NASA SP-430

A Review of the Significant Findings of the First Female Bed-Rest Study

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PHYSIOLOGICAL RESPONSES OF WOMEN TO SIMULATED WEIGHTLESSNESS

A Review of the Significant Findings of the First Female Bed-Rest Study

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PREFACE

This report is the first documentation on a group of female subjects studied under simulated space flight conditions. Contrary to voluminous data available on equivalently aged males, little or nothing was known regarding physiologic reactions during bed rest, centrifuge tolerance, or responses to lower body negative pressure. In these areas, the female subjects in this study did serve as pioneers.

The first study simulating weightlessness with prolonged bed rest, using all female subjects, was conducted in 1973 by the Biomedical Division of Ames Research Center, NASA. The objective was to determine whether women would exhibit the same physiological responses to prolonged bed rest that had been consistently observed previously in men. The study was a comprehensive effort that covered many of the physiological and psychological changes that might be expected to occur following simulated weightlessness. Various aspects of the research have been reported in journals and at meetings of the Aerospace Medical Association; however, complete documentation of the work has heretofore been unavailable.

The findings of this study should prove helpful in assessing the outlook for women in space and in determining criteria for selecting female passengers for Shuttle travel. Final verification of our findings must await operational Space Shuttle missions in the early 1980's when comparison of these data with actual measurements can be made during and after actual flights.

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This review of the first all-female bed-rest study conducted in 1973 at the NASA/Ames Human Research facility has been prepared to provide a single and comprehensive source of data concerning the study.

We express our deep appreciation for the magnificent cooperation and patience of the female subjects as we performed the many required tests. We also wish to thank the nurses, doctors, and support personnel of our Human Bed Rest Facility, for without their diligent efforts this complex task would not have become a reality. There are three individuals, however, who deserve particular mention for making this study possible. They are: 1) Brig. Gen. Claire Garrecht of Langley Air Force Base, who was so motivated to agree to this joint program of NASA-Air Force Nurse cooperation that two active duty nurses from her staff were provided to participate; 2) Major Dixie Lee Childs of Hamilton Air Force Base, who, under General Garrecht's direction, was allowed to recruit 10 nurse Air Force Reserve Officers from the San Francisco Bay Area; and 3) Dr. William F. Winter, Director of Medical Research, NASA Dryden Research Center, who made the original suggestion to recruit nurse subjects for this study and acted as the liaison between this study and General Garrecht and was one of the coprincipal investigators. Particular thanks is given to Mrs. Doris Furman and Ms. Mary Phares for their great help in compiling and formatting the data.

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SUMMARY

A survey is presented of the findings of the first bed-rest study using all female subjects. The 12 volunteer subjects (active Air Force nurses or reserves) were exposed to centrifugation, to lower body negative pressure (LBNP), and to exercise stress both before and after bed rest. Areas studied were centrifugation tolerance, fluid electrolyte changes and hematology, tolerance to LBNP, physical working capacity, biochemistries, blood fibrinolytic activity, female metabolic and hormonal responses, circadian alterations, and gynecology. The subjects were first tested to establish baseline values during a 14-day control period; on the basis of their baseline values, the 8 subjects most capable of tolerating acceleration and LBNP were selected for the bed-rest test. The bed-rest period lasted 17 days, after which the subjects underwent a 5-day recovery period. The 4 ambulatory controls underwent all requirements of the study except bed rest. Results were compared with the responses observed in similarly bed-rested male subjects. The bed-rested females showed deconditioning responses similar to those of the males, although with some differences. The surprising finding of the study was that the ambulatory control subjects also exhibited a degree of deconditioning, which was thought to result from the stress of confinement. The results of the study indicate that women are capable of coping with exposure to weightlessness and, moreover, that they may be more sensitive subjects for evaluating countermeasures to weightlessness and developing criteria for assessing applicants for Shuttle voyages.

INTRODUCTION

Women will play an increasing role in future space programs. They will be included as passengers in the upcoming Space Shuttle Program and will very likely participate in the Space Station Program envisioned for the distant future. The prospect of sending women into space, however, has raised a number of questions concerning the physiological capability of the female to withstand the deconditioning that has been observed consistently in both U.S. and Russian space crews after exposure to weightlessness.

Extensive data have been accumulated on male physiological responses to weightlessness both from actual flight experience (refs. 1,2) and from studies using bed rest (refs. 3,4) or water immersion (refs. 3,5) to simulate the weightless condition. The resulting data have demonstrated that young, healthy males undergo cardiovascular deconditioning after these exposures as manifested by reduced tolerance to lower body negative pressure, tilt, or centrifugation, or all three. With loss of orthostatic tolerance has come the regular manifestation of distinct symptoms which include tachycardia, narrowed pulse pressure, presyncope (bradycardia, diaphoresis, and nausea), and occasionally frank syncope. The mechanisms that cause this degradation are as yet unclear but may be related to a loss of total body fluid, plasma volume, neural influences regulating distribution of blood flow or strength of heart contraction, or other so-far undetected changes (ref. 6).

Although women will be exposed to weightlessness and to $+G_Z$ acceleration during Shuttle flights, data have not been available regarding the physiological responses of females to these conditions. Of the hundreds of bed rest and immersion studies (refs. 4, 5) that have been conducted, only one has included a female subject (ref. 7); that study was concerned with the effects of physical exercise on glucose tolerance. Our study was undertaken to develop much-needed information on the physiological responses of women to weightlessness as simulated by bed rest. The validity of bed rest as an analog for weightlessness has been confirmed by recent space flight experience (ref. 2).

The areas emphasized during the present study were tolerance to centrifugation and lower body negative pressure (LBNP), fluid and electrolyte shifts, decrements in work capacity, biochemistry responses, blood fibrinolytic activity, endocrinology, gynecology, and changes in biorhythms.

A major concern of the investigations was the establishment of low-level $+G_Z$ tolerance curves in healthy

female subjects; first when ambulatory, later to determine degradation following bed rest. Low levels of $+G_Z$ (not to exceed +3 G_Z) were emphasized because passengers and crew will be exposed to this level of acceleration during Space Shuttle reentry.

The investigators sought also to determine the degree of degradation in orthostatic tolerance that women would experience after bed rest. Male subjects exposed to prolonged bed rest have regularly exhibited decreased tolerance to 70° passive tilt or LBNP (refs. 3, 8, 9). Tolerance of males to $+G_Z$ is also greatly reduced (ref. 10). In the present study an effort was made to determine whether female subjects would exhibit similar responses, whether shifts in fluid volume were the root of the problem, and whether the female menstrual cycle, which is known to affect fluid volume, would affect their responses.

Finally, the investigators hoped to derive information that would be useful in promoting a better understanding of the physiological mechanisms that contribute to deconditioning following weightlessness or simulated weightlessness.

TABLE 1. VITAL STATISTICS OF FEMALE SUBJECTS

Subject	Age, yr	Height, m	Weight, kg	Surface area, m^2	Resting heart rate, bpm	Resting blood pressure, mmHg
Bed-rest group						
A	33	1.64	60.8	1.65	60	116/72
B	25	1.59	55.3	1.56	80	108/72
C	26	1.73	63.4	1.76	65	124/72
D	24	1.67	53.1	1.52	74	112/76
E	32	1.63	58.2	1.62	100	100/74
F	29	1.57	50.4	1.49	76	122/72
G	23	1.57	53.0	1.52	80	122/72
H	32	1.64	66.5	1.73	78	110/70
Mean	29	1.62	57.6	1.61	±66.9	114/73
SD	±5	±.05	±5.6	±.10	±29.5	
Ambulatory group						
I	27	1.59	47.7	1.47	67	120/78
J	29	1.70	61.5	1.71	60	108/76
K	23	1.70	64.1	1.74	62	96/64
L	25	1.64	51.0	1.54	72	100/60
Mean	27	1.66	56.1	1.62	±65.3	106/70
SD	±2	±.05	±8.0	±.13	±5.4	

PROCEDURES AND METHODS

Twelve nurses (23-34 yr) volunteered to serve as subjects during this study. Two were active duty Air Force nurses and 10 were reservists. All were in prime physical condition; all were well adjusted psychologically; and all had abstained from oral contraceptive medication for 3 months prior to the study in order to eliminate the possibility of chemical interference from such substances in subsequent biochemical determinations. Eight of the volunteers served as bed-rest subjects and four as ambulatory controls. The bed-rest subjects were selected on the basis of their higher tolerance to centrifugation and LBNP. The subjects' vital statistics are shown in table 1. All subjects were housed throughout the investigation in the Ames Human Research Facility, which provided a highly regulated environment with regard to temperature and a fixed photoperiod.

The study consisted of a 14-day control period, 17 days of absolute bed rest, and 6 days of recovery (fig. 1). During the bed-rest period, each bed-rest subject was required to refrain from excessive muscular movement, was furnished one pillow, and was allowed to raise up on one elbow during meals. All emunctory functions and bathing were performed in the horizontal position. Blood and urine samples were taken periodically throughout the study to measure biochemical and other physiological changes, and vaginal and rectal temperatures were monitored at 30-min intervals by means of temperature transducers and a biobelt (described in the section dealing with biorhythms). All subjects were given medical and gynecological examinations before the study was begun and again at its termination. The ambulatory controls underwent all tests and procedures except bed rest.

The control period was devoted to familiarizing the subjects with $+G_Z$ centrifugation, exposing them to LBNP and exercise tolerance testing, and to establishing consistent end-point responses and a valid baseline for each subject.

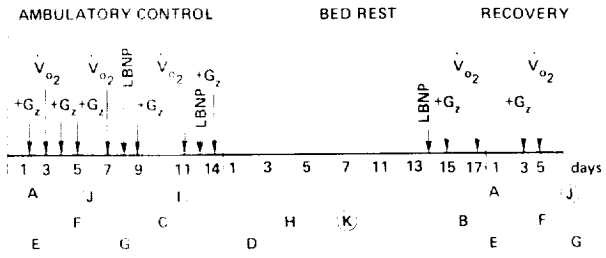


Figure 1. *Experimental protocol, with an indication of beginning of menstrual period of each subject. Circled letters are AMB group; V_{O_2} designates exercise testing procedures and G_Z is exposure to centrifugation.*

Centrifugation Tolerance

To establish a baseline for acceleration tolerance, each subject was exposed over a 1-week period to centrifugation at increasing levels of $+G_Z$. Each acceleration test consisted of three consecutive runs on the centrifuge with a 5-min rest period between runs. The runs began at $+2\ G_Z$ and were increased by 0.5 G to the point of advanced greyout. During all centrifuge runs, the subjects were instrumented noninvasively with a Doppler ultrasound device (ref. 11) to monitor ECG, blood pressure, and temporal artery flow. The system of lights used to determine loss of peripheral vision was modified slightly from that used by Rogge (ref. 12). Cessation of temporal blood flow at eye level, as monitored by the Doppler equipment, served as an additional means of obtaining objective end points for determining acceleration tolerance (ref. 13). Tolerance time, at an onset rate of 0.03 G/sec, was established at acceleration levels of +2.5, +3.0, +3.5, and $+4.0\ G_Z$. Each subject was taken to all four G levels in a random manner to negate the effects of fatigue. Exposure times at any given G level were arbitrarily limited to 20 min. The eight subjects showing the highest acceleration tolerance were selected to undergo bed rest to determine the magnitude of bed-rest induced decrements. The remaining subjects, who exhibited an average 42% lower tolerance to centrifugation, were assigned as ambulatory control subjects. Acceleration at $+3\ G_Z$ was selected as the G level that would produce a run of approximately 5 min before loss of peripheral vision during the control period. The subjects were centrifuged during the control period, on the last day of bed rest, and on the third day of recovery. Data were collected as shown in figure 2.

Fluid Electrolytes and Hematology

Fluid and electrolyte shifts were evaluated using antecubital venous blood samples obtained without stasis, before and immediately following each acceleration test. The blood samples were spun at 3400 rpm (International Model HN centrifuge), and the plasma was analyzed for sodium, potassium, chlorides, and phosphorus (Instrumentation Laboratory flame photometer) for osmolarity by freezing point depression (Advanced Instruments), and for total protein by using the method of Lowry *et al.* (ref. 14). The error of measurement for these analyses was less than ±1.0%.

Quadruplicate microhematocrit (Hct) determinations were made immediately after collection of each blood sample. The samples were centrifuged for 12 min at 11,500 rpm (International Model MB centrifuge) and read on a microcapillary tube reader (International). The

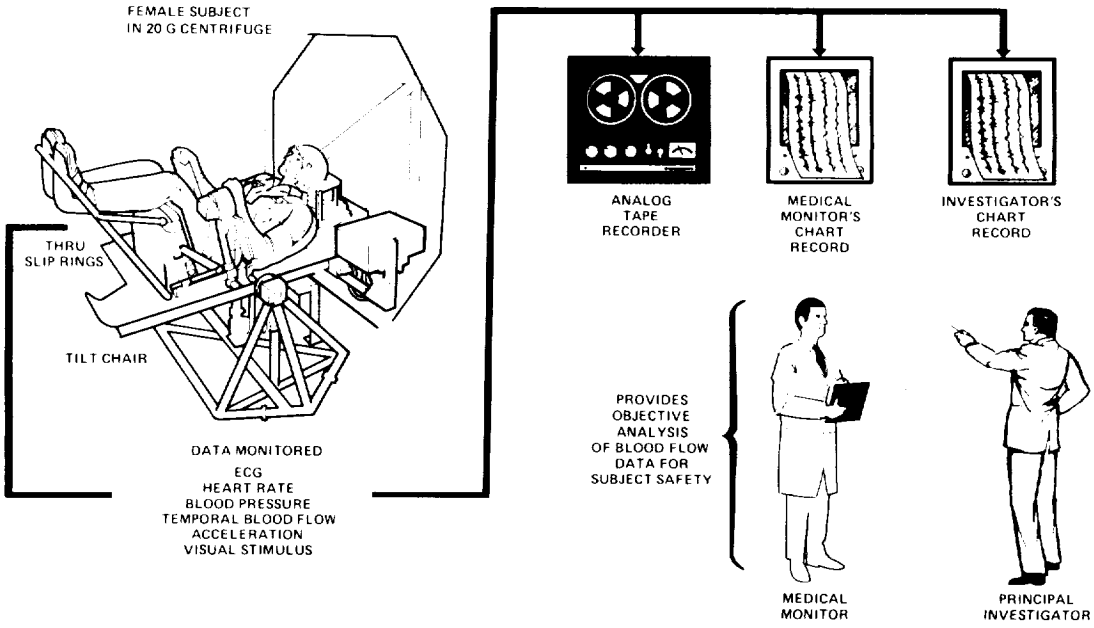


Figure 2.– *Data acquisition system:* $+G_Z$.

measurement error was ±0.25%. The raw Hct values were corrected for trapped plasma and whole-body Hct by multiplication with the factors 0.96 and 0.91, respectively. Hemoglobin was determined using the cyanmethemoglobin method, and red blood cell count was measured with a Coulter Model S counter.

Plasma renin activity and vasopressin were assayed because they are known to regulate fluid balance. Blood (3 ml) for the plasma renin activity was transferred immediately from a 30-ml syringe to a chilled test tube containing 7.5 mg of NaEDTA. For the vasopressin measurements, 10 ml of blood from the same syringe was placed in a chilled test tube containing 14 mg of NaEDTA. After the blood was centrifuged, the plasma was separated from the packed cells and stored at -50° C and was assayed several weeks later. Plasma renin activity was measured by radioimmunoassay for angiotensin I according to the method of Haber *et al.* (ref. 15) and calculated as nanograms of angiotensin I generated by renin per milliliter of plasma per hour during a 3-hr incubation at 37° C.

Plasma vasopressin levels were measured by radioimmunoassay. Antibodies to arginine vasopressin were generated in rabbits by the method of Goodfriend *et al.* (ref. 16). The iodination of vasopressin and other details of the assay, except for the plasma extraction procedure, are described by Husain *et al.* (ref. 17). Vasopressin was adsorbed with Bentonite from duplicate 1-ml aliquots of plasma according to the method of Skowsky *et al.* (ref. 18). Air-dried extracts were reconstituted to 0.5 ml with buffer (ref. 17), and two 0.2-ml aliquots were assayed from each tube. A typical standard curve and specificity of the antibody are shown in figure 3. Synthetic arginine vasopressin (Schwartz/Mann lot Y-2312), 262 ±20 U/mg, was used for standards, as well as iodination and antibody production. Vasopressin concentration is expressed as pg/ml of plasma. Although only 60-65% of added vasopressin could be recovered by Bentonite extraction, this percentage was consistent from assay to assay. The values reported have not been corrected for losses during extraction.

All data were analyzed using the Student t-test for paired observations and the analysis of variance. The null hypothesis was rejected when $P \leq 0.05$. Differences that were not significant were indicated by NS. Values are presented as means ± standard deviation (SD) or standard error (SE) or both. Data curves were fitted with the aid of a curve-fit computer program (Tymshare) that determined which of various applicable equations would best approximate the data.

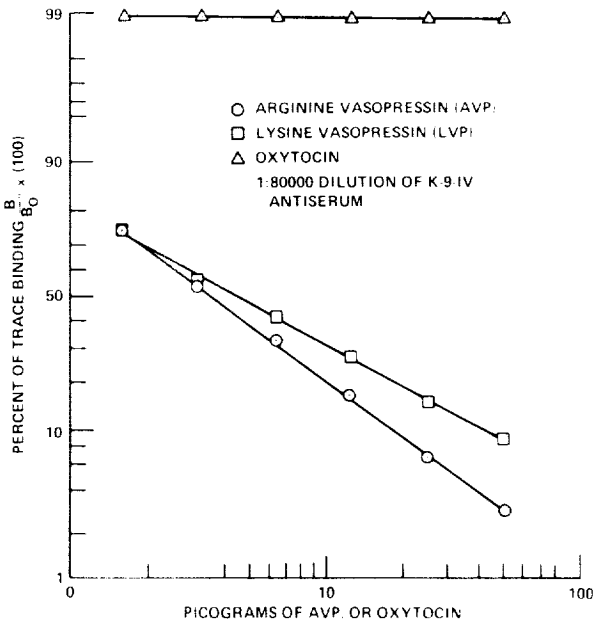


Figure 3. *Standard curve and specificity of antiserum for arginine vasopressin.*

The calculation of percentage changes in plasma volume from the hematocrit assumed that no changes occurred in red cell volume. Hemoglobin provides a reasonably stable point from which to compare red blood cell volume. The investigators compared the changes in plasma volume using the hematocrit data alone with those using the hematocrit and hemoglobin data combined. The results with both approaches agreed closely. Thus, when evaluating changes during $+G_Z$ acceleration, plasma volume changes can be calculated accurately using either approach.

Lower Body Negative Pressure

Previous studies of male subjects have demonstrated that exposure to -50 mmHg LBNP produced physiological responses similar to those produced by 70° tilt (ref. 19). LBNP was used in the present study as a provocative test to determine the degree of deconditioning occurring in female subjects following bed rest. Results provided a means of comparing female responses with those previously obtained in males of similar age.

The subjects were exposed to LBNP twice during the control period, again on the final day of bed rest, and finally 5 and 90 days after bed rest. LBNP was applied

with the subjects in the supine position as shown in figure 4, and pressure was applied from the iliac crests caudally using manually controlled vacuum equipment. During the training period prior to bed rest, exposure was begun at -20 mmHg and dropped by increments of 10 mmHg to -30 and -40 mmHg for 5 min at each level. Subsequent exposures before and after bed rest lasted 15 min at -50 mmHg or until the subjects exhibited the first symptoms of syncope. Control data were collected and averaged for 5 min before the onset of LBNP and for 3 min after the release of pressure.

The subjects were monitored noninvasively for heart rate, blood pressure, temporal artery flow, and changes in left ventricular volume using echocardiography. Heart rate was recorded continuously from sternal leads and averaged over 30-sec intervals in order to adjust for respiratory variations. Arterial blood pressure was measured and recorded each minute with a semiautomatic Doppler ultrasonic system (Hoffman-LaRoche Arteriosonde Model 1217) with the transducer placed over the right brachial artery. Temporal artery flow velocity was monitored continuously with a continuous wave ultrasonic Doppler system (ref. 11). The sensor was able to detect forward as well as reverse flow in the transduced artery.

Standard single-element echocardiographic recordings were made using a Smith Kline Ekoline 20 using a 2.25 MHz transducer placed in the fourth or fifth intercostal space at the left sternal border to record echoes from the left ventricular posterior wall and interventricular septum. A reference point was obtained by first positioning the transducer to obtain mitral valve motion and then rotating it inferolaterally until the motion disappeared. Echoes were recorded continuously over the final 60 sec of each 5-min LBNP exposure period using a Honeywell 1806A Visarecorder, as shown in figures 5 and 6. End-diastolic and end-systolic dimensions were measured from the tracings as previously described (ref. 20) and shown in figure 5, and cyclic volumes were calculated under the assumption that the ventricular shape was a prolate ellipsoid (ref. 20). The quality of the tracing and nature of measurements made during LBNP for one of the bed-rested subjects is shown in figure 6.

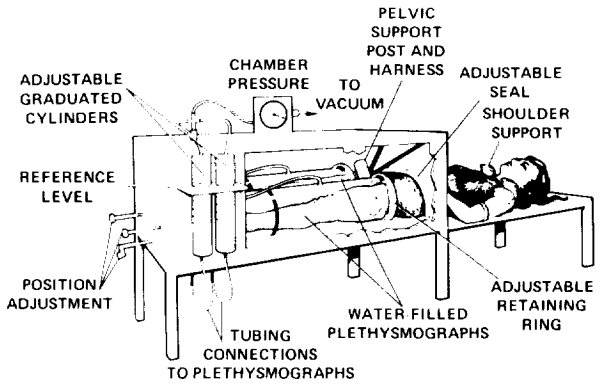
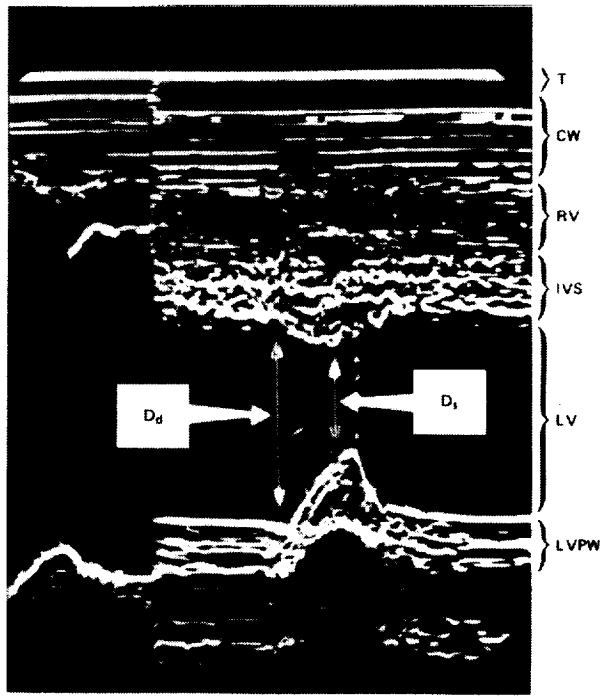


Figure 4. *LBNP pressure device.*



Legend:

Echo ↕ = maximum	LV = left ventricle
T = transducer	LVPW = left ventricular posterior wall
CW = chest wall	Dd = diameter at end-diastole
RV = right ventricle	Ds = diameter at end-systole
IVS = intraventricular septum	

Figure 5. *Representative echocardiographic tracing illustrating method of cardiac dimensional measurement.*

The left ventricular internal diameter D was derived from the difference between the septal and left ventricular posterior wall echoes. Left ventricular volume was then calculated as: $(7.0/2.4 + D)D^3$ (refs. 20, 21). Where no heart disease exists, the error in this method varies between 10% and 15% relative to results obtained with angiography (ref. 20). Stroke volume represented the difference between maximal or end-diastolic volume and

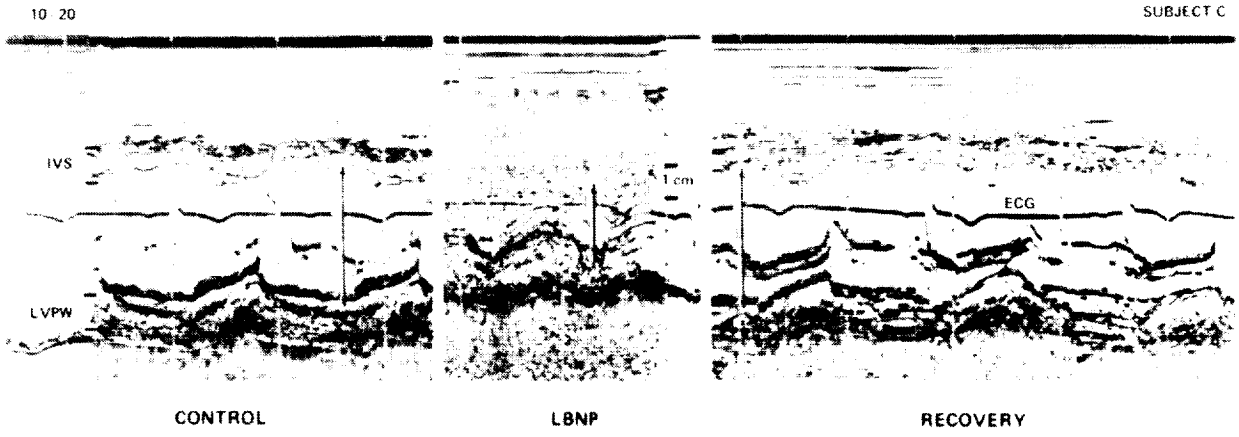


Figure 6. *Typical echocardiographic tracings obtained during control, LBNP, and recovery test periods.*

minimal or end-systolic volume. Cardiac output was the product of heart rate and derived stroke volume.

A water plethysmography technique similar to those of Musgrave (ref. 19) and Menninger (ref. 22) was used to measure changes in total leg volume. Water in the plethysmographic cylinders was maintained at a temperature of 33° to 35° C. Average hydrostatic pressure for the system was 13 mmHg, in order to produce a net negative pressure of −50 mmHg. A negative pressure of −63 mmHg was used in the box. Movement of the subjects was minimized by adjustable, padded shoulder and crotch supports (fig. 4). Test results were rejected when any movement was noted. Visual inspection verified the absence of air bubbles. Changes in leg volume were measured by conducting the water displaced from the plethysmographs through tubes to graduate volumetric cylinders outside the pressure chamber (fig. 7). Tubing from seals in the tops of the volumetric cylinders was connected to the interior of the pressure tank for pressure equilibration (fig. 7). A mark was made on the subject's thigh where it joined the plethysmograph, and the position was monitored during the test through an observation port. Constant hydrostatic pressure was maintained within the plethysmographs by manually adjusting the position of the external graduated volumetric cylinders to a constant reference level since the plethysmographs tended to empty or fill because changes in leg volume create an equal change in the volume of the graduated cylinders. The percentage change in volume was calculated by immersing the leg in an upright cylinder to the mark made during LBNP and

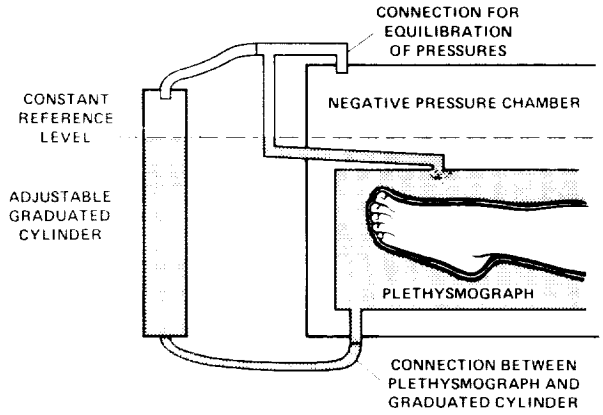


Figure 7. *Schematic of water plethysmograph used to detect change in total leg volume.*

measuring the displaced volume directly. After all instrumentation was in place, a minimum of 15 min was allowed for stabilization.

Data from all measurements were transferred to punch cards or digitalized on magnetic tape in real time and incorporated into a data base maintained in an IBM 360 computer. In the statistical analyses, the two-tailed independent t-test for comparing two means was applied at each 1-min interval or 5-min average of the 1-min values. Values are presented as means with standard deviations following the ± symbol.

Physical Working Capacity

Prolonged bed rest results in physiological deconditioning that affects most systems of the body. Maximal oxygen uptake, or physical working capacity, is an effective variable for measuring cardiorespiratory function. After prolonged immobilization, healthy young male subjects have exhibited decreases in maximal oxygen uptake (maximal VO_2) ranging from 17% to 31% (refs. 23, 24). Male subjects with normally high maximal VO_2, such as athletes, experience a greater absolute decrease, but lower percentage decrease, than individuals with low maximal VO_2 (ref. 24). Women in general have lower maximal VO_2 than men with similar anthropometric characteristics (ref. 25). The present study sought to determine whether the maximal VO_2 of bed-rested women would deteriorate to the extent observed in male subjects (refs. 23, 24).

The subjects were required to exercise, on a Collins bicycle ergometer (ref. 25), to maximum tolerance three times during the control period and again on the final day of bed rest. The exercise tests were performed with the subjects in the recumbent position (ref. 26) on a ventilated bed. Each test was begun at 0 W for a 3-min warmup period. The load was then increased by 40 W every 3 min to the point of subject exhaustion. Body weight (±5 g) was measured prior to each test, and oxygen uptake and heart rate (ECG record) were measured during the final 30 sec of testing. For the maximal VO_2 measurements, each subject was equipped with an Otis-McKerrow respiratory valve. The expired gas was measured using a Parkinson-Cowan high-velocity, low-resistance meter. Gas samples were collected in oiled 200-ml syringes and analyzed with a Beckman E2 oxygen analyzer and a Godart Capnograph CO_2 analyzer. Plasma volume was measured by intravenous injection of a saline solution containing 25 mg of Evans blue dye (ref. 27). The post-injection dye, recovered from the plasma through a chromatographic column, was compared with a standard dye solution at 615 nm with a Zeiss PMQ II spectrophotometer (ref. 28).

Hemoglobin was measured from antecubital blood in duplicate samples with the cyanmethemoglobin method (Hyland Laboratory). Blood for quadruplicate microhematocrit determinations was drawn into capillary tubes and spun for 12 min at 11,500 rpm on an International Model B centrifuge. Red blood cells were counted with the Model S Coulter counter. Additional red blood cell variables were calculated as follows:

Mean corpuscular volume,

$$MCV(u^3) = (Hct \times 10)/RBC$$

Mean corpuscular hemoglobin,

$$MCH(pg) = (Hb \times 100)/Hct$$

Mean corpuscular hemoglobin concentration,

$$MCHC(\%) = (Hb \times 100)/Hct$$

(where Hct = the microhematocrit; Hb = hemoglobin; and RBC = red blood cell count).

Biochemistries

The effects of bed rest on various measures of total body composition and on a number of biochemical constituents of the blood and urine were analyzed using techniques and equipment developed at the University of California at Berkeley. Because the subjects had to be transported to Berkeley for the measurements, the investigators, to facilitate scheduling, arbitrarily divided the subjects into two groups, each consisting of four bed-rest subjects and two controls. Measurements were made on the seventh day of the control period, on the last day of bed rest, and on the sixth day of recovery. The bed-rested subjects remained in the horizontal position during travel to and from Berkeley during the bed-rest period.

On arrival in Berkeley, each subject was asked to void and a 24-hr urine collection was begun. A heparinized venous blood sample was taken for biochemical analyses, and each subject drank 100 ml of D_2O to be used as a trace element in determining total body water. The subjects were then injected intravenously with a saline solution containing 25 mg of T-1824 (Evans blue) dye to determine plasma volume and placed in a 2π whole-body gamma counter for 20 min to determine the body potassium content from emissions of naturally occurring ^{40}K radioactivity. Venous blood samples were drawn 30 and 40 min after injection of the dye, and the separated plasma was analyzed spectrophotometrically for dye concentration; plasma volume was computed from these measurements. Upon completion of the 24-hr urine collection on the following day, a venous blood sample was drawn and analyzed for D_2O concentration by the falling-drop method. The urine pool was also analyzed for the trace element. After correcting for the D_2O lost in the urine over the 24-hr period, total body water was computed.

Plasma was separated from the original heparinized blood samples and analyzed for potassium concentration by atomic-absorption spectrophotometry and for total protein concentration colorimetrically by the biuret

reaction. An electrophoretogram was prepared; the fractional composition of the total plasma protein was measured photometrically, and the concentration of albumin, the globulins, and fibrinogen was computed.

The volume, specific gravity, freezing-point depression, and pH of the 24-hr urine collection were recorded, and the concentration of the following constituents was measured: choride, sodium, potassium, magnesium, calcium, phosphate, ammonia, urea, creatinine, creatine, hydroproline, glucose, citrate, 17-hydroxycorticosteroids, epinephrine, norepinephrine, and cyclic adenosine monophosphate. Excretion rates were computed for each of these constituents. Specific data compiled for each of these measured blood and urine variables as determined for each subject before and after bed rest are given in Appendix A.

Blood Fibrinolytic Activity

The observed loss of tolerance to $+G_Z$ acceleration consistently following prolonged bed rest may result from tissue hypoxia and associated increased pooling in dependent limbs. A drop in blood oxygen saturation or content is reported to provoke an increase in blood fibrinolytic activity (ref. 29). This condition is commonly attributed to the release of plasminogen activator in the vascular endothelium. Blood levels of plasminogen activator were compared following $+G_Z$ acceleration before and after bed rest. It was hypothesized that the magnitude of change in fibrinolytic activity would serve as an index of tissue hypoxia under these conditions. It was also an objective of these studies to determine whether bed rest per se was associated with increased fibrinolytic activity.

Fasted subjects were exposed to centrifugation in the morning. Blood samples were drawn before and 5 min after centrifugation from an antecubital vein using a 19-gauge needle and a plastic syringe. The tourniquet was released immediately upon entry of the needle into the vein, and several ml of blood were withdrawn without stasis. With the needle held in place, the syringe was replaced and 5 ml of blood were slowly withdrawn. Only the latter blood sample was used for fibrinolysin studies. A 4.5 ml aliquot was mixed with 0.5 ml of 3.2% trisodium citrate dihydrate, chilled in ice, and centrifuged to obtain platelet-poor plasma; the plasma was stored at -20° C. The plasminogen activator content of the plasma (euglobulin) was measured by the Astrup fibrin plate method (ref. 30), and the fibrinolytic activity expressed as the area (mm^2) of lysis. The results were evaluated by the Student t-test for paired data. The level of significance was $P < 0.05$.

Female Hormonal and Metabolic Responses

The present study was also concerned with measuring changes in female hormones and metabolism after bed rest and with determining what effect the menstrual cycle would have on acceleration tolerance. For these determinations, 8 ml of blood were collected every 4 hr for 24 hr on Days 5 and 11 of the control period, Days 5 and 13 of bed rest, and Day 6 of the recovery period. Twenty-four hour sampling was required because hormonal rhythms shift during bed rest. Single samples would have been inadequate for evaluation. Additional samples of 5 ml each for determining ACTH and cortisol were collected before, immediately after, and 10 min after each centrifugation run. The blood was collected in iced, heparinized containers and centrifuged immediately in refrigerated centrifuge at 4° C; the plasma was separated and frozen within 1 hr of withdrawal. Four-hour and 24-hr urine pools were collected throughout the study for urine cortisol determinations. The 4-hr pools were also used to determine urinary sodium, calcium, potassium, aldosterone, and 5-HIAA. The 24-hr aliquots were analyzed for 17-ketosteroids, estriol, catecholamines, and antidiuretic hormone.

Glucose tolerance tests were administered to all subjects on the final day of the control period, on the sixth and thirteenth days of bed rest, and after 2 days of recovery. On these days, after an overnight fast, the subjects were given a glucose load (300 ml lemon-lime drink with an average of 75 mg of glucose) followed by a standard 3-hr glucose tolerance test. Seven ml of blood were withdrawn 30, 60, 120, and 180 min after administration of the glucose load. The blood was placed in cold, heparinized containers and separated in a refrigerated centrifuge. Glucose levels were determined immediately, and the plasma for insulin determinations was frozen for later analysis. Serum glucose and insulin responses were compared for the control and bed-rest conditions. Serum glucose was expressed as mg per 100 ml of plasma (mg%) and serum insulin as μU/ml plasma.

The competitive binding procedure was used to determine cortisol, and the radioimmunoassay procedure to determine ACTH (ref. 31). Cortisol was expressed as μg/100 ml plasma or per total volume of pooled urine; ACTH was expressed as pg/ml plasma.

Biorhythms

Although shifts in light-dark periodicity and prolonged exposure to bed rest are known to result in desynchronization of certain biorhythms in male subjects (refs. 32, 33), similar data concerning such changes in women have not been available. The biorhythm portion of this study was directed toward determining whether the rhythmic changes occurring in women following bed rest would be similar to those observed in men.

The photoperiod was fixed at 18 hr of light and 6 hr of darkness (18L:6D) with light intensity of 40 foot candles at eye level for the bed-rested subjects. Ambient temperature was controlled at 70° ± 10° F and recorded continuously.

Rectal temperature, vaginal temperature, and heart rate were recorded for 5 min every 30 min throughout the study by means of a biobelt radio telemetry system. The unit consisted of two leads for electrocardiography and two for deep body temperature (fig. 8). One temperature sensor was a swallowable telemetry capsule; the other a standard, commercially available rectal thermistor probe which was used as a standard for comparison with the swallowed sensor. The biobelt unit (fig. 9) used for transmitting data from the body to a central receiving-recording station was small, battery operated, and capable of being worn for 24-hr periods. It has a transmission capability of 15–30 m (50 to 100 ft) within the FM radio band (88–108 MHz) so that individual, commercial FM band receivers can be used without interference. The ingestible telemetry pill shown in figure 10 has been miniaturized so that it can be packaged within a gelatin capsule and silastic-coated for protection during passage through the intestinal tract. Useful recordings of deep body temperature have been obatained for 48–96 hr in various subjects; the monitoring periods can be prolonged by placing subjects on low-residue diets (ref. 34). Figure 11 compares results obtained from the ingested unit with those from a rectal probe over a 24-hr period; a close linear correlation between the sensors is shown. In order to obviate problems of locating signals when the transmitter is swallowed, ingestible transmitters were inserted into each subject's vaginal tract. The biobelt receiving antenna for the temperature capsule was incorporated into each subject's underpants. An additional receiving antenna for the capsule was configured to encircle the subject's waist and thereby run orthogonally to the pelvic area, thus creating a two-dimensional antenna array. Capsules were replaced biweekly or as needed. Units also were usually

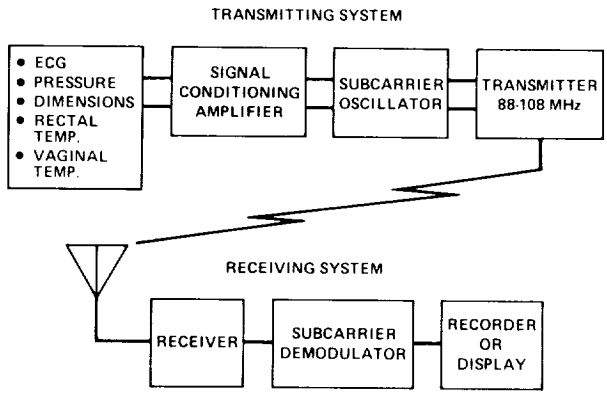


Figure 8. *Components of biotelemetry system.*

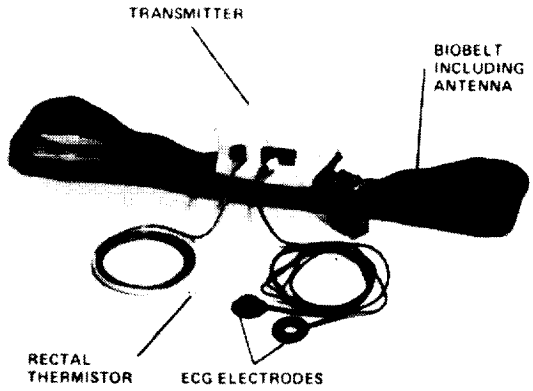


Figure 9. *Biobelt personal telemetry system.*

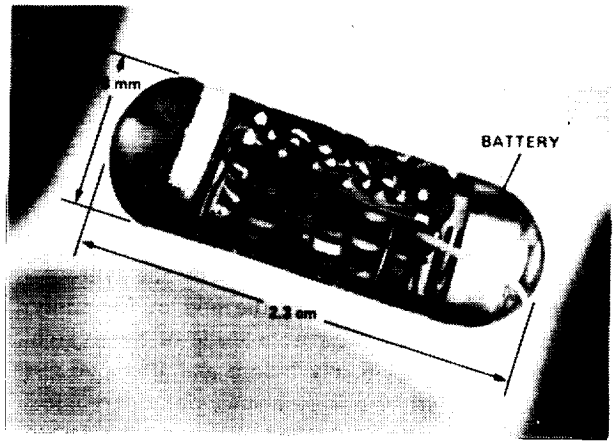


Figure 10. *Swallowable telemetry capsule.*

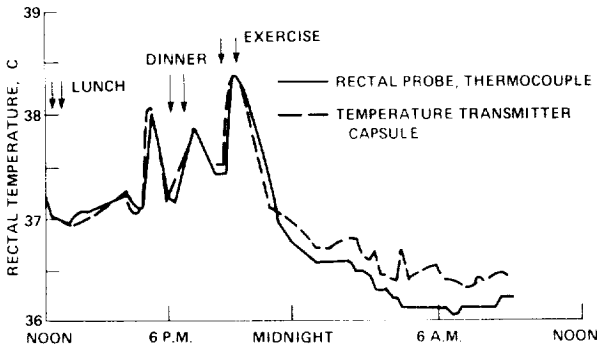


Figure 11. *Deep body temperature from rectal thermistor compared to that of swallowed temperature transmitter.*

changed during menstruation. In two of the subjects, the vaginal pills became dislodged during normal ambulation in the control period; however, in those cases the units were held in place with Tampons. The main transmitter antenna for the belt consisted of a single straight wire configuration attached to the external surface of the transmitter package.

Vaginal and rectal temperatures generally were very similar, but the vaginal data were less reliable because of technical limitations related to the use of a telemetric link for input to the biobelt system. The data were analyzed using the cosinor (ref. 35), periodogram, and summation dial (refs. 36, 37) methods.

Gynecology

Because this was the first study of simulated weightlessness in which all-female subjects were used, gynecological examinations and observations were an important part of the proceedings. All subjects were examined regularly by a medical team that included two gynecologists. Vaginal temperature was measured at 30 min intervals using a temperature transducer as described above; the transmitting devices were inserted by the gynecologists and removed by them at the end of the study. Bacteriological examinations were made of clean-catch, midstream urine immediately before and after bed rest to determine the effect of recumbency on urinary infections. Menstrual responses to bed rest were recorded to determine whether irregularities would occur.

RESULTS

Centrifugation Tolerance

Gradual onset runs of 0.03 G/sec were used prior to bed rest to determine physiologic response to low level prolonged acceleration as might occur in Shuttle flights. Each subject was exposed to levels of +2.5, +3.0, +3.5, and +4.0 G_Z (ref. 10). Results are shown in figure 12. A large variation in minutes at peak G was seen at +2.5 G_Z; 3 subjects, 2.3 to 5.4 min; 6 subjects, 9.1 to 13.4 min; and 3 subjects, 15.1 to 20 min. Variation decreased considerably at 3 G_Z: 4 subjects, 1.2 to 1.8 min; 4 subjects, 3.1 to 4.6 min; and 4 subjects, 6 to 6.8 min. At +3.5 G_Z 1 subject could not complete the ramp (1.9 min) to peak G, while tolerance for 7 subjects was 0.4 to 1.4 min, and 4 subjects, 2.8 to 4.7 min. At 4 G_Z, 3 subjects could not complete the ramp, 1 subject just did before blackout, the remaining 8 subjects tolerated peak G for 10 to 1.9 min.

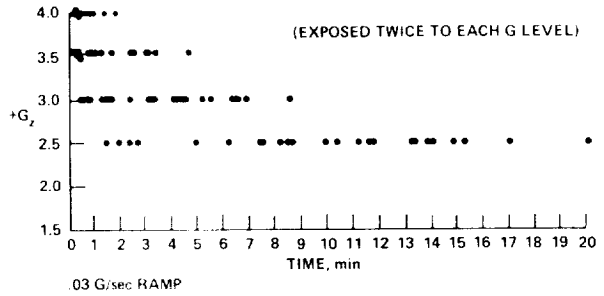


Figure 12. *Tolerance to $+G_Z$ of 12 female subjects before bed rest.*

All subjects exhibited a decrease in +3 G_Z tolerance following 14 days of confinement, but the most significant changes occurred in the bed-rested subjects (fig. 13 and table 2). Average tolerance (±SE) to +3 G_Z in these subjects declined significantly from 388 ±43 sec in the control period to 198 ±28 sec ($P < 0.001$) after bed rest. Tolerance of the ambulatory controls decreased significantly over the same period from 225 ±36 sec to 138 ±8 sec ($P < 0.01$). As shown in table 2, individual percentage changes ranged from -19.7% to -65.8%. Individual time performances at +3 G_Z for each subject before and after bed rest are given in table 3 for both bed-rested and ambulatory subjects. Menstruation, in general, did not appear to affect G_Z tolerance as indicated from the data in figure 1 and table 3. However, it

TABLE 2. INDIVIDUAL ANTHROPOMETRIC, BASE-LINE WORK CAPACITY, and $+G_z$ TOLERANCE DATA DURING THE CONTROL (C), BED-REST (BR), AND RECOVERY (R) PERIODS

Subject	Anthropometry: Age, year	Height, cm	SA, m^2	Body weight: C, kg	BR, kg	%Δ	Work capacity: Maximum O_2 uptake: C, l/min	BR, l/min	%Δ	Maximum ṼE BTPS: C, l/min	BR, l/min	%Δ	Maximum hr: C, beats/min	BR, beats/min	%Δ	Centrifugation: Tolerance: C, sec	BR, sec	(C-BR), %Δ	R, sec	(C-R), %Δ	Maximum hr: C, beats/min	BR, beats/min
Bed-rest group																						
A	32	161	1.62	59.75	55.70	6.8	1.82	1.76	3.3	61.39	62.49	+1.8	162	168	+3.7	460	133	71.1	382	17.0	145	156
B	34	159	1.54	55.00	53.12	3.4	2.15	2.28	+6.0	78.94	90.50	+14.6	174	186	+6.9	491	168	35.0	319	35.0	178	172
C	26	174	1.74	62.48	62.80	+0.5	2.41	2.33	3.3	104.06	117.19	+12.6	198	204	+3.0	178	143	19.7	274	53.5	186	186
D	24	156	1.54	56.52	55.50	1.8	1.89	1.89	0.0	87.58	82.93	5.3	180	186	+3.3	498	349	29.9	559	12.2	164	178
E	32	163	1.65	61.00	59.55	2.4	1.96	1.72	12.2	72.97	79.49	+8.9	168	180	+7.1	287	182	36.6	275	4.2	175	180
F	25	157	1.50	51.80	46.36	10.5	2.26	1.65	27.0	71.82	82.68	+15.1	180	180	0.0	378	271	28.3	313	17.2	153	156
G	23	157	1.50	52.65	52.40	0.5	1.41	1.26	10.6	57.79	52.46	9.2	186	192	+3.2	304	121	60.2	231	24.0	170	170
H	31	163	1.71	66.24	65.45	1.2	2.58	1.98	23.3	85.26	66.61	21.9	198	198	0.0	507	219	56.8	422	16.8	165	180
X	28	161	1.60	58.18	56.36	3.1[a]	2.06	1.86	9.7	77.48	79.29	2.3	181	187	3.3[a]	388	198	49.0[a]	347	10.6	167	172
±SE	2	2	0.03	1.79	2.17		0.13	0.12		5.31	7.03		5	4		43	28		37			
Ambulatory group																						
I	27	159	1.45	47.00	48.44	+3.1	2.39	1.84	23.0	110.01	81.53	25.9	186	186	0.0	206	158	23.3	222	7.8	160	156
J	28	170	1.69	60.20	60.53	+0.5	2.29	1.96	14.4	107.80	92.26	14.4	186	192	+3.2	171	132	22.8	167	2.3	180	186
K	26	170	1.74	64.74	64.00	1.1	1.96	1.70	13.3	92.60	64.76	30.1	180	168	6.7	192	141	26.6	170	11.5	180	168
L	25	164	1.53	50.88	49.64	2.4	1.62	1.97	+21.6	71.00	89.11	+25.5	168	162	-3.6	329	121	63.2	223	32.2	155	116
X	27	166	1.60	55.71	55.65	0.1	2.07	1.87	7.3	95.35	81.92	14.1	180	177	1.8	225	138	38.7	196	12.9	169	157
±SE	1	3	0.07	4.09	3.89		0.17	0.06		8.99	6.15		4	7	2.2	36	8		11			

[a] $P < 0.05$

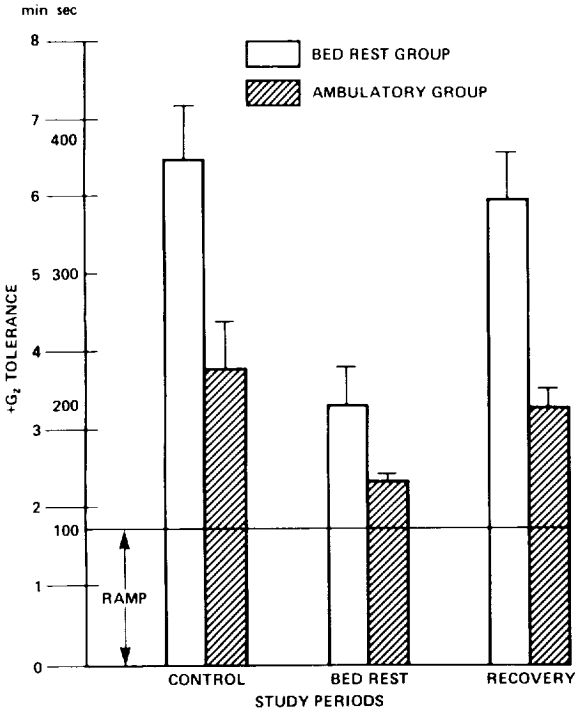


Figure 13.– *Acceleration tolerance of +3 G_z for the ambulatory and bed-rest groups during the control, bed-rest, and recovery periods. Ramp equals time to reach the plateau of 3.0 G.*

TABLE 3.– FEMALE TOLERANCE AT PEAK +3.0 G_z

Subject	Tolerance at peak +3.0 G_z, sec: Pre-bed rest	Post-bed rest	Recovery
Bed-rest group			
A	455	29	187
	338	39	278
	294	29	260
B	498	48	228
	298	72	195
	263	83	232
C	58	36	99
	69	50	214
	105	40	195
D	462	217	570
	399	293	427
	333	234	318
E	172	19	186
	207	120	177
	180	105	161
F	219	180	189
	281	158	204
	332	177	244
G	242	18	200
	196	20	88
	174	24	103
H	478	102	422
	347	128	302
	393	126	243
X	283	97.8	255
±SD	57.5	43.2	88.9

Subject	Tolerance at peak +3.0 G_z, sec: Pre-bed rest	Post-bed rest	Recovery
Ambulatory group			
I	102	65	117
	105	48	115
	109	59	131
J	56	18	61
	74	24	80
	79	52	59
K	90	39	98
	115	42	55
	68	40	56
L	128	38	37
	261	15	100
	245	9	231
X	123.5	37.4	95.0
±SD	71.3	15.6	31.0

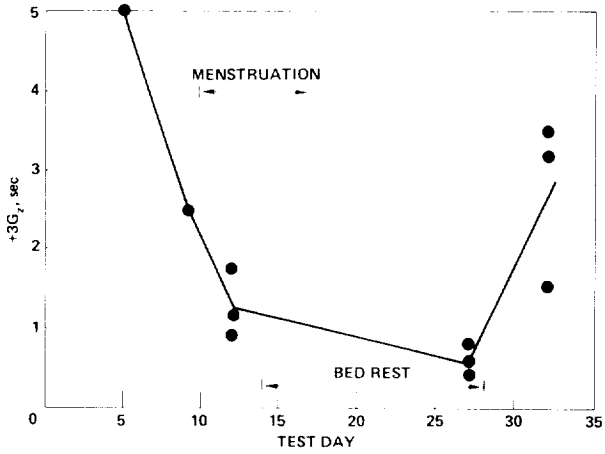


Figure 14. *Effect of menstruation on +G_z tolerance of one subject.*

did appear to have effects for 1 subject (C) as shown in figure 14. Her performance was 300 sec during the first trial of three runs. Menstruation began immediately following these exposures. It can be seen that two days later when her three pre-bed-rest tolerance runs were made, a very marked deterioration in endurance was found. A further decrease from pre-bed-rest values was found during post-bed-rest testing, which showed a marked recovery after bed rest toward pre-bed-rest values as shown. Subjects G and J were similarly studied during the control period while some phases of menstruation were in progress. Subject G also showed some slight changes in tolerance, as shown in table 3, but Subject J did not.

As a group, tolerance times for the ambulatory subjects were significantly lower than those of the bed-rested group. But this factor was biased by the selection process. The degradation of tolerance in the ambulatory controls during confinement, despite being ambulatory, was significant and not at all expected.

The tolerance of both groups improved during the recovery period. By the third day of recovery, the average tolerance of the bed-rested subjects had increased to 347 ±37 sec and that of the control subjects to 196 ±11 sec. The difference between the control and recovery values, therefore, was -10.6% (NS) for the bed-rested group and -12.9% (NS) for the controls. Thus, the recovery rates for the bed-rested and control subjects were 89.4% and 87.1%, respectively.

Maximum heart rate during centrifugation following bed rest ranged from 156 to 186 bpm (beats/min) (table 2) in the bed-rested subjects (mean, 172 bpm) and from 116 to 186 bpm (mean, 157) in the ambulatory controls. These data compare with pre-bed-rest (control) findings of 145 to 186 bpm (mean, 167 bpm) for the bed-rest subjects during centrifugation and 155 to 180 bpm (mean, 169 bpm) for the ambulatory controls. Heart rate responses during +3 G_z before and after bed rest for one bed-rested subject (Subject B) and one ambulatory control (Subject J) are shown in figures 15 - 18.

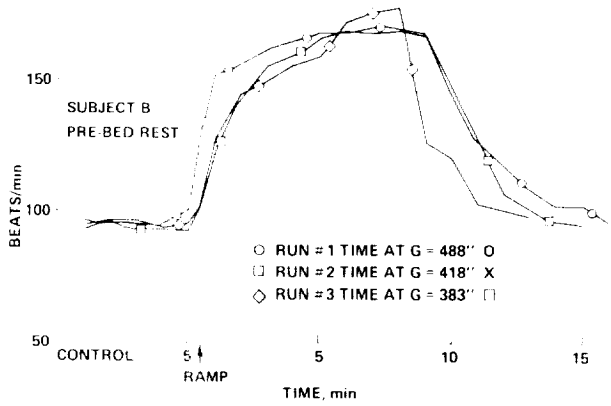


Figure 15. *Heart rate of bed-rest subject B during acceleration before bed rest.*

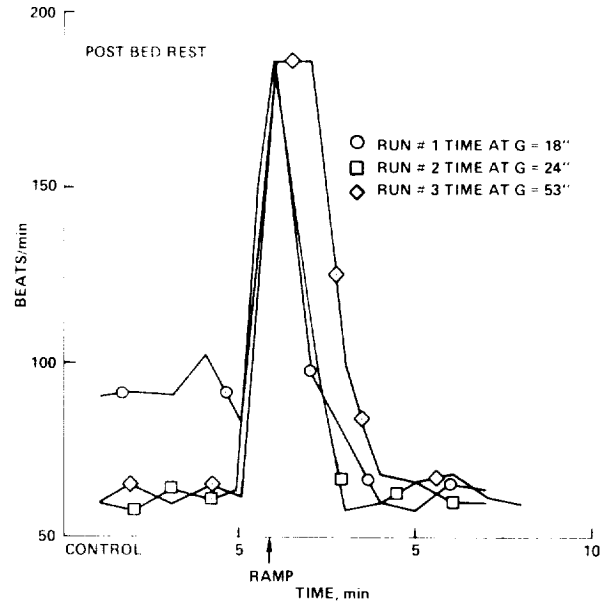


Figure 16. *Heart rate response of bed-rest subject B after bed rest.*

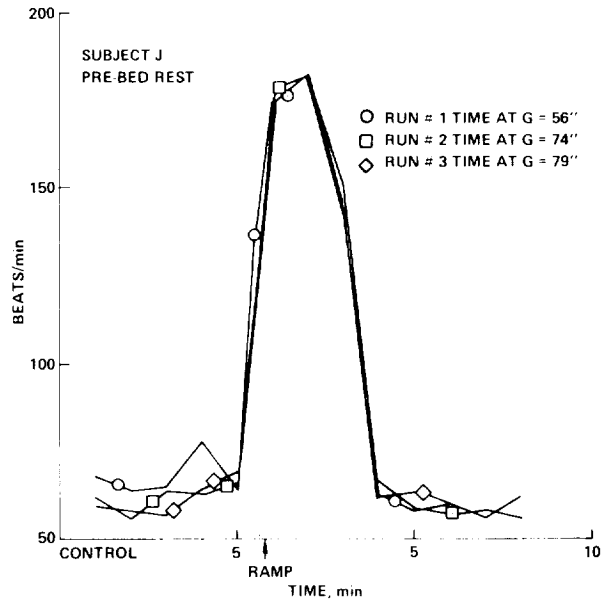


Figure 17. *Heart rate response of ambulatory control subject J during centrifugation before bed rest.*

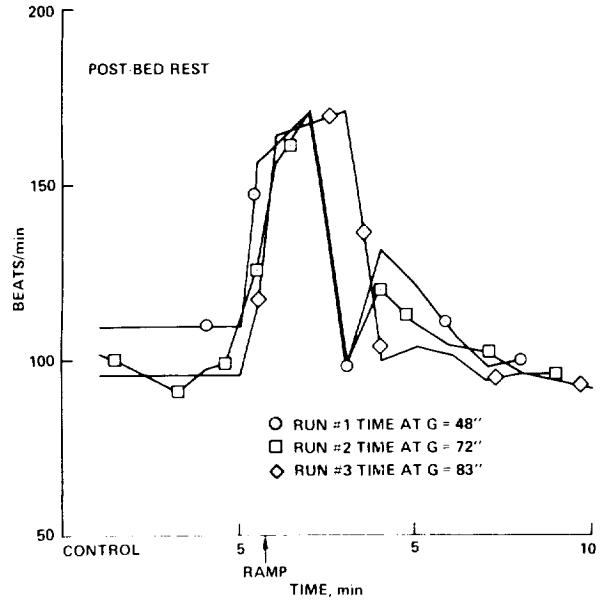


Figure 18.– *Heart rate response of ambulatory control subject J during centrifugation after bed rest.*

Fluid Electrolytes and Hematology

The percentage changes in plasma volume, blood protein, and electrolytes during centrifugation in the control, bed rest, and recovery periods are shown in figure 19 (upper half, %Δ concentration; lower half, %Δ content) (ref. 38). The percentage change data shown in the concentration graphs were also included in the content graphs for reference. The percentage change in all variable concentrations was determined from measured data as given in table 4; the percentage change in plasma volume was calculated using the following equation:

$$\%\Delta PV = 100/(100 - Hct_{pre}) \times 100(Hct_{pre} - Hct_{post}).$$

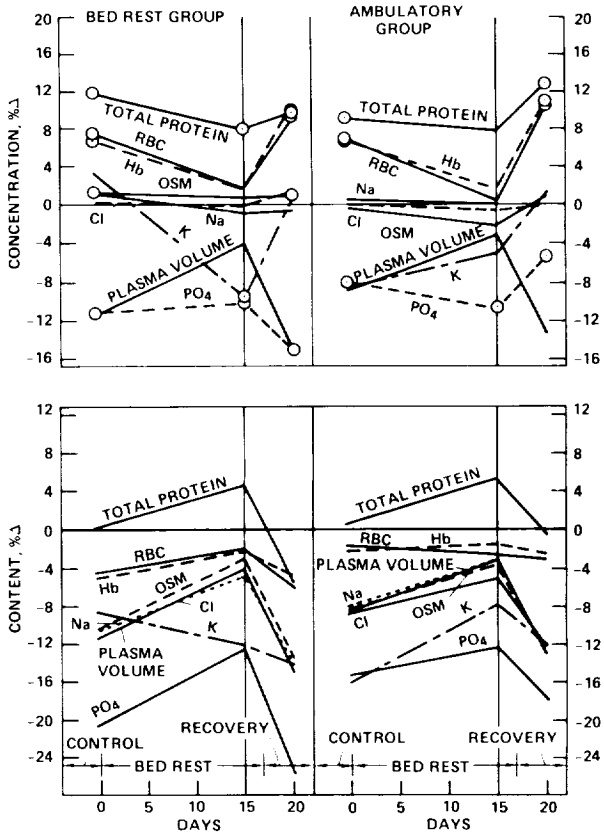


Figure 19.– *Mean percent changes in plasma volume, electrolyte, and protein concentrations* (upper half) *and contents* (lower half) *during centrifugation in ambulatory and bed-rest groups during control, bed-rest, and recovery periods.*

TABLE 4.— RESTING BLOOD AND PLASMA CONSTITUENTS DURING THE CONTROL (C), BED-REST (BR), AND RECOVERY (R) PERIODS

Blood and plasma constituents	Bed-rest group			Ambulatory group		
	C	BR	R	C	BR	R
WBC, 10^3/mm^3	6.2 ±0.3	5.8 ±0.4	8.0[a] ±0.7	6.2 ±0.3	5.6 ±0.6	8.0[a] ±0.4
RBC, 10^6/mm^3	4.01 ±0.06	4.04 ±0.07	3.54[a] ±0.06	3.70 ±0.25	3.63 ±0.21	3.28 ±0.19
Hct × 0.96, %	36.7 ±0.7	37.1 ±0.4	32.6[a] ±0.5	34.8 ±1.3	33.9 ±1.3	31.9 ±1.2
Hb, g/100 ml	12.3 ±0.2	12.5 ±0.1	10.8[a] ±0.1	11.8 ±0.5	11.5 ±0.4	10.5 ±0.4
Protein, g/100 ml	7.56 ±0.17	7.12 ±0.13	6.95[a] ±0.22	8.08 ±0.13	7.22 ±0.32	7.12 ±0.19
Na, meq/l	137.1 ±1.1	137.4 ±1.2	145.9 ±2.3	139.0 ±1.0	136.8 ±3.6	145.8 ±2.1
K, meq/l	4.11 ±0.12	4.17 ±0.11	4.16 ±0.08	4.28 ±0.10	4.19 ±0.13	4.22 ±0.06
Cl, meq/l	102.7 ±1.5	109.0[a] ±2.2	104.4 ±1.1	102.8 ±1.8	109.3[a] ±1.6	105.0 ±2.0
Osm, mosmol/l	282 ±1	290[a] ±1	285 ±1	286 ±1	291 ±1	289 ±2
PO_4, mg/100 ml	3.37 ±0.18	3.28 ±0.13	3.40 ±0.08	3.40 ±0.28	3.75 ±0.21	3.16 ±0.11

[a] $P < 0.05$ from C
NOTE: All values are ±SE.

The % Δ in content was calculated using:

$$\frac{CN_{post} - [Hct_{post}(100 - Hct_{pre})CN_{pre}]/Hct_{pre}(100 - Hct_{post})}{Hct_{post}(100 - Hct_{pre})CN_{pre}/Hct_{pre}(100 - Hct_{post})} \times 100$$

where in both equations, "pre" denotes before centrifugation and post denotes after centrifugation. The mean change in plasma volume in the bed-rested group after bed rest was -12.6% ($P < 0.05$) and +4.3% (NS) in the ambulatory controls.

The accuracy of the post-centrifugation data can be estimated for the bed-rested group from the percentage change in plasma volume (resting value -11.5%) and the percentage change in concentration of total protein (resting value +11.7%) and sodium (resting value +1.1%) from the control period (fig. 19, left panel). If no protein content were lost during centrifugation, a loss of -11.5% in plasma volume would result in an increase of +11.5% in protein concentration and a 0.0% change in protein content. With an actual change in protein concentration of +11.7%—which is slightly higher than the theoretical value of +11.5%—this calculated percentage change in protein content should be slightly higher than zero; and it was (+0.1%).

Sodium responded differently, shifting out of the vascular system – presumably with plasma – in approximately the same proportion as its normal plasma concentration; that is, in an isotonic shift. If sodium had exhibited a perfect isocontent loss, the percentage change in sodium concentration would have been zero and the percentage change in sodium content would have been -11.5%, or the same as the percentage change in plasma volume. The measured percentage change in sodium concentration, however, was +1.1%, which indicated that there was a small retention of sodium, and no measurement errors assumed. Consequently, the actual resulting change of -10.6% in content would be slightly less than the -11.5% loss in plasma volume. The changes observed in sodium, chloride, and osmotic content adhered closely to the changes in plasma volume, which indicated an isocontent loss in sodium chloride. The osmotic content followed closely the sodium content because sodium accounts for 80% of the plasma osmolarity.

The pattern of shifts in blood constituents and plasma volume was essentially the same in both the bed-rested and control subjects during the control, bed rest, and recovery periods (fig. 19; table 4). Concentration of RBC and Hb and content values were similar and evidenced a small (-2% to -5%) loss in content during centrifugation that was not affected by bed rest.

As shown in tables 4 and 5, there were few or no significant changes in RBC mean corpuscular volume (MCV), mean corpuscular hemoglobin content (MCH), or mean corpuscular hemoglobin concentration (MCHC) as a consequence of bed rest or centrifugation in any of the three experimental periods. MCHC showed slightly significant changes after the 14-day test period in the controls following centrifugation as compared to control baseline levels. Hematocrit (Hct) changed significantly for both subject groups, first as a consequence of acceleration; then as a manifestation of loss of plasma volume and/or marrow suppression from inactivity and confinement; and finally hemodilution or suppression in the recovery period. Values were significantly lower ($P < 0.02$) for the ambulatory group at the onset and persisted throughout the bed-rest period; they were not, however, significant during recovery.

Although the percentage change in phosphate content followed the change in plasma volume, phosphate content exhibited a change that was twice as great as that of plasma volume. During centrifugation, there was about 50% loss of plasma volume, Na, Cl, PO_4, and osmotic content after bed rest in both the test and control subjects, compared with values obtained during control and recovery periods. Correlation coefficients (r) were calculated for all data from the 12 subjects between the percentage change in plasma volume and the percentage change in the content of each of the blood or plasma constituents. The constituents exhibiting significant

TABLE 5.– CHANGES IN MEAN CORPUSCULAR VOLUME, MEAN CORPUSCULAR HEMOGLOBIN CONTENT, MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION, AND HEMATOCRIT BEFORE AND AFTER CENTRIFUGATION

Control			Bed rest			Recovery		
Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ
Mean corpuscular volume, μm^3								
Bed-rest group								
92.4 ±1.6	92.7 ±2.0	0.3	92.2 ±1.6	93.0 ±1.6	0.9	92.2 ±1.6	93.3 ±1.4	1.2
Ambulatory group								
94.7 ±4.0	95.2 ±3.2	1.6	94.0 ±2.9	96.0 ±3.2	2.1	97.6 ±2.8	96.4 ±3.5	1.2
Mean corpuscular hemoglobin content, pg								
Bed-rest group								
30.9 ±0.3	30.8 ±0.6	0.3	31.0 ±0.4	31.0 ±0.4	0.0	30.6 ±0.4	30.8 ±0.4	0.6
Ambulatory group								
32.1 ±1.3	31.8 ±1.1	0.9	32.0 ±1.2	32.2 ±1.3	0.6	32.2 ±1.3	32.8 ±1.4	0.3
Mean corpuscular hemoglobin concentration, %								
Bed-rest group								
33.5 ±0.3	33.3 ±0.2	0.6	33.6 ±0.2	33.3 ±0.4	0.9	33.2 ±0.3	33.0 ±0.1	0.6
Ambulatory group								
33.9 ±0.3	34.2 ±0.2	0.8	34.0 ±0.2	33.6 ±0.2	1.2	33.0 ±0.5	33.4 ±0.5	1.2
Hematocrit, %								
Bed-rest group								
36.7 ±0.6	39.7 ±0.7	+8.2[a]	37.1 ±0.4	38.1 ±0.7	+2.7	32.6 ±0.5	36.3 ±0.7	+2.7[a]
Ambulatory group								
34.8 ±1.3	36.9 ±1.1	+6.0[a]	33.9 ±1.3	34.7 ±1.1	+2.4	31.9 ±1.2	35.1 ±0.6	+10.0[a]

[a] $p < 0.05$

NOTE: All values are ±SE.

($P < 0.05$) correlations were sodium (0.90), osmolarity (0.93), chloride (0.83), PO_4 (0.74), total protein (0.69), Hb (0.68), and RBC (0.59). Potassium, on the other hand, exhibited a nonsignificant change ($r = 0.36$).

The reductions in fluid and electrolyte shifts following bed rest (table 4) were associated with decreases in centrifugation tolerance of -49% in the bed-rested subjects and -37.8% in the ambulatory controls. Plasma potassium had a variable response. In the bed-rested subjects, as indicated earlier, there was a progressive loss of potassium from a control value of -8.6% to -12.2% after bed rest and to -14.2% during centrifugation in the recovery period. In the control group, the potassium content followed the pattern of the other electrolytes, but at a lower level. Total protein content did not change during centrifugation in the control period, but showed an influx during centrifugation in the bed-rest period and a comparative loss during centrifugation in the recovery period.

The loss in plasma volume correlated significantly ($r = 0.72$, $P < 0.01$) with acceleration tolerance (fig. 20). The general hyperbolic equation, $Y = a + b/X$, fitted the data slightly better than the linear equation, $Y = a + bX$, where the correlation coefficient was 0.66 ($P < 0.01$). An analysis run omitting the three positive plasma data points did not change the best fit with the hyperbolic equation. The logarithmic function appears to be more reasonable because there is an upper limit to the loss of plasma volume that would not irrevocably compromise the integrity of the organism. Using this logarithmic relationship and extrapolating the curve until it becomes asymptotic with the x axis indicates that the upper limit of the plasma volume loss during centrifugation would be 16-18%.

As early as Day 2 and continuing through Day 14 of the bed-rest period, plasma arginine vasopressin (AVP) levels were reduced 33% compared with control values and plasma renin activity (PRA) was persistently elevated by 91% ($P < 0.01$) above control levels from Day 10 through Day 15. Exposure to $+G_Z$ centrifugation following the control period provoked a marked rise (2083%) in plasma arginine vasopressin but only a slight increase in plasma renin activity. Following bed rest, $+G_Z$ acceleration caused a significant increase in plasma arginine vasopressin (788%); however, this magnitude of

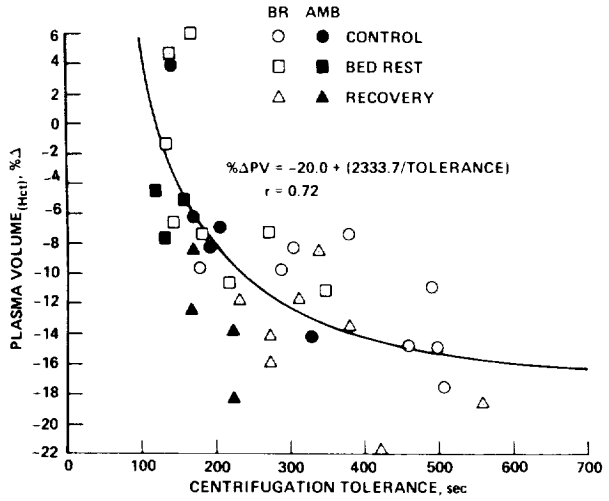


Figure 20.– *Regression of change in plasma volume on centrifugation tolerance utilizing data from all 12 subjects from three periods.*

change was noticeably less than that observed after centrifugation prior to bed rest. No significant increase in plasma renin activity was observed following +3.0 G_Z after bed rest (figs. 21 and 22; table 6).

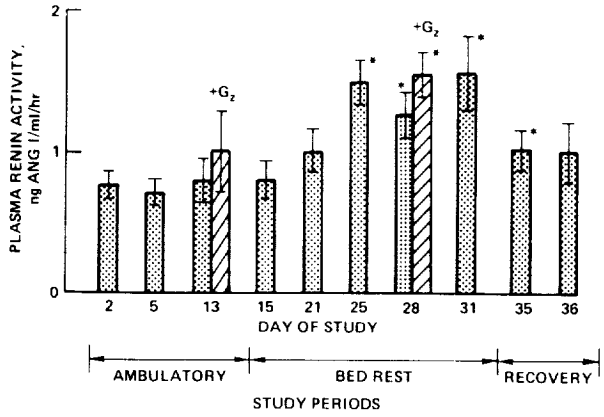


Figure 21.– *Effect of bed rest and +3 G_Z acceleration on plasma renin activity in women. Vertical lines represent the standard error of the mean for eight subjects. *P < 0.05 when compared to either* Day 2 *or* Day 5 *of the ambulatory control period.*

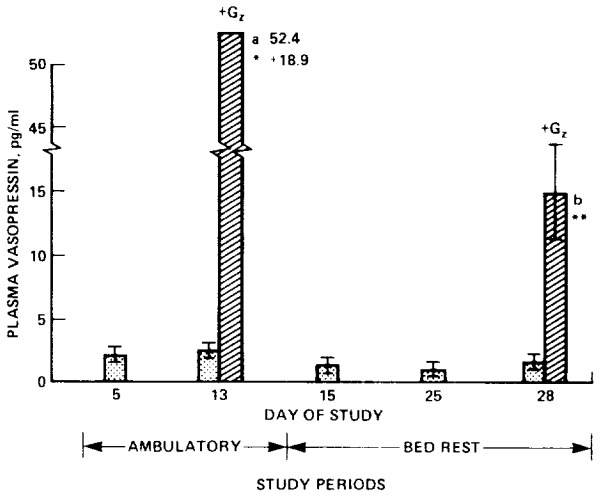
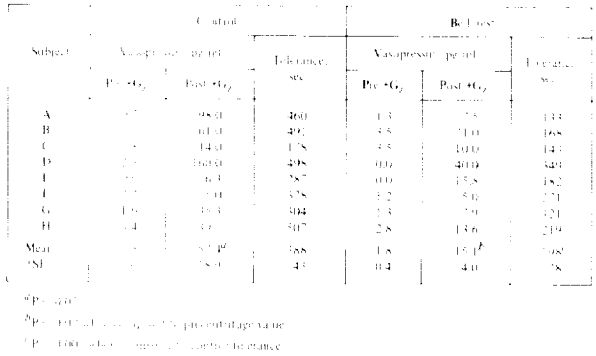


Figure 22.– *Effect of bed rest and +3 G_Z acceleration on plasma vasopressin. Vertical lines represent the standard error of the mean for eight subjects. P < 0.05; P < 0.02 when compared to preacceleration values on the same day.*

TABLE 6. PLASMA VASOPRESSIN RESPONSE AND TOLERANCE OF WOMEN EXPOSED TO +G_Z ACCELERATION



Lower Body Negative Pressure

Although all subjects were able to tolerate the complete 15-min exposure to LBNP during the control period, no one was able to complete the test following the bed-rest period; post-bed-rest tolerance times varied from 4.5 to 14 min. Tolerance to LBNP had completely improved to pre-bed-rest levels by 90 days. Blood pressure and heart rate findings for Subject D of this study, shown in figure 23, were typical for the rest of the subjects. Summaries of average values for heart rate and blood pressure measurements obtained before and after bed rest are shown in tables 7(a)–7(e). In the tables, "Test" indicates data from the eight bed-rested subjects and "Ambulatory" refers to the four ambulatory control subjects. Data were arbitrarily divided into 5-min intervals representing control (C) – early (first 5 min of LBNP), mid (second 5 min of LBNP), late (last 5 min of LBNP), and recovery periods. Average values over each period were determined; for heart rate, data were obtained from 30-sec coverages, and for blood pressure, from 1 min recordings.

Heart rate appeared to be the most sensitive indicator of changes in LBNP tolerance. Average 1-min changes are shown in figure 24; they increased significantly ($P < 0.001$) from pre-bed-rest levels as did average 5-min values shown in table 7(a). Prior to bed rest, resting heart rate values of the eight bed-rested subjects (test) were significantly higher ($P < 0.01$) than those of the controls (ambulatory), with values of 75 ±9 bpm for the test subjects and 64 ±12 for the ambulatory controls. These differences between resting values for the two groups persisted throughout all test phases. During LBNP,

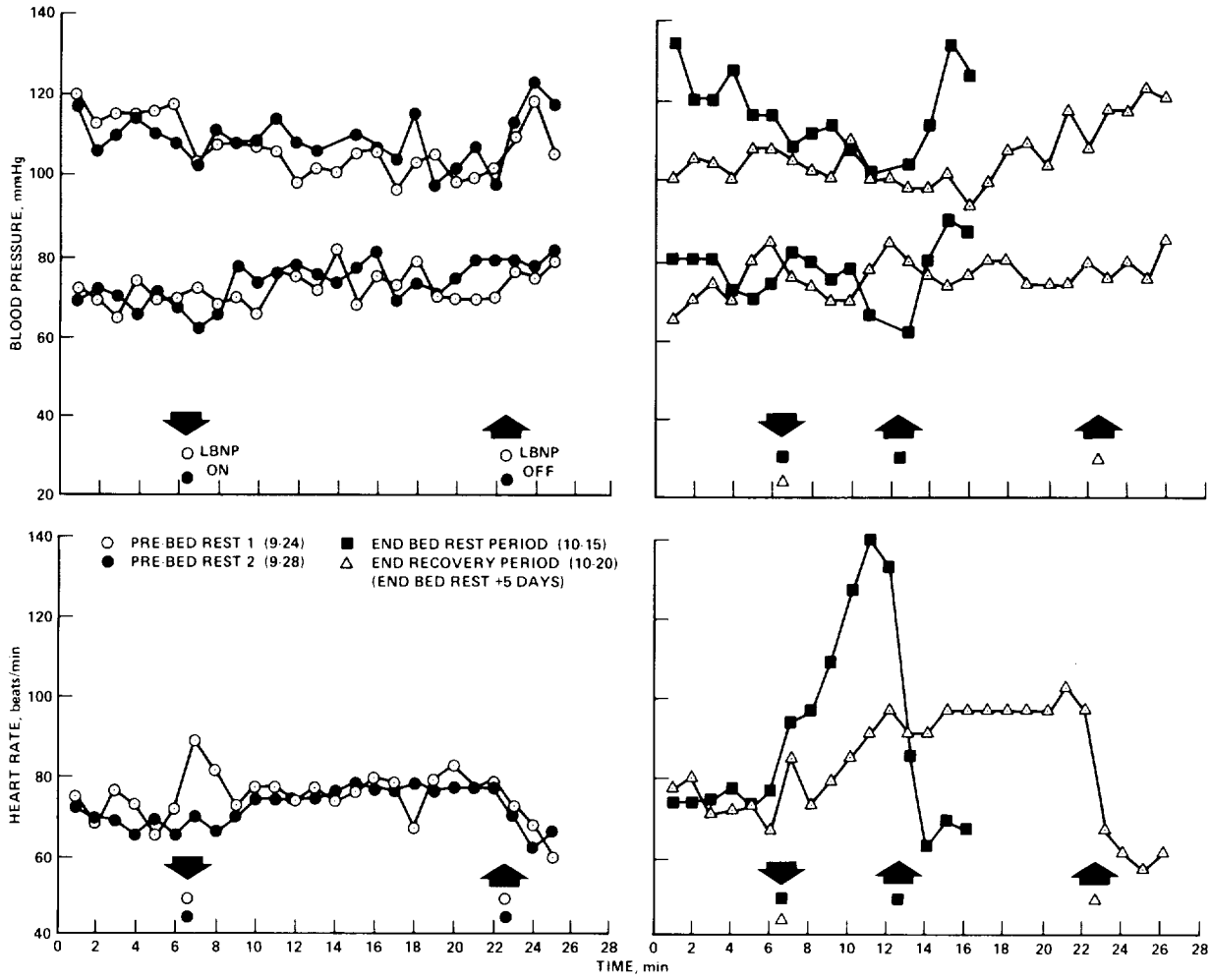


Figure 23.– *Typical hemodynamic changes during LBNP before and after bed rest. Duration of LBNP tolerance is noted along bottom axis by arrows. After bed rest this subject could only tolerate 6 min of suction, where prior to bed rest she could tolerate full 15-min protocol.*

TABLE 7. LBNP CARDIOVASCULAR DATA HEART RATE

Test conditions		n[a]	Pre-bed rest, mean ± SD	n[a]	End bed rest, mean ± SD	n[a]	5 Days post-bed rest, mean ± SD	n[a]	90 Days post-bed rest, mean ± SD
(a) Heart rate, beats/min									
Pre-LBNP (resting), 5-min mean	Test	(80)	75 ± 9[b]	(40)	80 ± 9[b,c]	(40)	81 ± 8[b,c]	(45)	74 ± 9[b]
	Ambulatory	(30)	64 ± 12	(15)	67 ± 7	(15)	62 ± 5	(25)	63 ± 11
LBNP elapsed time, 1-min values									
5	Test	(16)	94 ± 13[d]	(7)	129 ± 26[c]	(8)	114 ± 16[b,c]	(9)	95 ± 14
	Ambulatory	(6)	78 ± 17	(3)	112 ± 17[e]	(3)	92 ± 3	(5)	83 ± 22
10	Test	(16)	102 ± 16	(3)	136 ± 45[c]	(7)	110 ± 25	(9)	103 ± 19
	Ambulatory	(6)	86 ± 21	(2)	126 ± 17[e]	(3)	100 ± 9	(5)	91 ± 27
15	Test	(16)	100 ± 18	...	...	(6)	123 ± 16[d,e]	(7)	94 ± 14
	Ambulatory	(6)	89 ± 20	(2)	132 ± 8[e]	(2)	34 ± 17	(4)	81 ± 12
Maximum 1-min value during LBNP	Test	(16)	105 ± 18[b]	(2)	160 ± 16	(6)	127 ± 16	(8)	107 ± 24
	Ambulatory	(6)	89 ± 20	(2)	133 ± 18	(2)	105 ± 4	(5)	91 ± 27
Recovery, min									
+1	Test	(16)	81 ± 12[d]	(7)	95 ± 29	(8)	84 ± 18	(9)	77 ± 11[b]
	Ambulatory	(6)	67 ± 9	(3)	68 ± 9	(3)	68 ± 9	(5)	58 ± 7
+3	Test	(16)	70 ± 11[b]	(8)	71 ± 11	(8)	71 ± 8[b]	(9)	67 ± 13
	Ambulatory	(6)	55 ± 6	(3)	58 ± 12	(3)	52 ± 3	(5)	55 ± 9
(b) Systolic arterial pressure, mmHg									
Pre-LBNP (resting), 5-min mean	Test	(80)	103 ± 7	(40)	111 ± 6[b,c]	(40)	108 ± 6[e]	(45)	108 ± 6[c]
	Ambulatory	(30)	101 ± 7	(15)	102 ± 9	(15)	106 ± 5[e]	(25)	110 ± 8[c]
LBNP elapsed time, 1-min values									
5	Test	(16)	94 ± 6	(5)	87 ± 6[e]	(8)	99 ± 10	(9)	100 ± 5[e]
	Ambulatory	(6)	91 ± 5	(3)	93 ± 12	(3)	96 ± 7	(5)	104 ± 7[c]
10	Test	(16)	94 ± 6	(2)	88 ± 3	(6)	93 ± 7	(9)	93 ± 6
	Ambulatory	(6)	93 ± 8	(2)	99 ± 9	(3)	96 ± 2	(5)	98 ± 9
15	Test	(16)	89 ± 16	...	...	(5)	95 ± 9	(7)	99 ± 14
	Ambulatory	(6)	91 ± 7	(1)	95	(2)	97 ± 10	(4)	99 ± 5
Minimum value during LBNP	Test	(16)	89 ± 16	(1)	48	(8)	91 ± 14	(7)	90 ± 8
	Ambulatory	(6)	89 ± 7	(2)	81 ± 21	(3)	90 ± 9	(4)	96 ± 8
Recovery, min									
+1	Test	(16)	106 ± 15	(7)	103 ± 14	(8)	114 ± 12	(9)	113 ± 7
	Ambulatory	(6)	101 ± 10	(3)	98 ± 16	(3)	110 ± 10	(5)	112 ± 10
+3	Test	(16)	108 ± 11	(8)	116 ± 8	(8)	112 ± 7	(9)	112 ± 7
	Ambulatory	(6)	101 ± 6	(3)	109 ± 6	(3)	118 ± 2[c]	(5)	112 ± 10

[a] n = total number of test observations.

[b] $p < 0.01$ difference from control subjects.

[c] $p < 0.01$ difference from pre-bed rest.

[d] $p < 0.05$ difference from control subjects.

[e] $p < 0.05$ difference from pre-bed rest.

TABLE 7. Continued

Test conditions		n[a]	Pre-bed rest, mean ± SD	n[a]	End bed rest, mean ± SD	n[a]	5 Days post-bed rest, mean ± SD	n[a]	90 Days post-bed rest, mean ± SD
(c) Diastolic arterial pressure, mmHg									
Pre-LBNP (resting), 5-min mean	Test	(80)	65 ± 6[b]	(40)	69 ± 7[b,c]	(40)	69 ± 5[c]	(45)	69 ± 4[c]
	Ambulatory	(30)	62 ± 5	(15)	62 ± 5	(15)	67 ± 7[e]	(25)	68 ± 5[c]
LBNP elapsed time, 1-min values									
5	Test	(16)	67 ± 6[d]	(5)	68 ± 5	(8)	69 ± 9	(9)	68 ± 5
	Ambulatory	(6)	59 ± 6	(3)	61 ± 4	(3)	69 ± 7	(5)	70 ± 1[c]
10	Test	(16)	67 ± 8	(2)	66 ± 1	(6)	69 ± 6	(9)	68 ± 4
	Ambulatory	(6)	65 ± 6	(2)	69 ± 10	(2)	69 ± 10	(3)	71 ± 8
15	Test	(16)	67 ± 14			(5)	72 ± 5	(7)	70 ± 12
	Ambulatory	(6)	66 ± 5	(1)	82	(2)	65 ± 21	(4)	71 ± 5
Minimum value during LBNP	Test	(16)	64 ± 9	(1)	26	(8)	68 ± 10	(7)	67 ± 7
	Ambulatory	(6)	56 ± 7	(3)	61 ± 6	(3)	59 ± 20	(5)	67 ± 4
Recovery, min									
+1	Test	(16)	65 ± 10	(7)	58 ± 8[e]	(8)	69 ± 7	(9)	77 ± 9[e]
	Ambulatory	(6)	63 ± 4	(3)	56 ± 7	(3)	72 ± 9	(5)	70 ± 7[e]
+3	Test	(16)	71 ± 8	(8)	77 ± 6	(8)	77 ± 7	(9)	73 ± 5
	Ambulatory	(6)	64 ± 6	(3)	69 ± 5[c]	(3)	81 ± 7[c]	(5)	68 ± 4
(d) Arterial pulse pressure, mmHg									
Pre-LBNP (resting), 5-min mean	Test	(80)	38 ± 10	(40)	41 ± 7	(40)	39 ± 7	(45)	39 ± 6[b]
	Ambulatory	(30)	39 ± 8	(15)	40 ± 9	(15)	39 ± 6	(25)	42 ± 8
LBNP elapsed time, 1-min values									
5	Test	(16)	26 ± 6	(5)	19 ± 10	(8)	30 ± 11	(9)	31 ± 7
	Ambulatory	(6)	32 ± 8	(3)	33 ± 8	(3)	27 ± 1	(5)	34 ± 6
10	Test	(16)	27 ± 9	(3)	34 ± 4	(6)	24 ± 7	(9)	24 ± 6
	Ambulatory	(6)	28 ± 4	(2)	30 ± 1	(3)	27 ± 9	(5)	27 ± 2
15	Test	(16)	26 ± 9			(5)	22 ± 5	(7)	29 ± 8
	Ambulatory	(6)	24 ± 5	(1)	13	(2)	32 ± 11	(4)	28 ± 7
Minimum, value during LBNP	Test	(16)	24 ± 7	(2)	12 ± 3	(6)	22 ± 6	(7)	23 ± 6
	Ambulatory	(6)	24 ± 5	(1)	13	(2)	23 ± 1	(4)	24 ± 3
Recovery, min									
+1	Test	(16)	41 ± 12	(7)	44 ± 15	(8)	45 ± 11	(9)	37 ± 6
	Ambulatory	(6)	38 ± 8	(3)	42 ± 11	(3)	38 ± 2	(5)	42 ± 12
+3	Test	(16)	38 ± 7	(8)	38 ± 9	(8)	35 ± 7	(9)	39 ± 8
	Ambulatory	(6)	37 ± 11	(3)	39 ± 4	(3)	37 ± 9	(5)	44 ± 9

[a] n = total number of test observations.

[b] $p < 0.01$ difference from control subjects.

[c] $p < 0.01$ difference from pre-bed rest.

[d] $p < 0.05$ difference from control subjects.

[e] $p < 0.05$ difference from pre-bed rest.

TABLE 7. Concluded

Test conditions		n[a]	Pre-bed rest, mean ± SD	n[a]	End bed rest, mean ± SD	n[a]	5 Days post-bed rest, mean ± SD	n[a]	90 Days post-bed rest, mean ± SD
(e) Mean arterial pressure, mmHg									
Pre-LBNP (resting), 5-min mean	Test	(80)	78 ± 6[b]	(40)	83 ± 6[c,d]	(40)	82 ± 4[c]	(45)	82 ± 4[c]
	Ambulatory	(30)	75 ± 4	(15)	75 ± 5	(15)	80 ± 6[c]	(25)	82 ± 5[c]
			NS		0.001		NS		NS
LBNP elapsed time, 1-min values									
5	Test	(16)	75 ± 5[b]	(5)	74 ± 3	(8)	79 ± 8	(9)	79 ± 3
	Ambulatory	(6)	70 ± 5	(3)	72 ± 7	(3)	78 ± 7	(5)	81 ± 3[c]
10	Test	(16)	76 ± 6	(2)	73 ± 0	(6)	77 ± 5	(9)	77 ± 4
	Ambulatory	(6)	74 ± 6	(2)	79 ± 10	(3)	78 ± 7	(5)	70 ± 8
15	Test	(16)	71 ± 19			(5)	80 ± 6	(7)	75 ± 7
	Ambulatory	(6)	74 ± 5	(1)	86	(2)	76 ± 18	(4)	81 ± 4
Minimum value during LBNP	Test	(16)	71 ± 19	(1)	33	(8)	75 ± 11	(7)	75 ± 7
	Ambulatory	(6)	69 ± 4	(2)	69 ± 23	(4)	70 ± 19	(5)	74 ± 18
Recovery, min									
+1	Test	(16)	79 ± 11	(7)	73 ± 7	(8)	84 ± 7	(9)	86 ± 4
	Ambulatory	(6)	75 ± 5	(3)	70 ± 10	(3)	85 ± 9	(5)	84 ± 6[e]
+3	Test	(16)	83 ± 9	(8)	90 ± 6	(8)	89 ± 6	(9)	86 ± 4
	Ambulatory	(6)	77 ± 3	(3)	82 ± 5[c]	(3)	93 ± 4[c]	(5)	82 ± 6[c]

[a] n = total number of test observations.

[b] $p < 0.01$ difference from control subjects.

[c] $p < 0.01$ difference from pre-bed rest.

[d] $p < 0.05$ difference from control subjects.

[e] $p < 0.05$ difference from pre-bed rest.

heart rate increased substantially in all subjects after bed rest compared to pre-bed-rest values (table 7(a) and fig. 25). In the bed-rested subjects heart rate changes significantly exceeded those of the ambulatory controls only during the five-day recovery period and in maximal heart rate response during the test. Significant differences in the two groups did not occur during bed rest; this indicated that the ambulatory controls themselves underwent deconditioning.

Only half of the subjects were able to continue with LBNP for more than 6 min. Of these subjects, three continued for more than 9 min and two for more than 10 min. The significance of their changes in reaction to LBNP is shown in tables 7(a) through 7(e). The onset of presyncopal symptoms (bradycardia, hypotension, nausea, and sweating) or frank syncope during LBNP following the bed-rest period was abrupt in both groups.

Mean resting heart rate values did not change much by the fifth day after bed rest (table 7(a)). Heart rate levels during LBNP still remained above pre-bed-rest values in all such subjects; however, only the bed-rested subjects exhibited a statistically significant difference ($p < 0.01$), indicating that recovery from deconditioning had not as yet occurred by 15 days. On Day 90 after bed rest, heart rate values were nearly identical to those obtained at the outset of the study. The resting heart rate values of the bed-rested subjects still exceeded those of the ambulatory controls by a significant amount.

Changes in actual systolic, diastolic, mean and pulse pressures given in tables 7(b)–7(e) are shown as 1-min changes for one bed-rested subject in figure 23. Average 1-min changes for all bed-rested subjects are given in figure 26, and are compared with ambulatory controls in

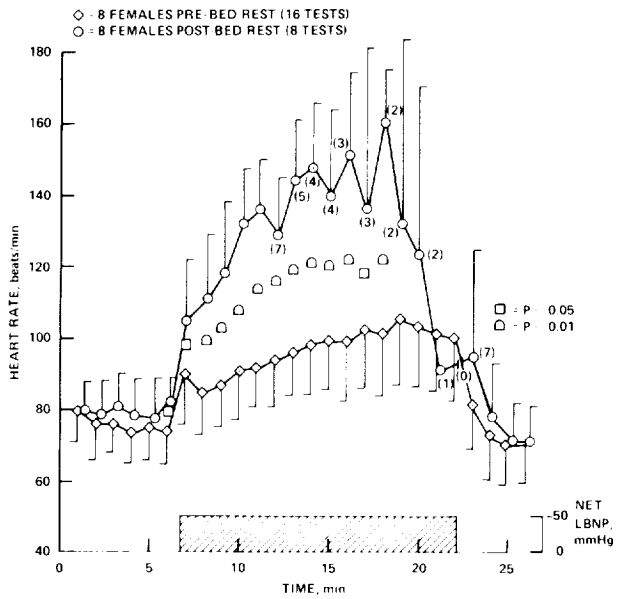


Figure 24.- *Average 1-min heart-rate changes during LBNP.*

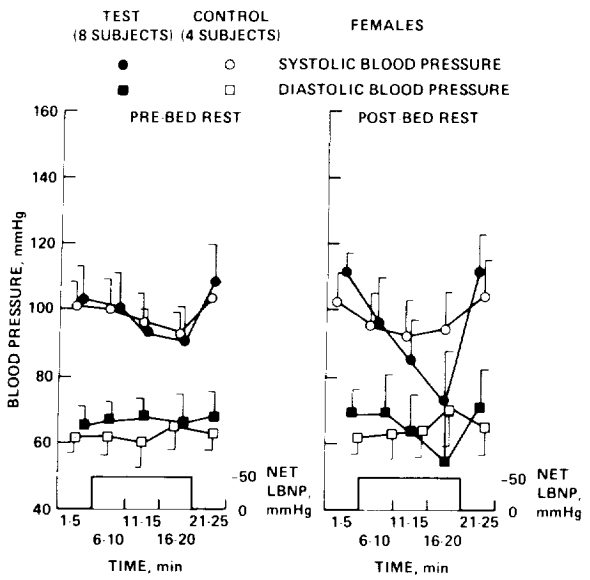


Figure 26. *Minute by minute changes in arterial blood pressure for the bed-rested subjects during LBNP.*

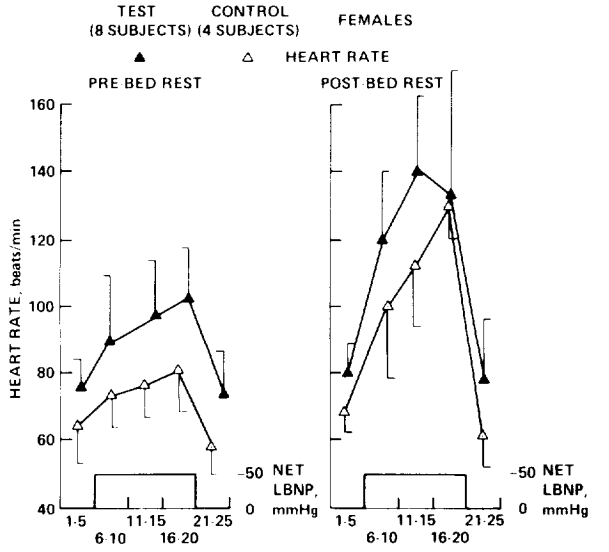


Figure 25. - *Comparison of heart rate responses in bed-rested subjects and ambulatory controls during LBNP.*

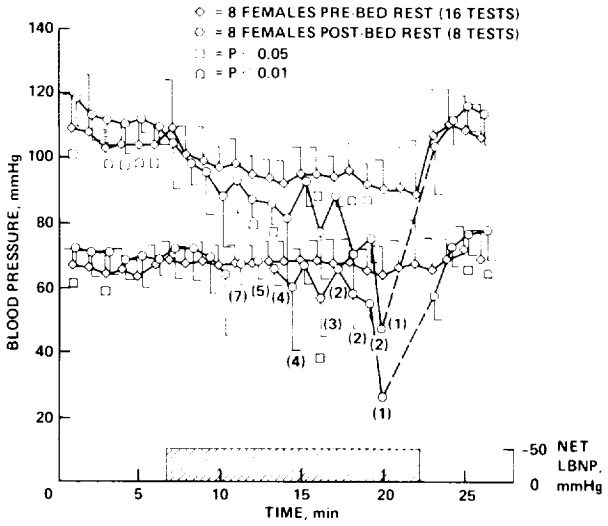


Figure 27. *Comparison of blood-pressure changes in bed-rested subjects and ambulatory controls during LBNP.*

figure 27. At rest prior to bed rest systolic blood pressure and pulse pressure values were similar between the bed-rested and ambulatory groups, but diastolic and mean pulse pressures were slightly higher ($P < 0.001$) in the bed-rested subjects. During LBNP prior to bed rest, systolic blood pressure decreased noticeably ($P < 0.05$) in both groups (table 7(b)); during the first 5 min of exposure diastolic and mean arterial blood pressures in the bed-rested subjects significantly exceeded those of the controls ($P < 0.05$), with values remaining similar

thereafter (tables 7(c)–7(d)). Pulse pressure decreased significantly from resting levels in both groups throughout LBNP before and after bed rest (test = $P < 0.01$; ambulatory = $P < 0.05$). This was associated with a slight fall in systolic blood pressure for both groups prior to bed rest (fig. 27). After bed rest the test subjects showed a marked and significant ($p < 0.001$) fall in systolic pressure while the ambulatory control subjects showed slight increase in diastolic pressure during the final 5 min of LBNP exposure.

Following bed rest, the test subjects exhibited significantly higher 5-min mean resting (control) systolic, diastolic, and mean blood pressure; however, pulse pressure remained unchanged (fig. 27). These control values remained elevated above pre-bed-rest levels after 5 days of recovery although systolic blood pressure dropped from 111 ± 6 mmHg at the end of bed rest ($P < 0.05$) to 108 ± 6 mmHg (still above pre-bed-rest levels). These findings persisted during the 90-day post-bed-rest tests in which all blood pressure variables in the bed-rested subjects continued to exceed significantly the pre-bed-rest values (resting systolic = $P < 0.01$; diastolic = $P < 0.001$; and mean BP = $P < 0.01$) and had not changed much from levels observed on the fifth day after bed rest. Pulse pressure continued unchanged. In contrast, resting or control values for the ambulatory group did not differ significantly from one test period to the other.

With exposure to LBNP, the bed-rested subjects exhibited significant decreases in: systolic blood pressure – from 108 ± 6 to 95 ± 9 mmHg ($P < 0.001$); mean blood pressure from 82 ± 4 to 78 + 7 mmHg ($P < 0.001$); and pulse pressure from 39 ± 6 to 26 ± 7 mmHg ($P < 0.001$). The subjects were able to maintain diastolic blood pressure at 60 ± 5 mmHg and showed no important changes until the last 5-min test period, during which significant decreases were observed. These changes are shown graphically in figure 26. The control group also exhibited decreases in systolic blood pressure and pulse pressure, but no significant change in diastolic or mean blood pressure (fig. 27).

Echocardiographic data suitable for analysis were obtained at rest and during LBNP for all bed-rest subjects (except Subject G) and the four ambulatory controls. Hemodynamic data on heart rate, ventricular volumes (end diastolic (EDV) and end systolic (ESV)), cardiac output, and mean blood pressures are given for the test subjects in table 8(a) and for the ambulatory controls in table 8(b). Values and means represent averages for the last minutes of each study period (control, early, middle, and late LBNP), during which time the echocardigraphic data were recorded and measured, and therefore differ from heart rate and blood pressure data given in tables 7(a)–7(d), which represent averages over the entire 5-min period of observation. Typical LBNP induced changes in end diastolic and end systolic volumes, stroke volume, cardiac output, and heart rate are shown for subject E before and after bed rest in figure 28.

In the four ambulatory controls, resting hemodynamic values after 14 days of confinement showed significant decreases in cardiac output (21.2%), stroke

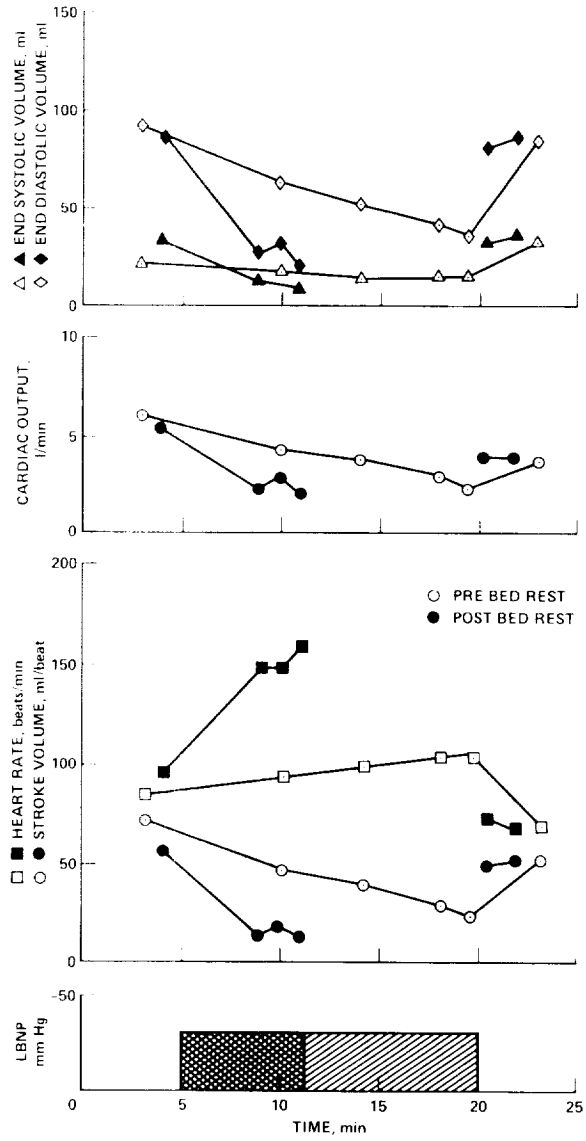


Figure 28. *Hemodynamic changes for subject E during LBNP before and after bed rest.*

volume (19.7%), and end-diastolic volume (13.1%). In comparison, there were decreases of 23.9% in stroke volume, 21% in cardiac output, and 12.8% in end-diastolic volume in the bed-rested subjects. Resting heart rate did not differ before or after bed rest in either group but post-bed rest resting heart rate was significantly higher in the test subjects ($p < 0.05$) compared to the ambulatory controls. This post-bed rest difference between the groups was also present during the first 5 min LBNP period. In all other instances the two groups showed comparable changes.

None of the subjects tolerated the complete 15 min of LBNP after bed rest (table 8(a)), but Subject C was able to withstand 14 min of it. Hemodynamic changes for this subject before and after bed rest are shown in figure 29. Data relating to heart rate, heart volumes, and cardiac output are given in table 8(a) for each individual bed-rested subject and in table 8(b) for each ambulatory control subject. Data were further divided into five periods of observation: Control, first 5 min of LBNP, second 5 min of LBNP (10 min), last 5 min of LBNP (15 min), and recovery period values. Data listed for each subject are the means for all values recorded during each respective period. As a group, heart rate increased significantly in the test subjects from control values during the first 5 min (table 8). These increases amounted to 18% before bed rest and 75% after bed rest. Heart volume decreased 48% before and 62% after bed rest, and cardiac output decreased 41% and 30%, respectively, for the same periods. During the second 5-min period (middle or 10-min portion), heart rate continued to increase significantly over the previous 5-min period, both before and after bed rest, and was the only hemodynamic variable to do so. The ambulatory control group showed similar findings but of lesser significance (table 8(b)). The heart volume changes in the ambulatory subjects which mimicked those found in the bed-rested subjects suggests that the required confinement of these subjects resulted in findings similar to those seen with bed rest alone.

The recording of end-diastolic volumes at rest and at peak LBNP allowed for a quantitative determination of fluid volume shifts from the heart to the periphery under these conditions. These changes are shown in table 9 and were obtained as the differences in end diastolic volume at rest (control) compared to the same values during LBNP prior to the onset of bradycardia or syncope. Of interest are the results that showed nearly identical fluid shifts of 57 ml which occurred before and after bed rest in the test subjects and in the controls. These shifts occurred with 50 mmHg suction despite significantly lower ventricular volumes after bed rest: $p < 0.001$ in the test subjects and $p < 0.02$ in the ambulatory controls. The lack of increased volume displacement under these conditions argues against significant peripheral venous pooling after bed rest. This was further confirmed by measurement of total leg volume as shown in figure 30 and table 10. These changes correlated with heart rate and blood pressure changes during LBNP are shown for a typical subject in figure 23.

Significant increases in leg volume during LBNP could not be detected after bed rest. For the bed-rested subjects, approximately 720 ml were displaced into the legs under resting conditions and 780 ml after bed rest; for the control subjects, these values were 780 and 800, respectively. Individual subjects varied in their response, as shown in figure 30. Four of the bed-rest subjects showed slightly lower volume displacement values after bed rest, two showed no change, and two were slightly greater. Of the ambulatory group, two subjects showed smaller volume displacement as the study progressed, and two showed no change. No difference was apparent in the rate of change or amount of fluid transferred between LBNP exposures that were abbreviated because of presyncopal symptoms and those that were completed. Repeated measurements, both with and without plethysmography, indicated that the plethysmographic equipment did not alter to any important degree the responses to LBNP or the symptoms of deconditioning. Paired t-tests were performed on the values at each minute and showed no substantial differences between the test and control subjects during either the end-bed-rest or post-bed-rest exposures.

Physical Working Capacity

The mean body weight of the subjects decreased during bed rest by 3.1% ($P < 0.05$), primarily because two of the subjects (Subjects A and F) voluntarily restricted their caloric intake (table 2, also appendix B). Maximal VO_2 in liters per minute decreased by −9.7% ($P < 0.05$); when expressed in milliliters per minute per kilogram the decrease was −7.8% (NS). Maximal ventilatory volume remained essentially constant ($\Delta = +2.3\%$, NS). Maximal heart rate was elevated from 181 bpm in the control period to 187 bpm following bed rest (table 11). After bed rest, the experimental subjects showed a significantly reduced ability ($P < 0.05$) to tolerate the exercise test, with the total time of the test reduced by 3.2%.

TABLE 8.-- ECHOCARDIOGRAPH DATA

		Control						5-min						10-min						15-min						Recovery				
		HR, beats/min	EDV, ml	ESV, ml	SV, ml/beat	CO, L/min	Mean BP, mmHg	HR, beats/min	EDV, ml	ESV, ml	SV, ml beat	CO, L/min	Mean BP, mmHg	HR, beats/min	EDV, ml	ESV, ml	SV, ml/beat	CO, L/min	Mean BP, mmHg	HR, beats/min	EDV, ml	ESV, ml	SV, ml/beat	CO, L/min	Mean BP, mmHg	HR, beats/min	EDV, ml	ESV, ml	SV, ml/beat	CO, L/min
(a) Bed rest group																														
A	Before BR	72	97	25	72	5.18	85.3	73	44	13	31	2.26	80.7	78	47	13	34	2.65	84.3	78	41	11	30	2.34	80.7	59	74	25	49	2.89
	After BR	73	79	16	63	4.60	89.3	134	30	10	20	2.68	78.0													61	79	14	65	3.97
B	Before BR	79	108	32	76	6.00	72.7	99	47	18	29	2.87	71.0	102	38	8	30	3.06	68.0	111	35	6	29	3.22	70.0	83	102	30	72	5.98
	After BR	85	92	44	48	4.08	80.7	131	35	18	17	2.23	70.7	151	41	25	16	2.42	52.0							90	108	38	70	6.30
C	Before BR	66	97	30	67	4.42	78.3	103	44	16	28	2.88	75.3	107	47	13	34	3.64	77.3	111	35	10	25	2.78	75.3	59	97	41	56	3.30
	After BR	70	79	35	44	3.11	80.7	120	35	8	27	3.24	80.0	150	32	7	25	3.75	72.7	91	13	3	10	0.91	56.7	63	92	41	51	3.21
D	Before BR	78	102	22	80	6.24	80.0	77	30	10	20	1.54	80.7	87	38	13	25	2.18	74.3	86	38	13	25	2.15	76.0	64	97	38	59	3.78
	After BR	74	92	32	60	4.44	88.0	141	27	4	23	3.24	74.0													72	88	27	61	4.39
E	Before BR	84	92	22	70	5.88	79.3	93	62	16	46	4.28	77.3	99	51	13	38	3.76	79.3	104	35	13	22	2.29	77.0	68	83	30	53	3.60
	After BR	96	88	32	56	5.38	85.3	150	32	14	18	2.70	73.3													75	83	32	51	3.83
F	Before BR	77	92	25	67	5.16	78.7	92	44	14	30	2.76	82.7	102	38	14	24	2.45	80.7	76	41	10	31	2.36	31.7	60	97	38	59	3.54
	After BR	78	88	35	53	4.13	80.7	134	20	5	15	2.01	80.0													60	83	30	53	3.18
G	Before BR	78	74	25	49	3.82	79.3	87	62	22	40	3.48	72.7	93	54	20	34	3.16	75.3	107	41	22	19	2.03	76.7	81	83	22	61	4.94
	After BR	84	54	18	36	3.18	78.7	139	Bad data																	78	66	25	41	3.20
H	Before BR	86	92	38	54	4.64	74.7	108	58	14	44	4.75	78.0	126	47	16	31	3.91	76.0	131	51	20	31	4.06	80.0	76	102	35	67	5.09
	After BR	81	83	32	51	4.13	80.7	172	41	16	25	4.30	76.0	174	30	13	17	2.96	72.3							74	113	35	78	5.77
Before BR Mean		78	94	27	67	5.17	78.5	92[a]	49[b]	15[b]	34[b]	3.10[b]	77.3	99[c]	45	14	31	3.10	76.9	101	40	13	28	2.66	70.9	69	92	32	60	4.14
±S.D.		6	10	6	11	.85	3.7	12	11	4	9	1.04	4.1	14	6	3	5	.64	4.8	19	5	5	4	.68	16.2	10	10	7	73	1.07
			d		e	f		d	d		e			d															
After BR Mean		80[g]	82	31	51	4.13	83.0	140[b,h]	31[b]	11[b]	21	2.91[i]	76.0	158[f,i]	34	15	19	3.04	65.7							72	89	30	59	4.23
±S.D.		8	12	9	9	.74	4.0	17	7	5	4	.77	3.5	14	6	9	5	.67	11.8							10	15	9	12	1.20
(b) Ambulatory group																														
J	Before BR	84	113	41	72	6.05	80.7	108	35	11	24	2.59	70.7													54	83	22	61	3.29
	After BR	70	102	32	70	4.90	76.0	90	25	7	18	1.62	16.7													63	97	38	59	3.72
I	Before BR	66	102	32	70	4.62	74.0	108	51	30	21	2.27	74.0	130	54	27	27	3.24	69.3	119	47	28	19	3.45	70.7	66	92	41	51	3.06
	After BR	72	92	35	57	4.10	79.3	132	27	10	17	2.24	76.0	138	32	13	19	2.62	85.7	141	35	11	24	3.38	80.7	65	92	41	51	3.32
K	Before BR	77	92	22	70	5.39	73.3	80	74	13	61	4.88	14.7	85	44	14	30	2.55	72.0	91	35	10	25	2.28	72.0	61	88	20	68	4.15
	After BR	72	79	30	49	3.53	73.3	114	30	10	20	2.28	76.3	126	32	13	19	2.39	80.7							66	83	32	51	3.37
L	Before BR	54	88	18	70	3.78	76.0	59	44	10	34	2.01	70.0	62	41	10	31	1.92	69.3	65	35	10	25	1.63	70.0	54	92	30	62	3.35
	After BR	60	70	18	52	3.12	70.0	96	30	3	27	2.59	64.0	102	22	3	19	1.94	71.7							48	66	20	42	2.02
Before BR Mean		70	99	28	71	4.96	76.0	89[k]	51[b]	16	35[k]	2.94	72.4	89	46	17	29	2.57	70.2	92	47	15	31	2.45	70.9	57	89	28	61	3.46
±S.D.		13	11	10	1	.98	3.3	24	17	9	18	1.31	2.3	29	7	9	2	.66	1.6	26	12	5	8	.92	1.0	4	4	10	7	.48
			f						e					e	e		e													
After BR Mean		69[g]	86	29	57	3.91	74.7	108[a,h]	28[i]	8	21[i]	2.18	58.3	122	29	10	19	2.32	79.4							61	85	33	52	3.11
±S.D.		6	14	8	9	.77	4.0	19	3	3	5	.41	28.3	18	6	6	0	.35	7.1							9	14	9	5	.75

[a] $p \leq 0.02$ difference compared to control.

[b] $p \leq 0.001$ difference compared to control.

[c] $p \leq 0.01$ difference compared to 5 minutes.

[d] $p \leq 0.001$ difference before and after bed rest.

[e] $p \leq 0.05$ difference before and after bed rest.

[f] $p \leq$ difference before and after bed rest.

[g] $p \leq 0.05$ difference between ambulatory control and bed rest subjects.

[h] $p \leq 0.02$ difference between ambulatory control and bed rest subjects.

[i] $p \leq 0.01$ difference compared to control.

[j] $p \leq 0.001$ difference compared to previous 5 minutes.

[k] $p \leq 0.05$ difference compared to control.

HR = heart rate
EDV = end diastolic volume
ESV = end systolic volume
SV = stroke volume
CO = cardiac output
BP = blood pressure

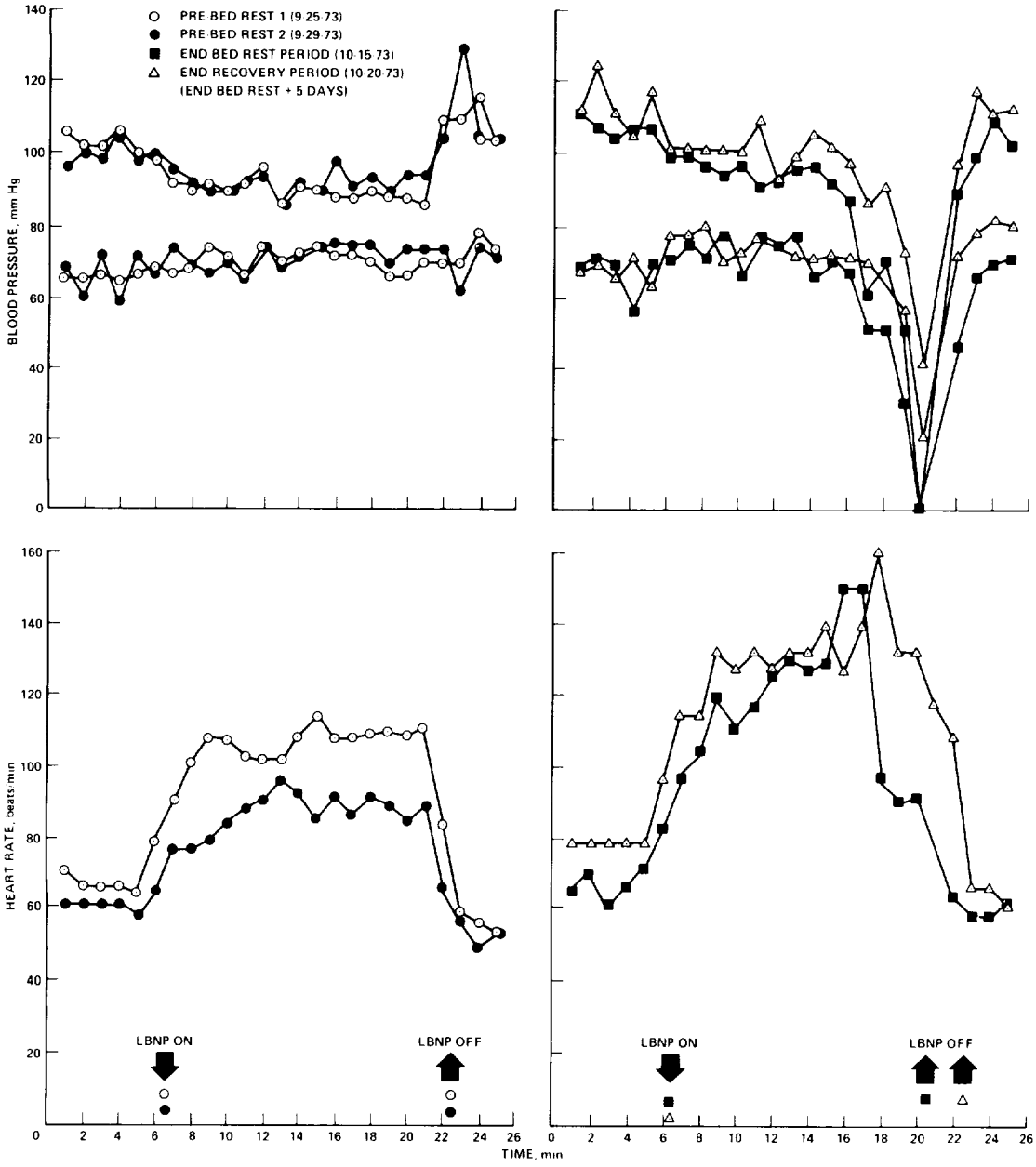


Figure 29.– *Minute by minute changes in heart rate and blood pressure in subject C during LBNP.*

TABLE 9.-- COMPARISON OF HEART RATE (HR) AND END DIASTOLIC VOLUME (EDV) AT REST AND AT PEAK RESPONSE (PRIOR TO ONSET OF SYNCOPE) DURING LBNP

Subject[a]	Control		Peak LBNP		ΔEDV[b]	%Δ[c]
	HR, beats/min	EDV, ml	HR, beats/min	EDV, ml	ml	ml
Bed-rest group						
1 Pre	85	95	173	54	41	43
1 Post	82	83	173	30	53	64
2	77	92	76	41	51	56
2	78	88	134	20	68	77
3	84	92	104	35	57	62
3	96	88	150	32	56	63
4	66	113	86	38	75	66
4	77	97	141	27	70	72
5	72	97	78	41	56	58
5	73	79	134	30	49	62
6	66	97	113	35	62	64
6	70	79	91	13	66	66
7	79	108	111	35	73	67
7	85	92	151	41	51	56
Average	76.9 ± 7.8 80 ± 8.6	99 ± 8.1 87 ± 6.7 $p < 0.001$	98 ± 18.4 134 ± 25.3 $p < 0.001$	40 ± 6.8 28 ± 9.0 $p < 0.001$	59 ± 12.0 59 ± 8.8	59 ± 8.3 66 ± 6.9
Ambulatory controls						
1 Pre	73	92	95	51	42	46
1 Post	72	79	126	32	47	59
2	84	113	108	35	78	69
2	70	102	98	25	77	76
3	84	88	95	35	53	60
3	60	70	102	22	48	69
4	66	102	120	44	58	57
4	72	92	141	35	57	52
Average	70 ± 13.1 68.5 ± 5.7	99 ± 11.2 86 ± 14.1 $p < 0.02$	97 ± 23.7 135 ± 23.0	41 ± 7.7 33.5 ± 13.4	58 ± 15.1 57 ± 13.9	58 ± 9.5 64 ± 10.6

[a] Female, LBNP = -50 mmHg.
[b] ΔEDV is difference in EDV during control (resting) and peak LBNP.
[c] Δ is ΔEDV/control EDV.

TABLE 10. LEG VOLUME RESPONSES OF FEMALE SUBJECTS TO LBNP

Test condition	Number complete	Number shortened by presyncope	% complete	Leg volume change after 4 min		
				ml	%	(n)
Before bed rest	14	1	96.0			
Immediately after bed rest	2	10	16.7	784	5.6	(30)
5 Days after bed rest	8	4	66.7	733	4.9	(31)
90 Days after bed rest	11	3	78.6	742	4.9	(31)
Control subjects (n = 4)						
Before bed rest (pre-op)	8	1	88.9			
Immediately after bed rest	2	2	50.0	796	5.6	(3)
5 Days after bed rest	2	2	50.0	667	4.3	(4)
90 Days after bed rest	4	1	80.0	783	4.9	(4)
Bed rest subjects (n = 8)						
Before bed rest	16	0	100.0			
Immediately after bed rest	0	8	0	779	5.6	(7)
5 Days after bed rest	6	2	75.0	771	5.2	(7)
90 Days after bed rest	7	2	77.8	709	4.8	(7)

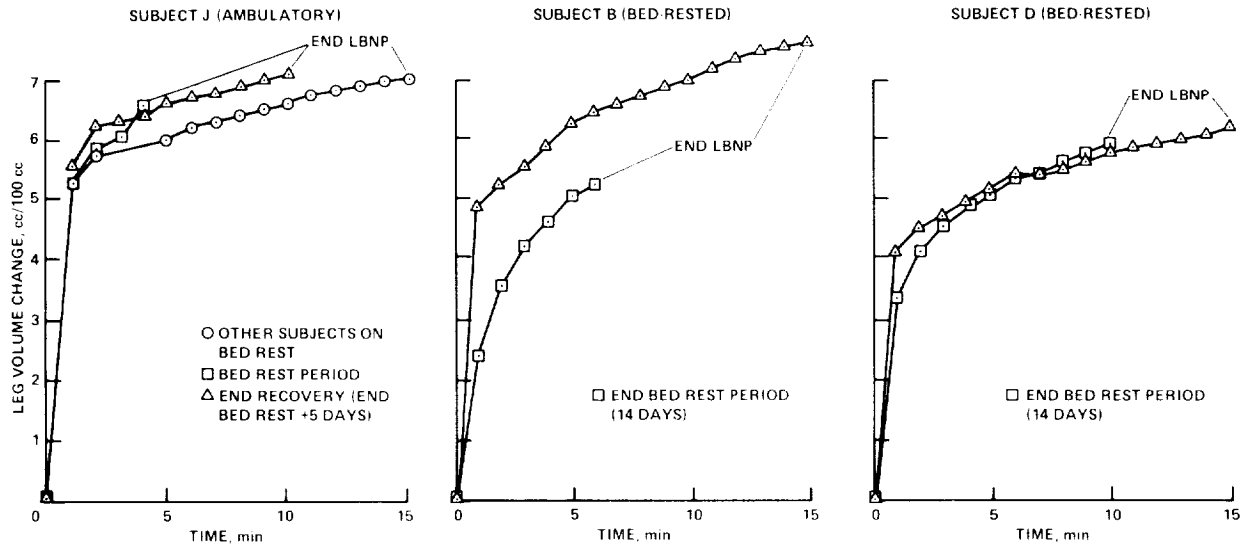


Figure 30. *Leg volume changes in representative subjects during LBNP.*

TABLE 11. EXERCISE TOLERANCE IN FEMALE SUBJECTS

Subject	Maximum $\dot{V}O_2$, liter/min			Maximum $\dot{V}O_2$, ml/min kg			Maximum ventilatory volume, liter/min			Maximum heart rate, BPM			Tolerance time, min		
	BBR[a]	ABR[b]	Δ	BBR[a]	ABR[b]	Δ	BBR[a]	ABR[b]	Δ	BBR[a]	ABR[b]	Δ	BBR[a]	ABR[b]	Δ
A	1.82	**1.76**	-3.3	29.79	**30.83**	+3.5	61.39	**62.49**	+1.8	162	**168**	+3.7	12.0	**10.6**	-11.7
B	2.15	**2.28**	+6.0	38.83	**43.01**	+10.8	78.94	**90.50**	+14.6	174	**186**	+6.9	13.3	**12.7**	-4.5
C	**2.41**	2.33	-3.3	**38.31**	37.42	-2.3	**104.06**	117.19	+12.6	**198**	204	+3.0	**13.7**	13.3	-2.9
D	**1.89**	1.89	0.0	**33.80**	34.66	+2.5	**87.57**	82.93	-5.3	**180**	186	+3.3	**12.7**	12.7	0.0
E	1.96	**1.72**	-12.2	32.02	**29.15**	-9.0	72.97	**79.49**	+8.9	168	**180**	+7.1	11.3	**10.2**	-9.7
F	2.26	1.65	-27.0	44.93	32.47	-27.7	71.82	82.68	+15.1	180	180	0.0	13.3	13.3	0.0
G	1.47	1.25	-15.0	27.50	24.11	-12.3	57.79	52.45	-9.2	186	192	+3.2	9.9	10.0	+1.0
H	2.58	1.98	-23.3	39.10	30.52	-21.9	81.80	66.61	-18.6	198	198	0.0	15.0	15.0	0.0
Mean	2.06	1.86	-9.7[c]	35.54	32.77	-7.8	77.48	79.29	+2.3	181	187	+3.3[c]	12.7	12.2	-3.2[c]
±S.E.	.13	.12		2.04	2.02		5.29	7.01		5	4		.6	.6	

[a] Before bedrest.

[b] After bedrest.

[c] $p < 0.05$.

NOTE: Bold numbers indicate ±2 days of menstrual flow.

Mean values of heart rate and oxygen uptake at submaximal and maximal workloads are given in figure 31. After bed rest, submaximal and maximal VO_2 at 80 to 160 W were lower ($P < 0.05$) than control values.

The subjects exhibited a similar pattern in submaximal and maximal heart rates which were significantly elevated over control values (fig. 31).

Data obtained within ±2 days of the onset of menstruation are shown in figure 1 and indicated in bold numbers in table 11. If menstruation had a detrimental effect on exercise performance, subjects' data would have shown lowered values. This was not the case. It is therefore concluded that menstruation did not have a significant effect.

When the subjects were exercised at 55-60% of their maximal VO_2, their submaximal VO_2 decreased after bed rest by 11.9% ($P < 0.05$). At the same time submaximal heart rate increased by +6.2%. Mean plasma volume decreased by −12.6% after bed rest (ref. 39). Hematocrit and red blood cell count were also lower, but mean corpuscular volume remained unchanged.

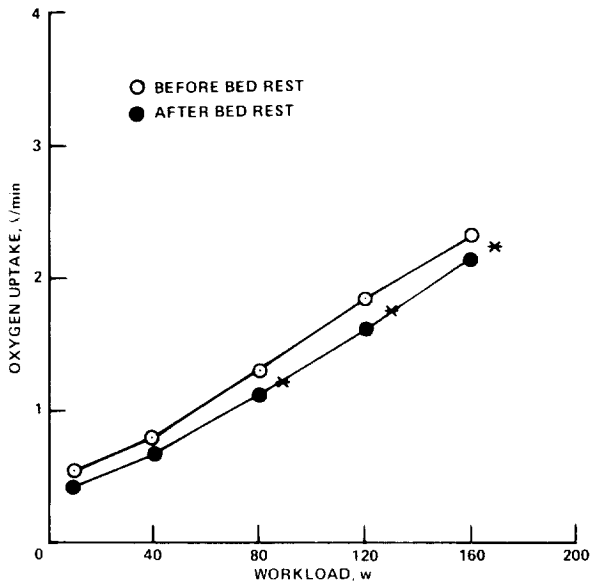
Biochemistries

A summary of selected plasma biochemical values associated with fluid shifts is given in table 12. At the end of bed rest, the bed-rested group showed statistically significant decreases of 12.6% in plasma volume, 3.3% in body potassium content, and 4.9% in plasma potassium concentration compared with control values (tables 13 and 14). Most of the eight subjects experienced a slight loss of body weight, as described above, and total body water content (table 15), but these changes were not statistically significant for the group as a whole. By the end of the recovery period, all variables except plasma potassium concentration had returned to base values. This latter constituent, however, remained significantly low by 9.0%. The control subjects exhibited no statistically significant changes in any of the variables during the study.

A summary of all plasma and urine analyzed variables obtained during the study is given in table 16. Specific values of each of these parameters are given in appendix A.

The findings of a substantial decrease in plasma volume and a small, but significant, decrease in body potassium content in the bed-rested females are in accord both qualitatively and quantitatively with results obtained for comparably bed-rested males (ref. 40). A comparison of these male and female values is given in figure 32.

Analyses of blood samples revealed no significant changes in total protein concentration in either the bed-rested or control groups. When the plasma protein electrophoretograms were examined, however, it was found that significant shifts in protein fractions had occurred. In the bed-rested group following recumbency, plasma albumin concentration decreased by 10.4%, and concentration of plasma globulins increased by 10.7%, resulting in a decrease in the albumin/globulin ratio of 20.5%. Plasma fibrinogen concentration rose by 53.2%. All these changes were reversed by the sixth day of the recovery



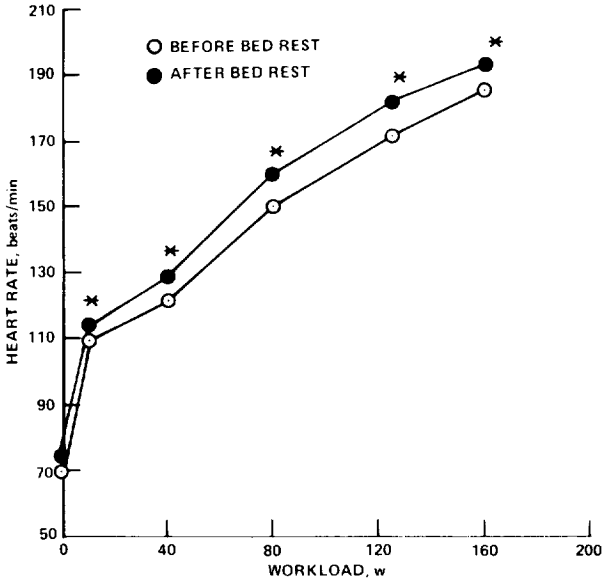


Figure 31. — *Workload capacity in female subjects.*

TABLE 12. SUMMARY OF BIOCHEMISTRY DATA

Parameter	Before bed rest	Bed rest, day 17
Body weight, kg	57.6 ± 5.6	56.4 ± 6.1
Body potassium, eq	2.50 ± .15	2.42 ± .16[a]
Body water, liters	31.6 ± 2.5	30.6 ± 3.5
Plasma volume, liters	2.62 ± .23	2.29 ± .21[a]
Plasma protein, g/100 ml	6.57 ± .44	6.65 ± .26
Plasma albumin, g/100 ml	3.86 ± .23	3.46 ± .09[a]
Plasma globulins, g/100 ml	2.24 ± .35	2.48 ± .19[a]
Plasma fibrinogen, g/100 ml	.47 ± .05	.72 ± .06[a]

[a] $p < 0.05$ that the mean values before and after the bed rest are the same.

TABLE 13. BODY POTASSIUM CONTENT

Subject	Body potassium, eq				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ Control	
				Bed rest	Recovery
Bed-rest group					
A	3.06	2.90	2.99	94.8	97.7
B	3.11	2.97	3.04	95.5	97.7
C	2.97	2.81	2.83	94.6	95.3
D	3.05	2.97	3.02	97.4	99.0
E	2.97	2.95	3.07	99.3	103.4
F	3.25	3.12	3.20	96.0	98.5
G	2.61	2.49	2.55	95.4	97.7
H	3.06	3.07	3.17	100.3	103.6
Mean	3.01	2.91[a]	2.98	96.7	99.1
S.D.	±0.18	±0.19	±0.21	±2.1	±2.9
S.E.	±0.07	±0.07	±0.07	±0.8	±1.0
Ambulatory group					
I	3.43	3.36	3.37	98.0	98.3
J	2.98	3.01	2.97	101.0	99.7
K	3.09	3.14	3.18	101.6	102.9
L	3.04	2.99	3.01	98.4	99.0
Mean	3.23	3.12	3.13	99.8[b]	100.0
S.D.	±0.20	±0.17	±0.18	±1.8	±2.0
S.E.	±0.10	±0.09	±0.09	±0.9	±1.0

[a] $p < 0.01$, bed rest vs control.
[b] $p < 0.05$, bed rest vs ambulatory control.

TABLE 14.– PLASMA POTASSIUM CONCENTRATION

Subject	Plasma potassium, meq/l				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ Control	
				Bed rest	Recovery
Bed-rest group					
A	4.42	4.18	3.95	94.6	89.4
B	4.23	3.94	3.60	93.1	85.1
C	4.81	4.52	4.70	94.0	97.7
D	4.14	4.38	4.30	105.8	103.9
E	4.81	4.14	3.85	86.1	80.0
F	4.33	4.33	4.10	100.0	94.7
G	4.23	4.04	3.65	95.5	86.3
H	4.71	4.42	4.30	93.8	91.3
Mean	4.46	4.24	4.06[a]	95.4	91.1
S.D.	±0.28	±0.20	±0.37	±5.7	±7.6
S.E.	±0.10	±0.07	±0.13	±2.0	±2.7
Ambulatory group					
I	4.14	4.14	4.00	100.0	96.6
J	4.23	4.38	4.15	103.5	98.1
K	4.04	4.33	3.95	107.2	97.8
L	4.04	4.47	4.15	110.6	102.7
Mean	4.11	4.33	4.06	105.3[b]	98.8
S.D.	±0.09	±0.14	±0.10	±4.6	±2.7
S.E.	±0.05	±0.07	±0.05	±2.3	±1.3

[a] $p < 0.01$, bed rest vs control.
[b] $p < 0.05$, bed rest vs ambulatory control.

TABLE 15.– BODY WATER VALUES

Subject	Body water, liters				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ Control	
				Bed rest	Recovery
Bed-rest group					
A	32.4	28.1	29.6	86.7	91.4
B	30.4	28.4	29.6	93.4	97.4
C	33.4	33.2	34.3	99.4	102.7
D	30.7	32.3	31.8	105.2	103.6
E	32.4	33.2	33.2	102.5	102.5
F	29.7	26.6	27.7	89.6	93.3
G	28.0	27.2	28.1	97.1	100.4
H	36.0	36.1	36.7	100.3	101.9
Mean	31.6	30.6	31.4	96.8	99.2
S.D.	±2.5	±3.5	±3.2	±6.4	±4.6
S.E.	±0.9	±1.2	±1.1	±2.3	±1.6
Ambulatory group					
I	30.6	30.1	29.9	98.4	97.7
J	32.7	32.4	33.2	99.1	101.5
K	34.4	33.9	33.4	98.5	97.1
L	32.1	31.5	31.9	98.1	99.4
Mean	32.5	32.0[a]	32.1	98.5	98.9
S.D.	±1.6	±1.6	±1.6	±0.4	±2.0
S.E.	±0.8	±0.8	±0.8	±0.2	±1.0

[a] $p < 0.005$, bed rest vs control.

TABLE 16.– SUMMARY OF TRENDS IN ALL 63 MEASURED BIOCHEMICAL PARAMETERS

Parameters	Bed-rest group	Ambulatory group	Bed-rest vs ambulatory	Parameters	Bed-rest group	Ambulatory group	Bed-rest vs ambulatory
Body weight				Plasma LDH-2			
Plasma volume	↓		a	Plasma LDH-3	↑	*	
Venous hematocrit	↓	↓		Plasma LDH-4			
Blood hemoglobin				Plasma LDH-5			
Body water		↓		Plasma GOT	↓	↓	
Extracellular water		↑	a	Plasma GPT			
Intracellular water		↓		Plasma ALP	↑	↑	
Body potassium	*		a				
Plasma potassium			a	Urine volume	↓		
Plasma sodium	↑	↑		Urine sp gr			
Plasma calcium				Urine osm act	↓		
Plasma magnesium	↑	↑		Urine pH	*		
Plasma chloride	↑	↑		Urine chloride	*		a
Plasma protein				Urine sodium	*		
Plasma albumin	↓			Urine potassium	*		
Plasma globulins	↑			Urine Na/K			
Plasma fibrinogen	↑	↑		Urine magnesium			
A/G ratio	*			Urine calcium			
Circ plasma protein	*		a	Urine phosphate			
Circ albumin	*		a	Urine total N	*		
Circ globulins				Urine ammonia			
Circ fibrinogen	↑	↑	a	Urine urea	*	↓	
Plasma α-1-globulin				Urine creatinine	*		
Plasma α-2-globulin				Urine creatine			
Plasma β-globulin	*			Urine hydroxyproline	*		
Plasma γ-globulin				Urine glucose	*	↓	
Circ α-1-globulin				Urine citrate			
Circ α-2-globulin				Urine 17-OHCS			
Circ β-globulin				Urine epinephrine			
Circ γ-globulin				Urine norepinephrine	*		
Plasma total LDH	*	*		Urine NEFA			
Plasma LDH-1	*	↓		Urine cyclic AMP			

[a] Mean change on Day 17 of bed rest for bed-rest group significantly different ($P < 0.05$) from ambulatory group.
↓ Mean value significantly lower ($P < 0.05$) on Day 17 of bed rest than 7 days before.
* Mean value significantly higher ($P < 0.05$) on Day 17 of bed rest than 7 days before.

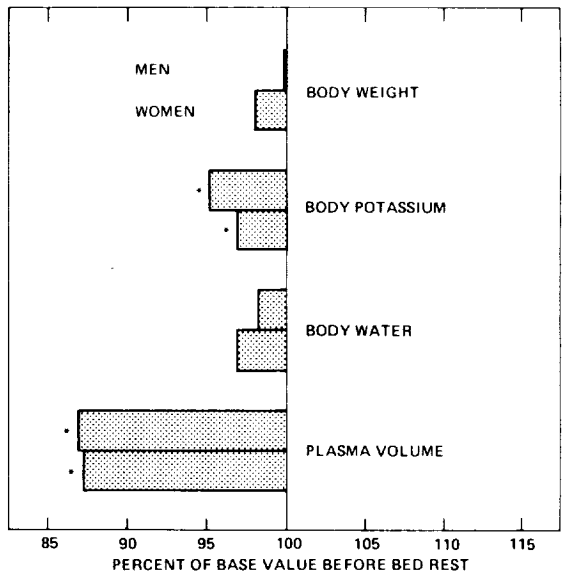


Figure 32.– *Mean values of four major body components measured in eight men after 14 days of bed rest and in eight women after 17 days of bed rest, expressed as percentages of the corresponding values measured before the start of bed rest. The asterisks indicate significant differences at the $P < 0.05$ level.*

period. There was no significant change in concentration of plasma albumin and globulins in the control subjects, but their plasma fibrinogen levels increased by 59.5% (table 17 and fig. 33). A comparison of these findings with those for males (fig. 33) showed that males exhibited a significantly greater increase in total plasma protein and females a decrease in plasma albumin and a large increase in plasma fibrinogen.

TABLE 17.- PLASMA PROTEIN CONCENTRATION

Subject	Plasma protein concentration, g/100 ml				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	% Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	6.26	6.58	6.12	105.1	97.8
B	7.31	7.05	6.74	96.4	92.2
C	6.97	6.58	6.31	94.4	90.5
D	6.72	6.58	6.01	97.9	89.4
E	6.38	6.55	6.56	102.7	102.8
F	6.35	7.05	7.01	111.0	110.4
G	6.67	6.55	6.71	98.2	100.6
H	5.93	6.28	5.88	105.9	99.2
Mean	6.57	6.65	6.42	101.5	97.9
S.D.	±0.44	±0.26	±0.40	±5.7	±7.1
S.E.	±0.15	±0.09	±0.14	±2.0	±2.5
Ambulatory group					
I	7.10	6.70	6.41	94.4	90.3
J	6.58	6.60	6.34	100.3	96.4
K	6.49	6.62	6.44	102.0	99.2
L	6.38	7.15	6.81	112.1	106.7
Mean	6.64	6.77	6.50	102.2	98.2
S.D.	±0.32	±0.26	±0.21	±7.4	±6.8
S.E.	±0.16	±0.13	±0.11	±3.7	±3.4

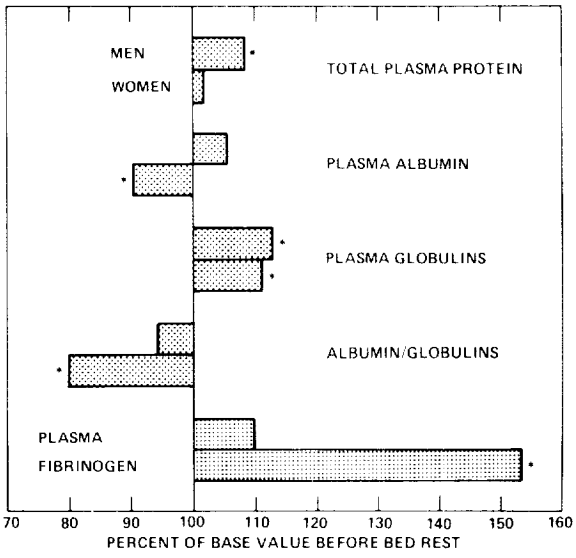


Figure 33. *Mean plasma protein concentrations measured in eight men and eight women after 14 and 17 days of bed rest, respectively, expressed as percentages of the values before bed rest.*

Interpretation of the observed changes in plasma protein concentration (table 17) in the bed-rested subjects required the computation of the circulating quantities of these parameters (fig. 34). This step was accomplished by multiplying plasma concentration by plasma volume in each case. In regard to similarly studied male subjects, circulating total plasma protein in the bed-rested female subjects was significantly reduced by 11.6% and circulating albumin was decreased by 22.5%, but concentration of circulating globulins showed no significant change. Circulating fibrinogen was increased by 33.3%. By the sixth day of recovery, quantities of circulating plasma proteins had returned to control values.

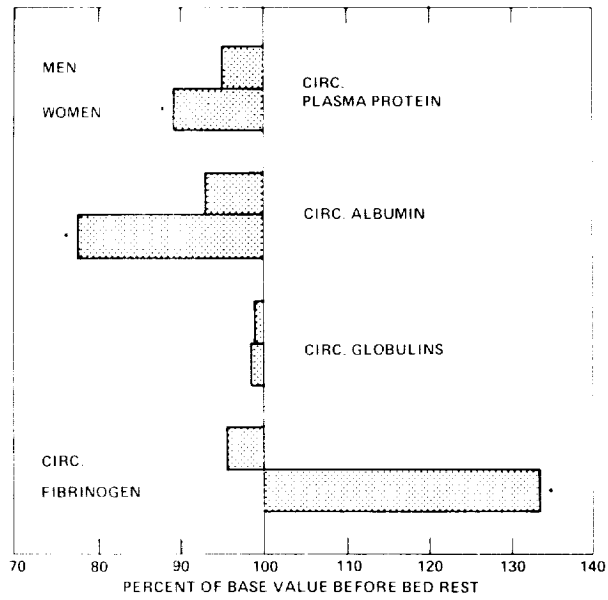


Figure 34. *Mean values for circulating plasma proteins in eight men and eight women after 14 and 17 days of bed rest, respectively, expressed as percentages of the values before bed rest.*

Analysis of the 24-hr urines revealed a number of statistically significant changes in various substances by the end of bed rest and after 6 days of recovery. The various substances are listed in table 15 and their qualitative changes shown. No changes of significance occurred for ammonia, creatinine, creatine, hydroxyproline, 17-hydroxycorticosteroids, epinephrine, and cyclic-AMP.

The excretion rate of total osmotically active substances was significantly reduced in both the bed-rested and control groups on the last day of bed rest (table 18). Individual electrolyte excretion rates in the bed-rested

group at that time showed a varied pattern of change; chloride, sodium, and potassium excretion rates were significantly lower, whereas magnesium, calcium, and phosphate were substantially elevated (tables 19–24). Excretion of electrolytes in both groups had returned to control levels by the end of the recovery period.

TABLE 18. URINE OSMOTIC ACTIVITY

Subject	Urine osmotic activity, osmols/24 hr				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	0.744	0.295	0.242	39.7	32.5
B	.571	.233		40.8	
C	.826	.708	.538	85.7	65.1
D	.814	.569	.600	69.9	73.7
E	.955	.466	.924	48.8	96.8
F	.799	.492	.542	61.6	67.8
G	.353	.312	.475	88.4	134.6
H	.996	.288	.847	28.9	85.0
Mean	0.757	0.420[a]	0.595[b]	58.0	79.4
S.D.	±0.208	±0.166	±0.230	±22.1	±31.5
S.E.	±0.074	±0.059	±0.087	±7.8	±11.9
Ambulatory group					
I	0.792	0.751	0.811	94.8	102.4
J	1.051	.761	.439	72.4	41.8
K	.950	.523	.785	55.1	82.6
L	.840	.343	.929	40.8	110.6
Mean	0.908	0.595	0.741	65.8	84.4
S.D.	±0.116	±0.200	±0.211	±23.3	±30.7
S.E.	±0.058	±0.100	±0.105	±11.6	±15.4

[a] $p < 0.005$, bed rest vs control.
[b] $p < 0.01$, recovery vs control.

TABLE 19. URINE CHLORIDE EXCRETION RATE

Subject	Urine chloride excretion rate, mmol/24 hr				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	163	42	48	25.8	29.4
B	152	37		24.3	
C	211	108	91	51.2	43.1
D	241	96	141	39.8	58.5
E	241	85	154	35.3	63.9
F	235	93	144	39.6	61.3
G	124	56	120	45.2	96.8
H	225	43	202	19.1	89.8
Mean	199	70[a]	129[b]	35.0	63.3
S.D.	±46	±28	±49	±11.1	±23.8
S.E.	±16	±10	±19	±3.9	±9.0
Ambulatory group					
I	182	156	178	85.7	97.8
J	241	125	126	51.9	52.3
K	144	107	167	74.3	116.0
L	239	63	251	26.4	105.0
Mean	201	113	180	59.6[c]	92.8
S.D.	±47	±39	±52	±26.2	±28.0
S.E.	±24	±19	±26	±13.1	±14.0

[a] $p < 0.001$, bed rest vs control.
[b] $p < 0.005$, recovery vs control.
[c] $p < 0.05$, bed rest vs ambulatory control.

TABLE 20. URINE SODIUM EXCRETION RATE

Subject	Urine sodium excretion rate, mmol/24 hr				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	159	39	46	24.5	28.9
B	159	49		30.8	
C	206	130	111	63.1	53.9
D	256	147	146	57.4	57.0
E	259	126	183	48.6	70.7
F	288	120	162	41.7	56.3
G	121	66	138	54.5	114.0
H	217	51	236	23.5	108.8
Mean	208	91[a]	146[b]	43.0	69.9
S.D.	±58	±44	±59	±15.3	±30.9
S.E.	±21	±15	±22	±5.4	±11.7
Ambulatory group					
I	170	179	185	105.3	108.8
J	267	121	126	45.3	47.2
K	127	145	189	114.2	148.8
L	267	81	275	30.3	103.0
Mean	208	132	194	73.8	102.0
S.D.	±71	±41	±61	±42.1	±41.8
S.E.	±35	±21	±31	±21.1	±20.9

[a] $p < 0.001$, bed rest vs control.
[b] $p < 0.05$, recovery vs control.

TABLE 21. URINE POTASSIUM EXCRETION RATE

Subject	Urine potassium excretion rate, mmol/24 hr				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	46.1	24.7	18.5	53.6	40.1
B	32.9	12.7		38.6	
C	67.2	52.8	61.2	78.6	91.1
D	85.9	42.0	32.4	48.9	37.7
E	79.2	46.3	67.7	58.5	85.5
F	65.3	39.6	34.6	60.6	53.0
G	41.8	19.4	20.2	46.4	48.3
H	77.5	15.6	54.0	20.1	69.7
Mean	62.0	31.6[a]	41.2[b]	50.7	60.8
S.D.	±19.5	±15.3	±19.8	±17.1	±21.6
S.E.	±6.9	±5.4	±7.5	±6.1	±8.1
Ambulatory group					
I	53.3	50.4	90.5	94.6	169.8
J	59.0	58.1	25.4	98.5	43.1
K	48.0	30.7	45.4	64.0	94.6
L	60.0	29.8	44.2	49.7	73.7
Mean	55.1	42.3	51.4	76.7	95.3
S.D.	±5.6	±14.2	±27.6	±23.7	±54.0
S.E.	±2.8	±7.1	±13.8	±11.9	±27.0

[a] $p < 0.001$, bed rest vs control.
[b] $p < 0.005$, recovery vs control.

TABLE 22.- URINE MAGNESIUM EXCRETION

Subject	Urine magnesium excretion, mmol/24 hr				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	2.58	2.08	0.85	80.6	32.9
B	2.66	2.38		89.5	
C	2.78	5.62	1.90	202.2	68.3
D	4.20	7.03	2.41	167.4	57.4
E	4.04	4.39	5.25	108.7	130.0
F	2.83	5.48	2.19	193.6	77.4
G	2.27	1.72	2.09	75.8	92.1
H	4.35	1.93	3.94	44.4	90.6
Mean	3.21	3.83	2.66	120.3	78.4
S.D.	±0.84	±2.06	±1.46	±59.4	±30.6
S.E.	±0.30	±0.73	±0.55	±21.0	±11.6
Ambulatory group					
I	3.74	5.87	2.87	157.0	76.7
J	2.82	4.17	1.64	147.9	58.2
K	2.34	3.59	3.60	153.4	153.8
L	5.60	3.08	4.66	55.0	83.2
Mean	3.63	4.18	3.19	128.3	93.0
S.D.	±1.44	±1.21	±1.27	±49.0	±41.9
S.E.	±0.72	±0.61	±0.63	±24.5	±21.0

TABLE 23. URINE CALCIUM EXCRETION

Subject	Urine calcium excretion, mmol/24 hr				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	3.84	2.70	1.59	70.3	41.4
B	2.76	3.30		119.6	
C	5.20	6.15	2.08	118.3	40.0
D	5.77	5.94	4.15	102.9	71.9
E	5.31	5.36	6.66	100.9	125.4
F	4.51	5.40	3.64	119.7	80.7
G	2.35	1.37	2.44	58.3	103.8
H	5.59	2.08	5.32	37.2	95.2
Mean	4.42	4.04	3.70	90.9	79.8
S.D.	±1.31	±1.89	±1.84	±31.7	±31.7
S.E.	±0.46	±0.67	±0.69	±11.2	±12.0
Ambulatory group					
I	4.16	5.32	3.79	127.9	91.1
J	4.65	4.99	2.56	107.3	55.1
K	4.66	3.87	4.70	83.0	100.9
L	3.64	2.24	4.59	61.5	126.1
Mean	4.28	4.11	3.91	94.9	93.3
S.D.	±0.48	±1.39	±0.99	±28.9	±29.4
S.E.	±0.24	±0.69	±0.49	±14.4	±14.7

TABLE 24. URINE PHOSPHATE EXCRETION

Subject	Urine phosphate excretion, mmol/24 hr				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	17.0	13.6	8.8	80.0	51.8
B	16.8	15.1		89.9	
C	28.7	30.9	23.1	107.7	80.5
D	34.4	28.6	20.3	83.1	59.0
E	23.2	25.8	36.2	111.2	156.0
F	18.8	24.9	18.6	132.4	98.9
G	17.8	11.4	13.7	64.0	77.0
H	24.5	11.7	34.4	47.8	140.4
Mean	22.7	20.3	22.2	89.5	94.8
S.D.	±6.4	±8.1	±10.1	±27.2	±39.8
S.E.	±2.2	±2.9	±3.8	±9.6	±15.0
Ambulatory group					
I	23.3	32.2	24.0	138.2	103.0
J	26.8	29.5	11.5	110.1	42.9
K	19.0	21.0	29.0	110.5	152.6
L	21.8	10.7	32.2	49.1	147.7
Mean	22.7	23.4	24.2	102.0	111.6
S.D.	±3.2	±9.7	±9.1	±37.6	±50.9
S.E.	±1.6	±4.8	±4.5	±18.8	±25.5

TABLE 25. URINE UREA EXCRETION RATE

Subject	Urine urea excretion rate, mmol/24 hr				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	456	154	99	33.8	21.7
B	273	111		40.7	
C	535	399	257	74.6	48.0
D	624	300	269	48.1	43.1
E	677	372	473	54.9	69.9
F	331	292	299	88.2	90.3
G	260	131	177	50.4	68.1
H	426	123	334	28.9	78.4
Mean	445	235[a]	273[b]	52.5	59.9
S.D.	±156	±119	±118	±20.1	±23.5
S.E.	±55	±42	±45	±7.1	±8.9
Ambulatory group					
I	393	332	315	84.5	80.2
J	549	421	166	76.7	30.2
K	359	194	323	54.0	90.0
L	312	136	368	43.6	117.9
Mean	403	271[a]	293	64.7	79.6
S.D.	±103	±130	±88	±19.1	±36.6
S.E.	±51	±65	±44	±9.6	±18.3

[a] $p < 0.005$, bed rest vs control.
[b] $p < 0.01$, recovery vs control.

Urea excretion decreased noticeably by the last day of bed rest in both groups and persisted during recovery (table 25). Glucose excretion was similar to the pattern for urea in both groups following bed rest and confinement, but returned to control values by the sixth day of recovery (table 26). Citrate excretion rates were significantly elevated in the bed-rested group at the end of bed rest and remained so during recovery (table 27). The same pattern occurred in the control subjects, but the degree of elevation was not significant.

TABLE 26.– URINE GLUCOSE EXCRETION RATE

Subject	Urine glucose excretion rate, mmol/24 hr				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	0.401	0.084	0.139	20.9	34.7
B	.526	.149		28.3	
C	.518	.451		87.1	
D	.691	.329	.502	47.6	72.6
E	.588	.449	1.162	76.4	197.6
F	.922	.473	.936	51.3	101.5
G	.302	.197	.233	65.2	77.2
H	.386	.108	.437	28.0	113.2
Mean	0.542	0.280[a]	0.568	50.6	99.5
S.D.	±0.197	±0.165	±0.402	±24.2	±55.2
S.E.	±0.070	±0.058	±0.164	±8.6	±22.5
Ambulatory group					
I	0.480	0.386	0.386	80.4	80.4
J	.494	.317	.288	64.2	58.3
K	.406	.211	.355	52.0	87.4
L	.526	.185	.509	35.2	96.8
Mean	0.477	0.275[b]	0.385	58.0	80.7
S.D.	±0.051	±0.094	±0.093	±19.1	±16.4
S.E.	±0.025	±0.047	±0.046	±9.6	±8.2

[a] $p < 0.001$, bed rest vs control.
[b] $p < 0.05$, bed rest vs control.

TABLE 27.– URINE CITRATE EXCRETION RATE

Subject	Urine citrate excretion rate, mmol/24 hr				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	1.07	0.98	0.77	91.6	72.0
B	2.43	1.42		58.4	
C	2.10	3.48	3.46	165.7	164.8
D	2.18	2.54	3.26	116.5	149.5
E	4.25	5.46	7.70	128.5	181.2
F	3.50	5.75	2.90	164.3	82.9
G	1.92	2.15	2.95	112.0	153.6
H	2.86	1.75	3.84	61.2	134.3
Mean	2.54	2.94	3.55	112.3	134.0
S.D.	±0.99	±1.81	±2.08	±41.0	±41.3
S.E.	±0.35	±0.64	±0.79	±14.5	±15.6
Ambulatory group					
I	2.61	3.53	6.39	135.2	244.8
J	3.12	3.32	2.71	106.4	86.9
K	2.39	4.10	3.67	171.5	153.6
L	4.63	3.66	4.60	79.0	99.4
Mean	3.19	3.65	4.34	123.0	146.2
S.D.	±1.01	±0.33	±1.57	±39.6	±71.8
S.E.	±0.50	±0.16	±0.78	±19.8	±35.9

Excretion of norepinephrine decreased during bed rest by 28.9% in the bed-rested subjects, but did not change in the ambulatory controls (table 28). On the final day of recovery, however, both groups showed large and significant increases in this constituent over control values of 135.3% in the bed-rested subjects and 91.3% in the controls.

TABLE 28.– URINE NOREPINEPHRINE EXCRETION RATE

Subject	Urine norepinephrine excretion rate, mmol/l				
	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
Bed-rest group					
A	203	110	261	54.2	128.6
B	103	54		52.4	
C	134	106	421	79.1	314.2
D	134	104	189	77.6	141.0
E	226	88	387	38.9	171.2
F	126	68	229	54.0	181.7
G	133	36	121	27.1	91.0
H	167	50	287	29.9	171.9
Mean	153	77[a]	271[b]	51.7	171.4
S.D.	±42	±29	±106	±19.6	±70.4
S.E.	±15	±10	±40	±6.9	±26.6
Ambulatory group					
I	116	146	267	125.9	230.2
J	90	121	106	134.4	117.8
K	142	68	243	47.9	171.1
L	112	62	180	55.4	160.7
Mean	115	99	199	90.9	170.0
S.D.	±21	±41	±72	±45.6	±46.3
S.E.	±11	±20	±36	±22.8	±23.2

[a] $p < 0.001$, bed rest vs control.
[b] $p < 0.05$, recovery vs control.

Plasma Renin and Arginine Vasopressin Activity

Average values of plasma renin activity throughout the control period measured 0.75 ±0.09 ng Ang I/ml/hr. Immediately following centrifugation, mean plasma renin activity rose to 1.11 ±0.28 ng Ang I/ml/hr (NS). During the first 8 days of bed rest, plasma renin activity began to rise above the ambulatory control values. By Day 10 of bed rest, plasma renin activity was 1.49 ±0.16 ng Ang I/ml/hr ($P < 0.05$) compared with 0.72 ±0.09 on Day 2 of the control period. This elevation in plasma renin activity was maintained throughout the remainder of the bed-rest period. Exposure to +3.0 G_Z centrifugation following bed rest also provoked a 17% rise in plasma renin activity, but this level was not significant when compared with pre-acceleration values obtained a few hours prior to centrifugation. During the ambulatory recovery period, mean plasma renin activity began to decline but did not return to control levels by the fifth day of recovery.

On Days 5 and 13 of the control period, the mean pre-acceleration levels of arginine vasopressin were 2.1 ±0.05 and 2.4 ±0.5 pg/ml, respectively. Exposure to +G_Z acceleration resulted in a significant rise ($P < 0.05$) in plasma arginine vasopressin above the pre-centrifugation level. During bed rest, the mean plasma

arginine vasopressin levels were 33% lower (NS) than the values obtained during the control period when the subjects were ambulatory. The plasma concentration of arginine vasopressin remained relatively constant throughout the bed-rest period with levels ranging from 1.2 ±0.5 to 1.7 ±0.5 pg/ml. Exposure to $+G_Z$ acceleration after 14 days of bed rest again induced a significant rise ($P < 0.02$) in the mean plasma arginine vasopressin levels from 1.7 ±0.5 to 15.1 ±4.0 pg/ml. This rise, however, was not as great as that observed before bed rest.

The rise in arginine vasopressin following centrifugation was variable. At the end of the control period, a correlation coefficient (r) of +0.639 ($P < 0.05$) was calculated for the relationship between post $+G_Z$ vasopressin levels and acceleration tolerance. After bed rest, the correlation between post-centrifugation values and tolerance was significant ($r = 0.666$; $P < 0.05$). Thus, a decrease in $+G_Z$ tolerance appears to be associated with a significant increase in plasma arginine vasopressin during centrifugation.

Biorhythms

The results of the biorhythm experiments are shown in table 29. The circadian wave forms of heart rate were similar in all subjects during the control period. The mean daily heart rate for the ambulatory control subjects was lower (74 bpm) than that of the bed-rested subjects (82 bpm) throughout the study, and the variability of the ambulatory controls was generally greater at all times of day. The differences between the heart rate means of the control and bed-rested subjects correlated well with the difference in their tolerances to $+G_Z$ acceleration, which was the basis for their selection. The integrated amplitudes of the heart rate rhythms of individual subjects varied considerably before bed rest.

During bed rest, the heart rate rhythms of the bed-rested subjects became more sinusoidal in shape than they had been during the control period, and the integrated amplitude decreased significantly. In general, the subjects exhibited a smaller decrease in mean heart rate during bed rest than had previously been observed in similarly bed-rested male subjects (ref. 41). The control subjects also exhibited similar, but lesser, decreases in mean heart rate, integrated amplitude, and rhythmic variability as compared with the responses of the bed-rested subjects. These changes were not statistically significant, however, and probably occurred because of the pronounced individual differences in mean heart rate and integrated amplitude that these subjects exhibited. Moreover, these changes may have represented a psychological response on the part of the subjects to their prolonged confinement during the study. There was also

TABLE 29. CIRCADIAN RESPONSES OF FEMALE SUBJECTS

Test condition		Daily mean		Integrated amplitude		Phase angle		Period length		Number of subjects
		Pre-bed rest	Bed rest	Pre-bed rest	Bed rest	Pre-bed rest	Bed rest	Pre-bed rest	Bed rest	
HR	Control	74.1 ±4.7[a]	70.6 ±2.8	223.0 ±26.4	216.9 ±15.5	165.4	159.7	24.05 ±.13	24.08 ±.02	4
	Bed rest	81.6 ±1.6	75.5[b] +1.7	235.5 ±17.1	155.6[b,c] ±11.5	158.1	161.6	24.07 ±.08	24.07 ±.06	7
RT	Control		37.41 +.21		7.3 ±.1		172.2		24.15 ±.06	4
	Bed rest	37.26 ±.11	37.20 +.18	7.2 +.4	6.3[c] ±.4	159.3	179.3[d]	23.94 ±.10	24.04 ±.05	5

[a] Standard error.

[b] Difference between bed rest and pre-bed-rest values is statistically significant ($P \leq 0.05$).

[c] Difference between bed rest and control subjects is statistically significant ($p \leq 0.05$).

[d] Difference between bed rest and pre-bed-rest phase angles is statistically significant ($P \leq 0.05$) as determined by the Cosinor method.

HR = heart rate

RT = rectal temperature

a significant shift in the time of the peak rectal temperature for the subjects in this study (see table 29).

Peak urine excretion (fig. 35) occurred in the subjects between 1200 and 2000 hr as compared with 0800 and 1200 hr in comparable male subjects; excretion was significantly less than excretion of comparable males during the early morning hours (0800 1200 hr, $P < 0.05$). The mean daily urine volume of the female subjects was 2258 ml/24 hr. The rhythm in the excretion of sodium (fig. 36) followed a pattern similar to that of urine volume; peak excretion of sodium occurred between 2000 and 2400 hr. The excretion rate of 143.9 meq Na/24 hr in these female subjects exceeded that in an equivalent group of males (106.3 meq Na/24 hr).

The female subjects also showed a greater excretion of potassium than males as a result of a more sustained

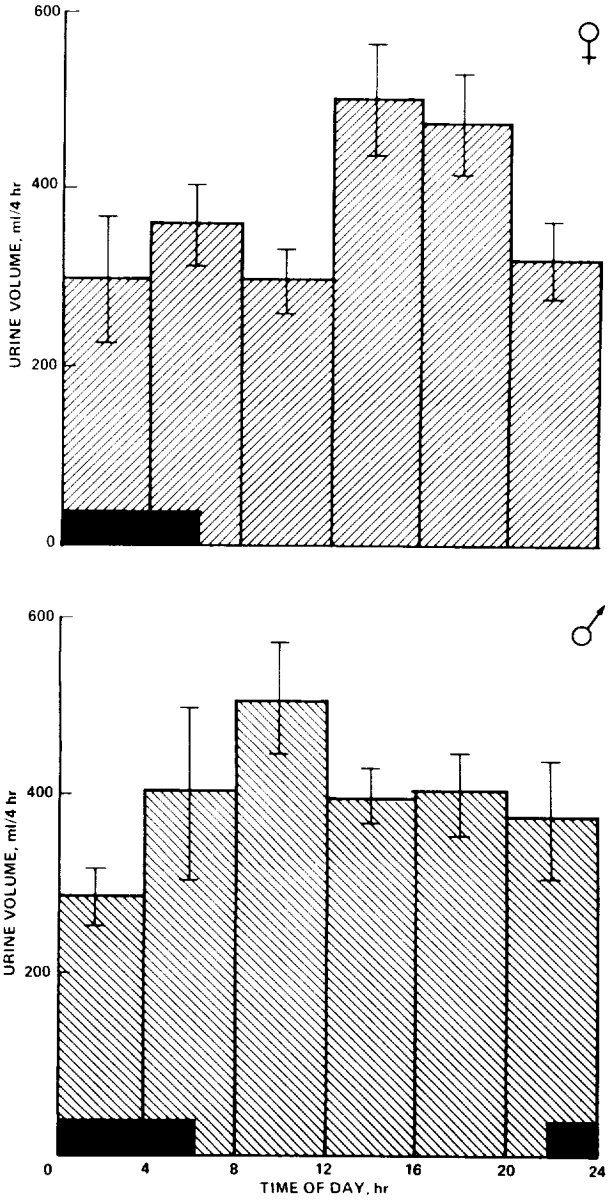


Figure 35. *Diurnal rhythm in urine volume. Mean of four consecutive days.*

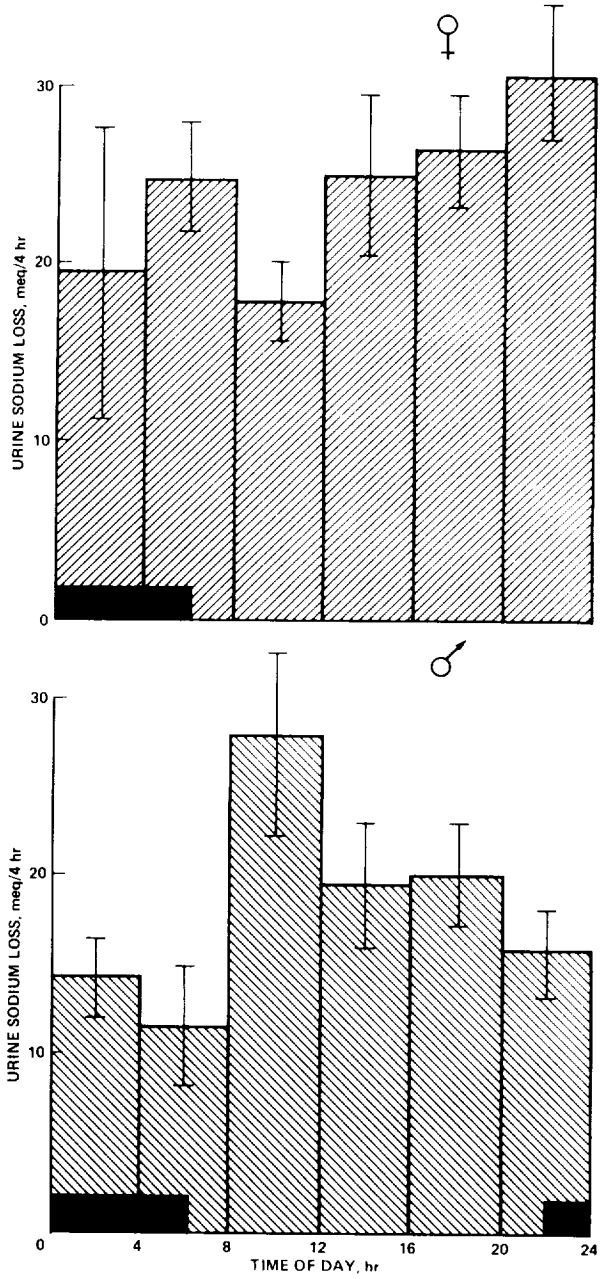


Figure 36. *Diurnal rhythm of sodium excretion.*

increased excretion during the light hours (fig. 37). Peak urinary excretion of potassium occurred between 0400 and 2400 hr. The mean daily excretion was 67.69 meq K/24 hr, as compared with 43.11 meq K/24 hr in male subjects. Maximum Na/K ratios (fig. 38) occurred during the dark hours in both sexes, but the minimal excretion occurred 4 hr earlier in the female subjects.

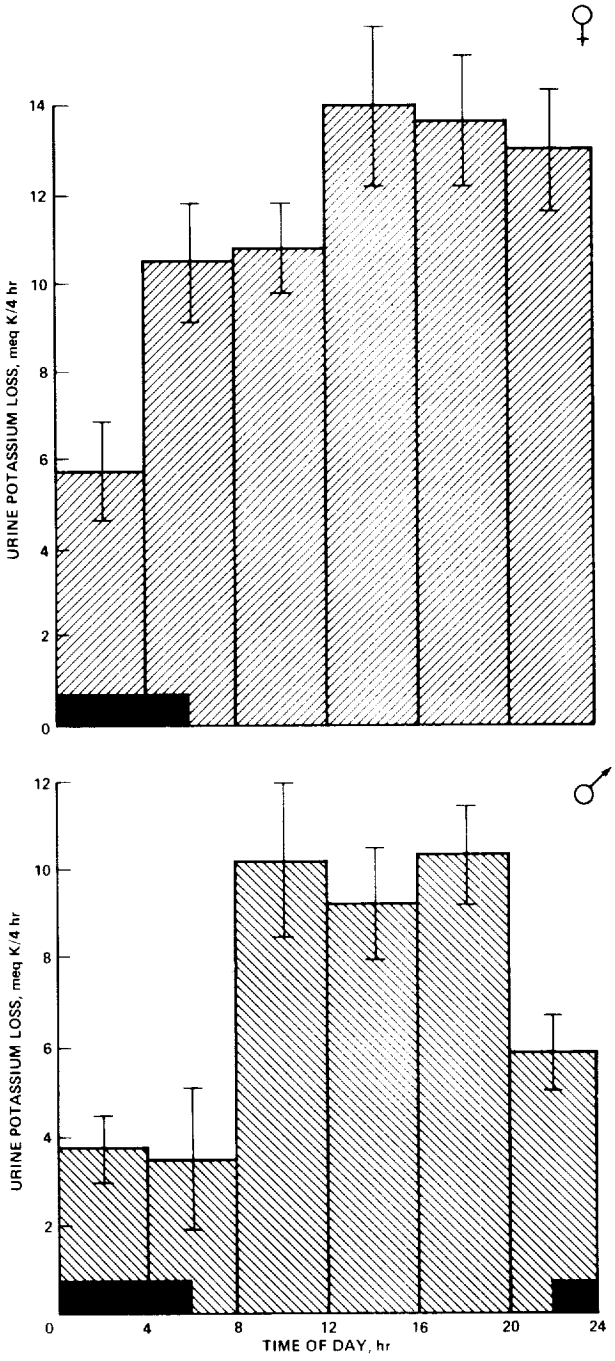


Figure 37. - *Diurnal rhythm of potassium excretion.*

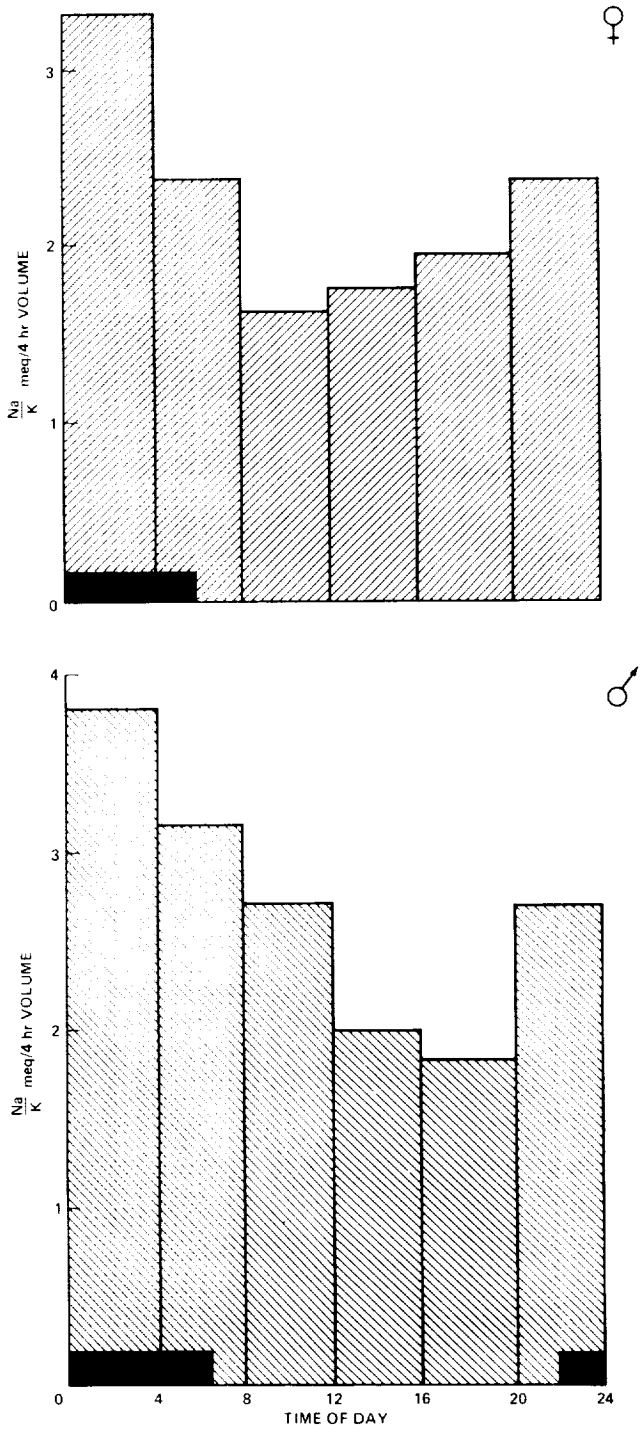


Figure 38. *Maximum sodium/potassium ratios.*

The subjects in this study excreted 4.00 mg of 5-Hydroxy indol acetic acid every 24 hr, with the peak excretion occurring between 0400 and 0800 (fig. 39). This finding differed from the response of male subjects who excreted a greater amount (6.27 mg/24 hr) and exhibited the maximum excretion during the dark hours.

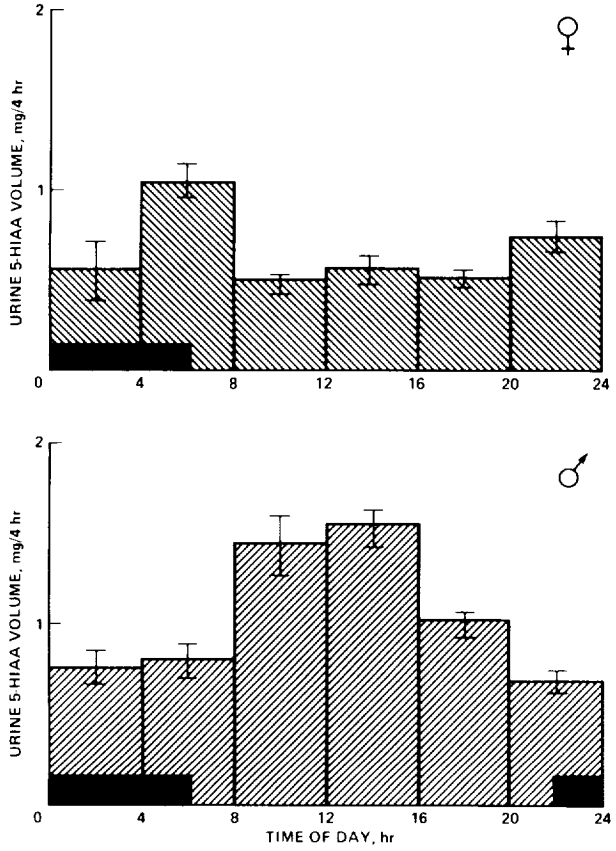


Figure 39. *Diurnal rhythm of 5-HIAA excretion.*

Peak urine cortisol excretion occurred between 0800 hr and 1600 hr and was similar to that found in males (fig. 40). Peak plasma cortisol levels (fig. 41) occurred at 0800 hr in the subjects and declined as the day progressed, reaching the lowest level at 2400 hr; they declined less rapidly in the female subjects than in the males and the minima in the males was also significantly ($P < 0.05$) less.

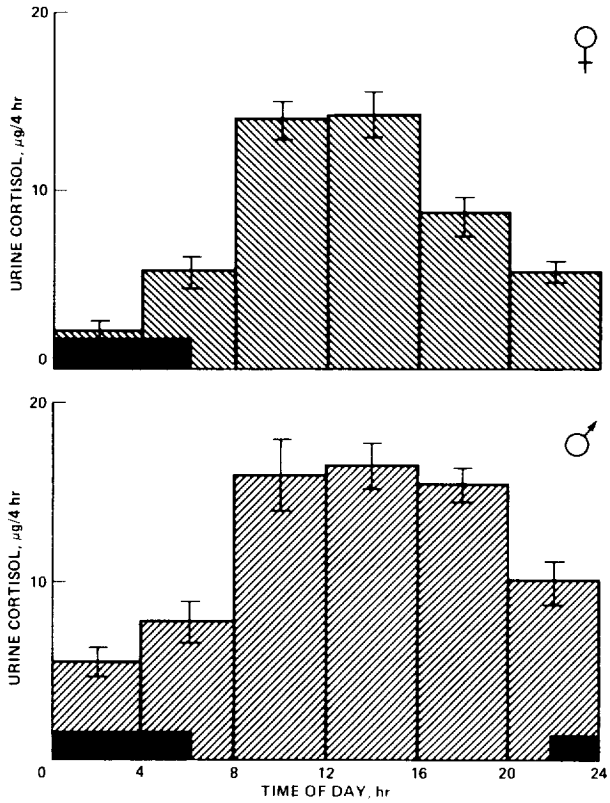


Figure 40. *Diurnal rhythm of urine cortisol excretion.*

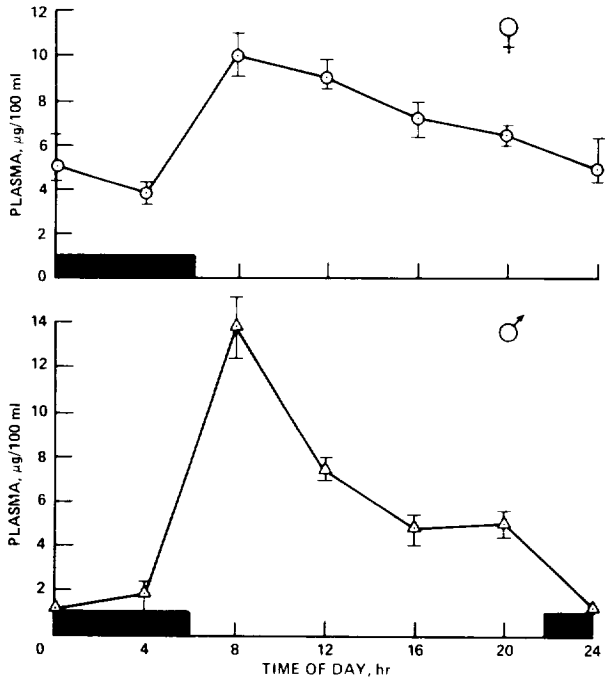


Figure 41. *Diurnal rhythm of plasma cortisol.*

Female Adrenal Hormonal and Metabolic Responses

A marked increase in plasma ACTH occurred in all subjects following centrifugation (fig. 42). Although no difference existed in the plasma cortisol response to centrifugation between those subjects with a high versus a low acceleration tolerance, increases in plasma ACTH were significantly greater in the higher tolerance group that was subsequently bed rested. These changes are shown in figure 43 where +3.0 G_Z tolerance is compared for the ambulatory controls (low acceleration tolerance) and the test subjects during the pre-bed-rest period. Good correlation was found between the diurnal amplitude in plasma cortisol and tolerance to $+G_Z$ acceleration (fig. 44). Subjects with low tolerance are again shown in cross-hatched bars. The amplitude in plasma cortisol decreased during bed rest as did the tolerance of the subjects to centrifugation (fig. 45). However, the apparent decrease in adrenocorticol secretion was not reflected in the urinary excretion of cortisol (fig. 46). Twenty-four-hr urine cortisol levels were somewhat elevated as has been reported previously for male bed-rest subjects (refs. 42 and 43). The decreased circulating cortisol levels did not necessarily imply a reduction to stress since plasma ACTH responses to centrifugation were significantly greater after bed rest, and plasma cortisol changes were comparable to those observed during bed rest. The ambulatory control subjects exhibited a similar response to $+G_Z$ exposure but of lesser magnitude as a function of the time of confinement.

Responses of glucose and insulin to bed rest and recovery for the eight bed-rested subjects are shown in figure 47. Serum glucose and insulin levels were normal at rest and with loading (glucose tolerance test) during the ambulatory period prior to bed rest. After 1 week of bed rest, mean resting plasma glucose (0 hr) had dropped significantly ($P < 0.05$) to 81 mgm% from 93 mgm%. Peak glucose response increased to 146 mgm% from 143 mgm%, which was not significant. Plasma insulin response at 1 hr after loading increased significantly ($P < 0.01$) from 48 μU/ml to 82 μU/ml. By the close of 2 weeks of bed rest, there were no significant changes in these findings except that peak insulin response occurred 2 hr after loading compared with changes at 1 hr being similar to the ambulatory state. The elevated serum insulin response to loading had disappeared by 2 days after recovery.

In order to better estimate the total effect, the areas under the responses shown in figure 47 were compared and plotted in figure 48. These data demonstrated that

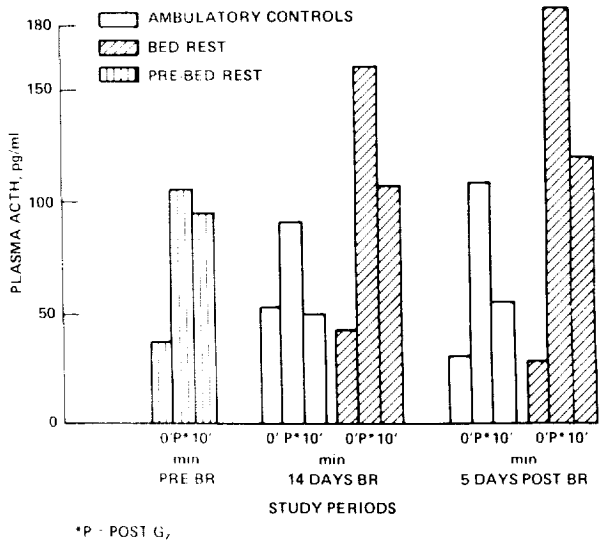


Figure 42. *Plasma ACTH response to G_Z centrifugation stress before and after bed rest.*

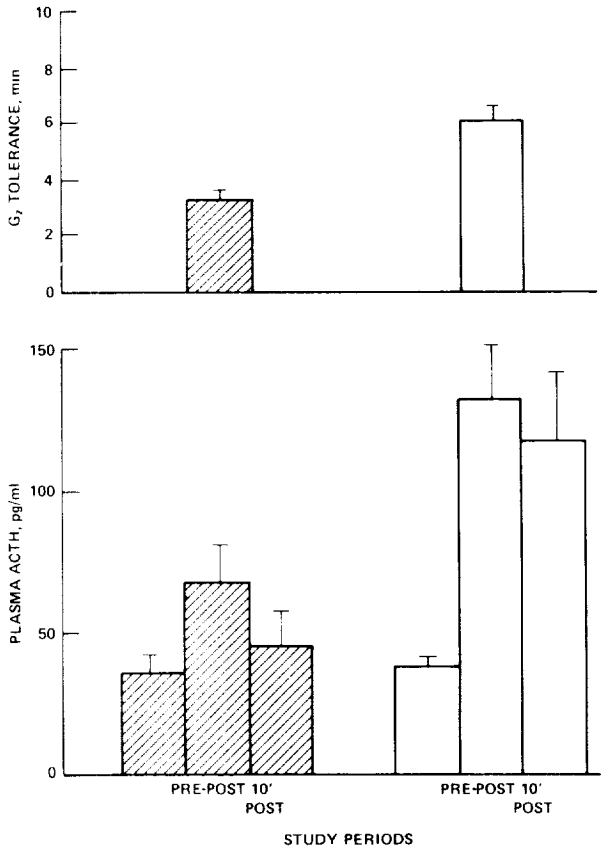


Figure 43. *Comparison of $+G_Z$ tolerance and changes in plasma ACTH levels during pre-bed-rest period.*

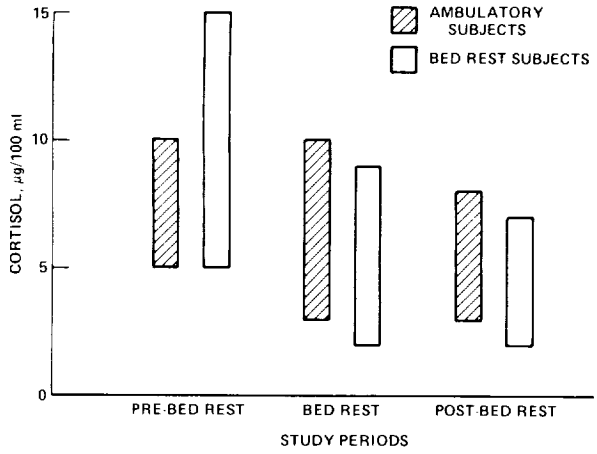


Figure 44. *Effect of bed rest or confinement on plasma cortisol amplitude in female subjects.*

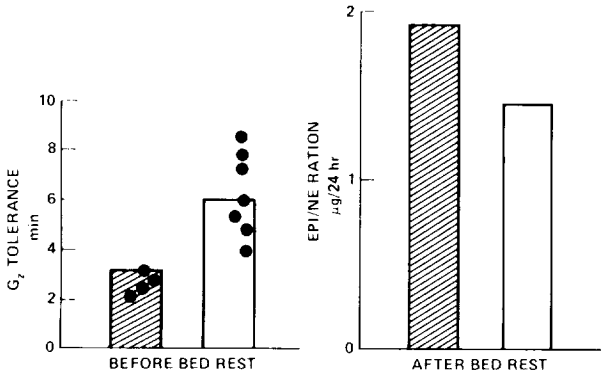


Figure 45. *Comparison of $+G_z$ tolerance and diurnal amplitude of plasma cortisol during pre-bed rest period.*

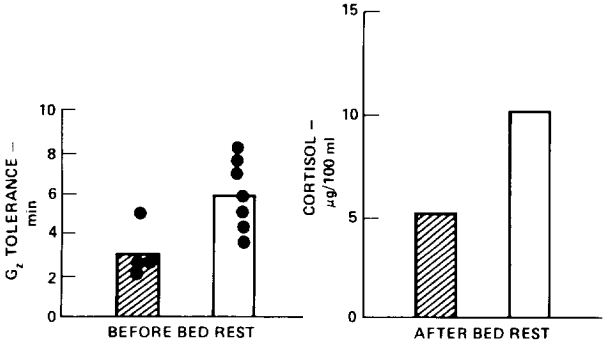


Figure 46. *Urinary excretion cortisol expressed as Epi/NE ratio compared to $+G_z$ tolerance.*

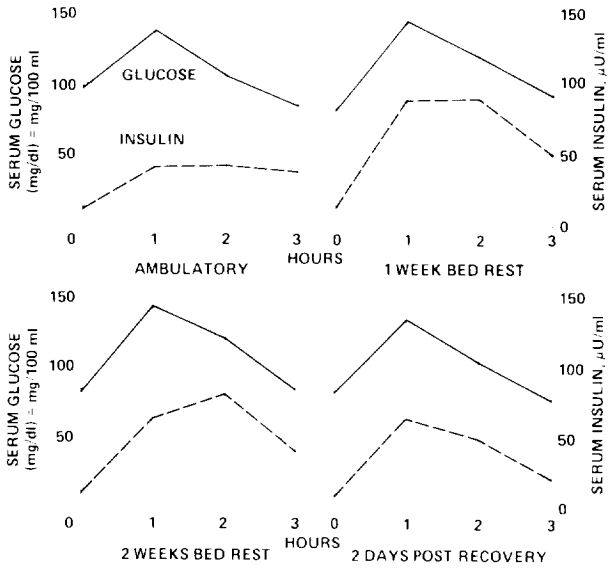


Figure 47. *Glucose and insulin responses of female bed-rest subjects.*

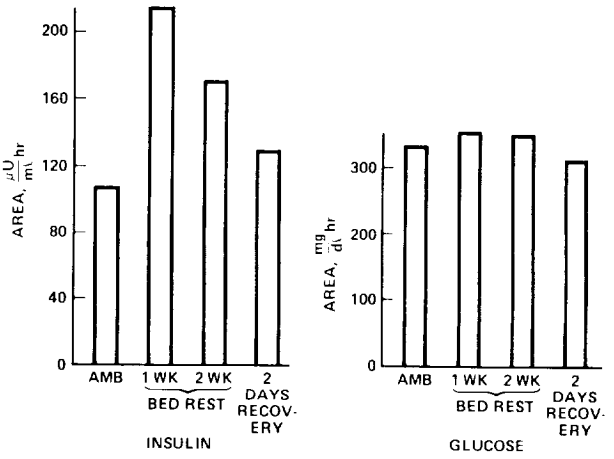


Figure 48. *Female insulin and glucose areas in oral glucose tolerance.*

mean insulin response increased markedly (98%) by 1 week of bed rest and persisted (58% increase) after 2 weeks of bed rest. After 2 days of recovery the overall insulin response was not significantly different from the ambulatory state. Replotting glucose response further demonstrated that it did not follow this pattern and showed little difference from ambulatory state values.

Gynecology

Table 30 summarizes changes in fluid balance (determined as the difference between daily oral intake and urine output) and body weight over the course of the study. (Daily values for these changes are given in tables 41(a) and 41(b) of appendix B). Time of menstrual cycle occurrence is indicated in the tables in appendix B. Average values for menstrual periods ±SD are given in table 30 and compared to nonmenstrual period values. Identical values comparing body weight changes with and without menstruation are also indicated in this table. Hematocrit changes in relation to various phases of the study are also included for comparison.

Duration of menstrual periods averaged 5.1 ±1.1 days (N = 11; range: 4 to 7 days). Flow was within normal limits; no one flowed excessively. Subject D spotted for 5 days prior to onset and was the only subject to do so. One of the ambulatory subjects (Subject L) was amenorrheic over the study period. As shown in figure 1, six of the subjects had their menstrual periods during the 14 days of control; periods for Subjects C and G ended just before bed rest began; for the other four subjects, periods occurred over Days 2 to 9 of the control period. Subject J of the ambulatory group had her period from Day 10 of the control period to the second day of bed rest. Subjects D and H had their periods between Days 2 and 8 of bed rest. Subjects A and E had two periods of significance during the study, one during control and the other during the recovery period (Subject A) or just prior to termination of bed rest (Subject E). Subjects F, G, and K also had two menstrual periods, but the second in both cases occurred during the terminal days of the recovery period just prior to release from the study. Of the ambulatory group, Subjects I and J had periods late and mid-term in the control period, Subject K over Days 7 to 11 of the bed-rest period, and Subject L not at all.

Subject A, the only individual to show a significant fluid balance change during menstruation ($P < 0.02$) and retained fluid during her periods. However, she also was one of the two subjects who lost significant weight. Data in table 30 for this subject represent the average for two menstrual cycles and indicate no average weight change compared to average of nonmenstrual days. When each respective menstrual period was compared with the latter average weight value, significant changes were noted: weight during the first menstrual period was 60.78 ±0.48 kg and during the second was 56.13 ±0.69 kg. In each case the changes were greater than 2 kg compared with the average weight of 58.14 ±2.09 kg during nonmenstrual periods. Subject E was also observed over two cycles. During the first cycle, body weight averaged 54.78 ±2.94 kg; during the second cycle which occurred on the terminal days of bed rest, values were significantly different ($P < 0.01$) and averaged 59.8 ±2.12 kg. Findings suggested that this subject lost weight with menstruation when she was able to ambulate but changed her response to maintaining weight with menstruation when at bed rest. Subjects F and G had findings that showed significant weight gain during menstruation, but their data are again difficult to interpret. Subject F lost significant weight over the course of the study and her period occurred early. Subject G had her period just prior to bed rest and had a slight but significant weight loss during bed rest, which may have influenced the results.

Hematocrit did not seem unduly influenced by menstruation or bed rest when values during the control were compared with those obtained on the last day of bed rest as shown in table 30. Such values did not change in two subjects, did not increase or decrease 1% in four subjects, and did increase 2% in one subject and 3% in another. At the same time, hematocrit differences in the ambulatory controls showed no change for two subjects, a decrease of 1% in one subject, and 3% in the last subject. Everyone had at least one complete menstrual cycle during these periods as indicated in figure 1, except Subject B who started her period on the last day of bed rest. During recovery all subjects, except B and G, demonstrated hematocrit drops of 2 to 6% compared to values obtained during the control period. The absence of a menstrual cycle did not stop a slight fall in Hct during recovery in Subject L and a significant fall in Subject G. No singular findings occurred for Subjects H and B, who had their periods during bed rest, or for Subject E when her bed-rest data were compared with average nonmenstrual study values.

DISCUSSION

Centrifugation Tolerance

Following bed rest, there was a 49% reduction in +3 G_z tolerance sec (range: −19.7% to −71.1%) in the bed-rested group and a 38.7% decrease (range: −22.8% to −63.2%) in the control group. These mean percentage losses in the female subjects were about 50% greater than comparable tolerance data for young men after

TABLE 30. SUMMARY OF AVERAGE FLUID AND WEIGHT LOSS DURING MENSTRUAL PERIODS

Subject	Oral hormone status	Menses	Daily fluid balance difference, intake vs output, ml			Body weight, kg			Hematocrit, %		
			Sample size (days)	Average	±SD	Sample size (days)	Average	±SD	Control	Bed rest	Recovery
Bed-rest group											
A	Never	Yes	8	646.9	484.4	8	58.70	2.46	38	40	34
		No	24	186.5	435.2	28	58.14	2.09	38	40	34
		Diff.		460.4[a]			-0.56				
B	None for 6 months	Yes	7	279.6	478.7	6	53.57	.35			
		No	25	54.1	266.1	30	54.44	1.23	40	40	40
		Diff.		225.5			-0.87				
C	Never	Yes	5	140.6	251.0	5	62.70	.21			
		No	30	424.4	376.9	31	62.65	.62	40	39	36
		Diff.		-283.8			.05				
D	Never	Yes	7	-196.1	554.2	7	55.45	.98			
		No	28	-266.0	728.5	29	55.86	1.20	37	38	34
		Diff.		-69.9			-0.41				
E	None for 90 days	Yes	8	324.6	628.1	9	57.04	3.39			
		No	27	105.9	674.8	27	59.87	1.88	39	39	35
		Diff.		218.7			-2.83[b]				
F	None for 60 days	Yes	4	-532.0	427.9	5	50.45	.28			
		No	29	-63.9	704.1	31	48.22	1.81	40	39	35
		Diff.		-595.9			2.23[b]				
G	None for 1 year	Yes	5	-122.0	338.8	6	53.55	.31			
		No	29	76.9	345.2	30	52.78	.50	34	37	35
		Diff.		-198.9			.77[b]				
H	Never	Yes	4	628.0	276.1	4	65.96	1.04			
		No	28	203.4	479.6	32	65.82	.69	38	39	34
		Diff.		415.6			.14				
Ambulatory group											
I	Never	Yes	6	573.7	323.4	7	47.74	0.58			
		No	28	555.4	330.8	29	48.27	.64	35	35	33
		Diff.		18.3			-0.53	.27			
J	None for 90 days	Yes	5	70.6	427.7	6	60.93	.63			
		No	28	82.1	376.0	30	60.17	.51	39	36	33
		Diff.		-11.5			.76[b]	.24			
K	Never	Yes	4	167.5	220.4	4	64.70	.23			
		No	31	-11.3	499.7	32	64.29	.69	38	38	36
		Diff.		178.8			.69	.35			
L	Never	Yes									
		No	31	-181.0	670.9	36	50.54	.65	33	32	30
		Diff.									

[a] $p < 0.05$. [b] $p < 0.01$.

Note: Yes indicates menstruation occurred for duration indicated by sample size. No indicates period of no menses. Diff. represents difference of average values for menstrual days minus that for nonmenstrual days. Subject L was amenorrheic for the duration of these studies.

14 days bed rest, but the ranges of loss in tolerance were similar (ref. 44). The 38.7% loss in tolerance in the female controls was only slightly greater than that of the bed-rested men (−29% to −33%) (ref. 44). The reason for such changes in the ambulatory controls remains unexplained. Although the subjects were free to move about in the research facility, they were relatively confined to its limits because of the need to record ECG and body temperature data by telemetry. Lamb, in previous studies, demonstrated marked alterations of cardiovascular response in males as a result of loss of physical activity without resorting to bed rest: in one instance through confinement in a flight simulator (ref. 45), in the other, by the use of chair rest over an 8-hr period (ref. 46). The present results suggest that confinement and physical inactivity have an effect on acceleration tolerance that nearly equals that associated with the reduction of hydrostatic pressure resulting from bed rest.

TABLE 31. VENOUS HEMATOCRIT VALUES FOR THE FEMALE SUBJECTS

Subject	Venous hematocrit values, %				
	Control (Day 0)	Bed rest (Day 16)	Recovery (Day 4)	%Δ of control	
				Bed rest	Recovery
Bed-rest group					
A	38.0	39.8	34.2	104.7	90.0
B	39.8	39.8	34.7	100	87.2
C	40.2	38.6	35.6		88.6
D	37.2	37.5	33.8	100.8	90.9
E	39.1	39.2	34.5	100.3	88.7
F	39.6	38.6	34.8	97.5	87.9
G	36.3	36.8	30.6	107.0	89.0
H	37.3	39.2	33.6	105.1	90.1
Mean	38.2	38.6	34.0	101.4	89.1[a]
S.D.	±1.0	±1.1	±1.8	±3.9	±1.2
S.E.	±0.7	±0.4	±0.5	±1.4	±0.4
Ambulatory group					
I	34.6	34.5	32.8	99.7	94.8
J	38.9	36.4	33.4	93.6	85.6
K	38.1	38.4	36.2	100.8	95.0
L	38.7	32.1	30.4	96.7	91.6
Mean	36.6	35.4	33.2	97.7	91.8[b]
S.D.	±2.0	±2.7	±2.4	±3.2	±4.4
S.E.	±1.3	±1.3	±1.2	±1.6	±2.2

[a] $p < 0.001$.
[b] $p < 0.05$.

TABLE 32. BLOOD HEMOGLOBIN CONCENTRATION

Subject	Blood hemoglobin concentration, g/100 ml				
	Control (Day 0)	Bed rest (Day 17)	Recovery (Day 6)	%Δ of control	
				Bed rest	Recovery
Bed-rest group					
A	13.9	14.5	12.1	104.3	87.1
B	13.4	13.9	12.3	96.5	85.4
C	13.3	13.9	13.1	90.8	85.6
D	14.4	13.8	12.5	95.8	86.8
E	13.8	14.1	13.3	102.2	96.4
F	14.8	14.3	13.1	96.6	88.5
G	13.8	12.3	11.8	89.1	85.5
H	13.7	13.8	12.6	100.7	92.0
Mean	13.8	13.8	12.6[a]	97.0	88.4
S.D.	±0.6	±0.7	±0.5	±5.3	±3.9
S.E.	±0.2	±0.2	±0.2	±1.9	±1.4
Ambulatory group					
I	14.0	12.2	11.2	87.1	80.0
J	14.1	12.6	13.0	89.4	92.2
K	13.1	13.0	12.9	90.1	85.4
L	12.3	12.6	11.8	101.6	95.2
Mean	13.4	12.8	12.2[b]	92.1	88.2
S.D.	±1.1	±0.6	±0.9	±6.5	±6.8
S.E.	±0.6	±0.3	±0.4	±3.2	±3.4

[a] $p < 0.001$.
[b] $p < 0.05$.

Fluid Electrolytes and Hematology

The bed-rested group exhibited a highly significant fall of 12.6% in their mean plasma volume whereas the ambulatory controls showed no significant change. The change in the bed-rested group was reversed by Day 6 of the recovery period. Total body water content was lower in both groups by the end of the bed-rest period on the average, but the change was not statistically significant. Extracellular fluid volume (measured as bromide space) showed similar findings. Water compartment data suggested a net loss of almost 1 liter of body water with recumbency. There was a slight loss of body potassium (3.3%) in the bed-rested group and a small but significant elevation of plasma sodium, magnesium, and chloride concentration in the blood. Total plasma protein did not change, but analyses of electrophoretic patterns showed some decrease in plasma albumin and elevation of plasma globulin and fibrinolytic concentration. A statistically significant increase in plasma alkaline phosphatase, which occurred in controls and in bed-rested subjects, remains unexplained.

Individual values for venous hematocrit (Hct) and hemoglobin (Hgb) at rest, before, after bed rest, and recovery are given in tables 31 and 32. The study day on which the blood samples were taken are given in the tables. Summary values for Hct, Hgb, and red blood cell count (RBC) and calculated values for RBC size and hemoglobin content at rest compared with those of a similar group of male subjects are given in table 33. Changes as a consequence of centrifugation are also given in table 2. Changes in white blood cell count (WBC) at rest are summarized and compared to fluid and electrolyte changes in table 5. Also given in tables 4, and 5 are Hct red cell values taken from blood samples obtained immediately before and after exposure to $+G_z$ acceleration. Hematocrit values given in table 30 were

TABLE 33. MEAN (±SE) HEMATOLOGICAL PARAMETERS IN THE WOMEN AND MEN BEFORE (PRE) AND AFTER (POST) BED REST

Parameters		Women			Men		
		Pre	Post	Δ	Pre	Post	Δ
Hematocrit	Mean	42.5[a]	43.1	+1.6	47.0		
	SE	2	1		1		
Hematocrit	Mean	40.4[a]	37.1[a]	+11.1	42.9	42	-1
(vol)	SE	2	4		0	1.0	
Red blood cells	Mean	4.92[a]	4.64[a]	+2.8	4.88	4.71	-3.5[b]
(millions/mm³)	SE	0.1	0.1		0.1	0.1	
Mean corpuscular	Mean	85	92	+7.1	88	90	+2.3
volume (μ³)	SE	2	2		2	2	
Mean corpuscular	Mean	31.4[a]	31.5	+0.3	34.0		
hemoglobin (pg)	SE	1	1		0		
Mean corpuscular							
hemoglobin con-	Mean	34.0[a]	34.3	+0.6	39.6		
centration (%)	SE	2	1		0		

[a] Statistically different (p < 0.05) than corresponding male value
[b] Significant at p < 0.05

obtained from the medical screening records prior to entry into the study, on the last day of bed rest, and prior to discharge from the research facility. In all cases a significant change in Hct did not occur during bed rest. In comparison with similarly treated aged males, female subjects showed significantly lower Hct and RBC values, both before and after bed rest. These findings undoubtedly can be attributed to the presence of menstruation. Careful study in subsequent groups of subjects is needed.

The values for most blood constituents at rest did not change significantly after bed rest despite the 10% to 12% loss of plasma volume. However, there were significant increases in plasma osmolarity and serum chloride, as well as slight, insignificant increases in Hct; these increases were undoubtedly associated with such plasma volume changes. The ambulatory controls demonstrated similar changes to those of the bed-rested subjects, but to a much lesser degree. There were no significant changes in any of the parameters when the two groups were compared except for venous hematocrit which was significantly lower in the ambulatory control group from the outset.

During recovery and after centrifugation, significant changes were observed in several parameters. During recovery, Hct, Hgb, and RBC all decreased in the bed-rested subjects. These changes were not associated with significant changes in MCV, MCH, or MCHC (see tables 2 and 33) which suggested that they were most likely induced by a shift of interstitial fluid to the vascular space during this period. Bone marrow suppression associated with inactivity may have been a factor since similar changes have been seen in other studies (ref. 45) and after space flight (ref. 2). The ambulatory controls showed similar changes, but they were not significant, which also suggested that this group demonstrated deconditioning solely as a result of confinement. WBC counts increased significantly in both groups during recovery and may be indicative of altered fluid and hormonal state.

During acceleration, changes occurred in plasma volume, electrolytes, and blood constituents, as shown in figure 19 and table 2. The pattern of change was essentially the same in both bed-rested and ambulatory groups. Acceleration induced an 11.5% loss in plasma volume before bed rest and 4.1% after bed rest; changes for the ambulatory controls were 8.5% and 3.1%, respectively. These changes were accurately reflected by significant changes in Hct as shown in tables 2 and 31, and demonstrated by Greenleaf *et al.* (ref. 38) to reflect altered plasma volume state. With an average change in plasma volume during bed rest of −12.6%, the shift of plasma during centrifugation was almost one-third as great as during control or recovery runs. During recovery, with an induced increase in plasma volume, acceleration was associated with a significantly greater loss in plasma volume in both groups of subjects (fig. 19). During each of these cases, shifts in plasma Na, Cl, and PO_4, and osmotic contents accompanied these outward shifts in plasma volume during exposure to $+G_Z$. Plasma potassium content did not respond in a manner consistent with other cations. Changes in the ambulatory controls followed the pattern of percentage change in plasma volume. In the bed-rested group, the reverse occurred, indicating a reasonably large loss of potassium from the plasma (−8.6% to −12.2%) after bed rest and to −14.2% during centrifugation in the recovery period. The reason remains unexplained. Similar losses have been previously found in normal ambulatory men during centrifugation when they were hypohydrated compared with the control state (ref. 45).

Lower Body Negative Pressure

In the present study, exposure to LBNP produced a consistent response pattern that is appropriate for evaluating changes produced by weightlessness and bed rest. During LBNP prior to bed rest, the subjects exhibited increased heart rate, decreased systolic blood pressure, and decreased pulse pressure. Throughout LBNP, heart rate increased progressively. In general, blood pressure stabilized as the LBNP exposure progressed; continuing declines in blood pressure therefore indicated the onset of syncope. Heart rate, systolic blood pressure, and pulse pressure were the key indicators of deconditioning following bed rest.

Compared to pre-bed rest state, resting hemodynamic state shifted significantly as a consequence of bed rest. Heart rate increased by 6% ($P < 0.05$); stroke volume decreased by 23% ($P < 0.001$); cardiac output decreased by 17% ($P < 0.01$); and mean arterial pressure increased by 5.7% ($P < 0.005$). Similar changes were seen in the ambulatory controls, but the bed-rested subjects exhibited significantly higher heart rates ($P < 0.01$) and mean arterial pressure ($P < 0.02$) than did the ambulatory controls.

Exposure to LBNP resulted in significant decreases in end-diastolic volume that were associated with significant increases in heart rate. Peak heart rates attained after bed rest varied from 120 to 174 bpm (before bed rest, values were 73 to 126 bpm, $P < 0.001$) for the bed-rest subjects; values for the ambulatory controls were lower (90 to 141 bpm after bed rest compared to 59 to 120 bpm before, $p < 0.001$). Minimal or end-systolic left ventricular volumes associated with LBNP decreased significantly from 40 ml to 28 ml ($P < 0.001$) as a consequence of bed rest. The application of LBNP produced a shift of 710 to 760 ml of volume to the lower extremities (table 10). This response was associated with an average decrease in end-diastolic volume of 59 ml, which was the same before and after bed rest. The decreases in end-diastolic volume and cardiac output at rest following bed rest indicated a shift to a lower point on each subject's left ventricular function curve, which resulted most probably from a decrease in left ventricular preload and concomitant regular losses in total blood and plasma volume that are seen with this condition. Smaller end-diastolic volume was noted regularly during LBNP after bed rest, but this condition was also associated with an increased heart rate. Comparison of heart rate versus end-diastolic volume during the course of LBNP before and after bed rest showed a linear inverse relationship until approximately 100 bpm, after which the slope changed. Further increases in heart rate were related to gradually decreasing values of end-diastolic volume that reached a plateau at the post-bed rest values given in table 8. All subjects for whom data are included in these tables experienced near or actual vasovagal syncope. Only one of the subjects was able to withstand LBNP suction for longer than 12 min. It is hypothesized on this basis that the minimal EDV values given in the table may represent the minimal volume levels associated with, or causing, vasovagal syncope in human subjects.

During LBNP, cardiac output is maintained principally by an increase in heart rate, and as much as 30 to 60% of end-diastolic volume may be shifted to the periphery during suction. The findings suggest that restoring plasma volume and blood volume before LBNP testing may prove to be beneficial countermeasures for averting the orthostatic intolerance observed after bed rest and exposure to weightlessness.

Following both space flight and bed rest, a reduction in cardiac size was noted (refs. 19 and 47). Heart size was observed to decrease by 10.5% to 17.9% after 20 to 70 days of bed rest (refs. 19 and 48). Prolonged bed rest also resulted in decreased stroke volume (refs. 19 and 49) which may have resulted from decreased venous return due to a reduction in circulating plasma, red blood cell volume (refs. 50 and 51), and skeletal muscle tone (ref. 49). The initial smaller size of the female heart, the degree of decrease in end-diastolic volume in females, as well as their high heart rate and low arterial pressure, are compatible with a diminished reserve for coping with body fluid shifts that occur during LBNP. This lowered stress response was evidenced by the high rate of syncope in the females during LBNP following bed rest.

Significant leg volume changes occurred during LBNP, but the changes did not differ markedly before and after bed rest. These findings argue the hypothesis that an increased venous compliance is associated with bed rest which is accompanied by increased volume shifts to the legs, and result in significantly altered cardiovascular responses seen after bed rest. No evidence was obtained to evaluate the effect of LBNP on the lower abdominal and pelvic organs, but the basic physiological makeup of the female suggest that further investigation should be undertaken to determine whether women will experience a greater transfer of blood into and out of the pelvic region than has been observed in men.

Although the female subjects in the present study exhibited a greater change in cardiovascular dynamics than had been previously observed in males, the results indicate that women are capable of tolerating the stresses of weightlessness and, furthermore, that they may serve as a more sensitive subject group for evaluating countermeasures to deconditioning and for developing criteria for selecting Shuttle passengers.

Physical Working Capacity

The magnitude of the decrease in VO_2 in women after bed rest was close to the range of responses noted in male subjects in previous studies (refs. 19, 52, and 53). In most of these studies, the maximal work capacity tests were performed with the subjects in the

upright position. When the exercise tests are undertaken immediately after bed rest and in the upright position, the resultant orthostatic hypotension would result in a variable decrease in the maximal working time and maximal VO_2. On the other hand, when the subjects perform the exercise test in the recumbent position, as they did in the present study, orthostatic responses are minimized. Georgievskii *et al.* (ref. 53) observed an 8.6% decrease in maximal VO_2 after 13 days of bed rest when male subjects were tested in the supine position on a bicycle ergometer. In contrast, Saltin *et al.* (ref. 24) observed an average reduction in maximal VO_2 of −26.4% in subjects exercised in the supine position following 20 days of bed rest; these subjects, however, had undergone 55 days of physical training prior to the bed-rest period. From the foregoing results, it is clear that more work is necessary to assess the deconditioning effect on maximal work capacity that occurs following bed rest.

Despite the close relationship of ventilation and oxygen uptake and heart rate during submaximal work, maximal ventilatory volume appears to operate independently and did not change significantly from control values. The increase in submaximal and maximal heart rates during exercise after bed rest agreed with the results of previous studies in men (refs. 19, 49, and 53). The significant decreases noted in submaximal and maximal heart rates probably resulted from an attempt by the body to sustain cardiac output. Georgievskii *et al.* (ref. 53) observed a significant decrease in maximal $\dot{V}O_2$ following 20 days of bed rest, but saw no change in cardiac output. They concluded that decreased oxygen uptake resulted from reduced oxygen utilization by the tissues. Saltin *et al.* (ref. 24) on the other hand, observed the following responses after 20 days of bed rest: A reduction in maximal $\dot{V}O_2$ of 26.4%, a decrease in maximal stroke volume of 28.8%, a decrease in maximal cardiac output of 26.0%, a slight increase in maximal heart rate of 2.1%, and no change in the A-$\dot{V}O_2$ difference. These results suggest that the reduction in maximal $\dot{V}O_2$ resulted primarily from impaired heart function (a central effect) rather than from altered utilization of oxygen by the tissues (a peripheral effect).

The women in our study exhibited a statistically significant decrease in oxygen uptake during the last two submaximal workloads in contrast to male subjects in previous studies (ref. 54). The reduced submaximal $\dot{V}O_2$ observed in the female subjects could have resulted from increased mechanical efficiency, but such an occurrence seems unlikely in the presence of deconditioning. It would seem more plausible that a change occurred in the time constant for the oxygen uptake to reach equilibrium. If the time constant lengthened following bed rest, oxygen uptake might not have reached a steady state in 3 min and, consequently, the measured $\dot{V}O_2$ would be lower than the steady-state submaximal value. Thus, submaximal $\dot{V}O_2$ would be lower after bed rest. Since this response has been observed only in the female subjects, it is possible that their lower physical fitness influences their $\dot{V}O_2$ time constants.

Hypovolemia (refs. 55–57) and hemoglobinemia (refs. 50 and 51) have been observed during prolonged bed rest and may have contributed to the observed decrease in submaximal oxygen uptake. There was no significant decrease in resting hematocrit (table 31) after bed rest but a 12% decrease occurred during recovery. Similar but less significant changes occurred in the ambulatory controls. Similar decreases in blood hemoglobin concentration (table 32) reached their lowest values (12% decrease) during the recovery period. The hemoglobinemia exhibited by the female subjects could be an important contributing cause to the reduction in submaximal $\dot{V}O_2$ through the reduced oxygen-carrying capacity of the blood. Other possible factors include decreased muscle mass, decreased enzyme activity in the mitochondria, decreased O_2 perfusion, and altered nervous stimulation to the blood vessels and muscle fibers.

Menstruation occurred in most of the subjects during the control and recovery periods, as shown in table 1. The menstrual period, however, appeared to have no consistent effect on the cardiorespiratory variables.

Finally, although the absolute working capacity of women is much lower than that of men, our findings indicate that the relative deconditioning responses resulting from bed rest are essentially the same in both sexes.

Biochemistries

It may be concluded that the decrease in plasma volume associated with prolonged bed rest entails a loss of circulating plasma albumin and plasma water, but no change in circulating globulins so that the total plasma protein concentration remains the same while the concentration of plasma globulins is elevated. There also appears to be a true increase in circulating fibrinogen but, because the absolute quantity of fibrinogen is small compared with other plasma proteins, this change had little effect on the concentration of total plasma protein.

In the ambulatory control subjects, both plasma fibrinogen levels and circulating fibrinogen were also significantly elevated following the bed-rest period. This

condition again reflected the presence of the deconditioning process which resulted most probably from prolonged bed rest or confinement of these subjects. It is possible, therefore, that the observed rise in plasma fibrinogen may have been caused by the inactivity of both groups rather than the prolonged recumbency of the bed-rested subjects. The clinical implications of this finding deserve further consideration since it is known that elevated fibrinogen levels result in a greater tendency toward intravascular clotting.

Exposure to $+G_Z$ acceleration provoked elevated fibrinolytic activity and produced near maximal fibrinolytic responses even before exposure to prolonged bed rest. The response of the female subjects was greater than that observed in male subjects under similar conditions (ref. 58).

Since the $+G_Z$ tolerance time of the female subjects was lowered by 69%, it follows that the blood pooling induced by centrifugation was sustained for a similarly reduced period of time. Despite the shorter period of blood pooling, the subjects continued to manifest maximal fibrinolytic responses. Because the vascular endothelium is the reservoir of plasminogen activator, it is concluded that deconditioning following bed rest produces changes in the vascular integrity leading to more active secretion of plasminogen activator in response to hypoxia. Consequently, it is proposed that an elevated fibrinolytic response to $+G_Z$ stress following bed rest may be a manifestation of deconditioning and a potential means of measuring this condition.

The parallel nature of the changes in the various electrolytes and metabolites in both the bed-rested and control subjects may indicate that the changes are dietary in origin rather than being related to prolonged bed rest. On the other hand, since the control subjects were almost entirely sedentary during the bed-rest period, some or all of the changes in excretion rates may well have resulted from the physical inactivity of both groups. The latter possibility is reinforced by the observations of other investigators (ref. 48) which revealed that magnesium, calcium, and phosphate urinary excretion rates are characteristically elevated during periods of prolonged bed rest or weightlessness.

Since the excretion rate of norephinephrine is markedly affected by changes in the level of physical activity, it can be postulated that the significant decrease noted in the bed-rested subjects following recumbency resulted from that state. The large increase observed in both study groups on the final day of recovery probably reflected the high level of physical activity during the recovery period.

Studies of glucose-insulin metabolism demonstrated marked alteration in insulin secretion without change in the plasma glucose level. This finding agrees with results of previous studies using male subjects (refs. 59–61). The mechanisms of the change remain unknown, but the change does not appear to result from altered insulin responsiveness due to altered secretion of such substances such as glucagon or growth hormone. The cause may be related to altered tissue reactivity to secreted insulin or to plasma binding of secreted insulin. These possibilities remain open to further study.

In general, it may be concluded that the response of women to prolonged bed rest is very similar to that observed in male subjects, at least insofar as the biochemical variables measured in this study are concerned. Consequently, women may be expected to respond metabolically in a similar manner to men when subjected to periods of prolonged weightlessness.

Female Adrenal Hormonal and Metabolic Responses

The increased cortisol excretion and increased output of ACTH in response to the stress of centrifugation suggest that the low plasma cortisol levels observed in the subjects may result from an increased turnover or binding of this steroid during bed rest or from both. The unchanged adrenal response to centrifugation despite increasing levels of ACTH may indicate a decreasing sensitivity of the adrenal to circulating ACTH. Similarly, the increased response of the pituitary to acceleration stress may reflect a change in the effectiveness of negative feedback mechanisms. This response has also been observed in animals exposed to stressful situations to which they appear to have adapted (ref. 62). On the basis of these findings, it appears that the magnitude of ACTH plasma levels and the daily plasma cortisol changes may serve as indicators for selecting subjects who will be capable of tolerating acceleration stress. Potential predictive indices should be sought and may be found among other hormonal responses that traditionally have been considered as stress indicators. For example, the work of Oparil (ref. 63) has shown that subjects who do not faint when tilted respond to a considerably greater increase in plasma renin/angiotensin than do those who faint upon exposure to tilt.

Biorhythms

The heart rate rhythms of the bed-rested subjects changed significantly following recumbency. Although

the control subjects also exhibited a change, the difference was not statistically significant and could have represented a psychological response to prolonged confinement. The heart rhythm responses in the bed-rested subjects were indicative of cardiovascular deconditioning following bed rest. The bed rested subjects showed less rhythmic desynchronization than male subjects who were previously studied, but the difference may be attributable to the fact that the bed-rest period was not of sufficient duration for the subjects to exhibit maximum desynchronization.

The hormonal and metabolic rhythmicity of the bed-rested subjects in most cases was similar to the responses observed in male subjects (refs. 43 and 44). Phase differences did exist, however, in the excretion of urine, electrolytes, and 5-HIAA. Rhythmic variations in adrenal function (ref. 63), as measured by urinary excretion and levels of plasma 17-OH-corticosteroids, have been observed consistently (ref. 64). The findings related to plasma-free cortisol in the present study agree with those of Perkhoff *et al.* (ref. 65) in their study of the responses of five males and six females. Peak values observed in the present study occurred at 0800 hr and declined thereafter to a minimum between 2000 and 0400 hr; the decrease was more rapid in previously studied male subjects (refs. 45, 46, and 65).

The rhythm of 5-HIAA excretion in the female subjects differed considerably from that of the male subjects (ref. 65). In our subjects, this rhythm increased between 0400 and 0800 hr; Wadsworth *et al.* (ref. 66) observed a similar response when studying one female subject. Their study also noted that the maximum urinary excretion of 5-HIAA in male subjects occurred during the night and early morning hours. Our investigators, on the other hand, have repeatedly observed that the increase occurred in male subjects between 0800 and 2000 hr.

The female subjects also exhibited differences from male subjects in the day-night variations in urine volume and sodium and potassium excretion. This finding was particularly interesting because these rhythms are considered to be endogenous and thus independent of the effect of various environmental factors. Many investigators have observed that males show a marked decrease in the excretion of sodium, potassium, and urine at night (refs. 67–71). The nocturnal decrease persists whether the electrolyte intake occurs during the day or is distributed evenly over the 24-hr period. The findings suggest that the rhythmical secretion of adrenal glucocorticoids could cause the change in excretion of these elements (ref. 72). Although it has been shown that manipulation of circulating 17-OHCS levels is accompanied by appropriate changes in sodium and potassium, variations in adrenal secretions do not always account for the rhythms of these cations (ref. 71). Consequently, some investigators have suggested that some additional factor that has a rhythmical influence on tubular function may be responsible. The findings of the present study further justify the need for a search for such a factor.

During this study the female subjects evidenced a clear dissociation between the cortisol and electrolyte rhythms. The cortisol rhythms peaked in the morning hours, a response similar to that of the males. The urinary electrolyte rhythm, on the other hand, did not peak until late in the evening, which was several hours out of phase with male responses. The data suggest that the normal physiological states in males and females may be described by the variations in internal phase relationships and synchrony. These differences by sex may prove useful in studying the coupling or regulation of various physiological rhythms. The data also suggest that circadian rhythm characteristics may be useful in assessing individual tolerance to $+G_Z$ acceleration.

Gynecology

The absence or presence of menstrual blood and associated body fluid loss as summarized in table 30 and appendix B did not appear to alter physiological responses of the subjects, except for the suggested acceleration responses of Subject C whose data are shown in figure 14. Subjects G and J, whose periods occurred at a similar time, were not so affected. The conclusions concerning menstruation are further complicated by three factors: (1) the periodic withdrawal of blood (677 ml from each subject) over the course of the study (fig. 1); (2) the random time of occurrence of individual menstrual periods; and (3) significant weight losses of 6.8% and 10.5% of total body weight (4.0 and 4.5 kg) in two subjects (A and F).

From the findings of the present study, it does not appear that women sent into space will have additional problems because of menstruation. However, since the data in this study were limited and since this is the first all-female bed-rest study reported, additional research would be useful in determining the gynecological responses of women in the weightless environment. It is known that women experience shifts in blood and fluid balance as a result of menstruation. This factor should be investigated further to determine whether women will be able to cope with all aspects of weightlessness.

APPENDIX A

SUPPORTING DATA ON BIOCHEMISTRY CHANGES IN FEMALE BED REST SUBJECTS

The following tables contain supporting biochemical data on each subject. These data were obtained from blood and urine specimens taken during the course of these investigations. References have been made throughout the paper to those instances where significant changes have occurred when data were compared to pre-bed-rest control values or to values present for the ambulatory controls.

TABLE 34.– BODY WATER VALUES

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(a) Extracellular water, liters					
Bed-rest group					
A	17.2	15.7	17.3	91.3	100.6
B	16.7	15.4	16.9	92.2	101.2
C	17.8	17.4	19.5	97.8	109.6
D	17.3	17.7	17.4	102.3	100.6
E	17.4	18.1	21.4	104.0	123.0
F	15.0	14.7	15.1	98.0	100.7
G	14.7	13.8	14.3	93.9	97.3
H	19.3	19.7	22.4	102.1	116.1
Mean	16.9	16.6	18.0	97.7	106.1
S.D.	±1.5	±2.0	±2.9	±4.9	±9.2
S.E.	±0.5	±0.7	±1.0	±1.7	±3.2
Ambulatory control group					
I	16.4	17.5	16.7	106.7	101.8
J	16.9	17.3	18.2	102.4	107.7
K	17.2	18.0	17.3	104.7	100.6
L	17.3	18.0	19.6	104.0	113.3
Mean	17.0	17.7[a]	18.0	104.4[b]	105.8
S.D.	±0.4	±0.4	±1.3	±1.8	±5.9
S.E.	±0.2	±0.2	±0.6	±0.9	±2.9
(b) Intracellular water, liters					
Bed-rest group					
A	15.2	12.4	12.3	81.6	80.9
B	13.7	13.0	12.7	94.9	92.7
C	15.6	15.8	14.8	101.3	94.9
D	13.4	14.6	14.4	109.0	107.5
E	15.0	15.1	11.8	100.7	78.7
F	14.7	11.9	12.6	81.0	85.7
G	13.3	13.4	13.8	100.8	103.8
H	16.7	16.4	14.3	98.2	85.6
Mean	14.7	14.1	13.3[c]	95.9	91.2
S.D.	±1.2	±1.6	±1.1	±9.9	±10.4
S.E.	±0.4	±0.6	±0.4	±3.5	±3.7
Ambulatory control group					
I	14.2	12.6	13.2	88.7	93.0
J	15.8	15.1	15.0	95.6	94.9
K	17.2	15.9	16.1	92.4	93.6
L	14.8	13.5	12.3	91.2	83.1
Mean	15.5	14.3[c]	14.2[a]	92.0	91.2
S.D.	±1.3	±1.5	±1.7	±2.9	±5.4
S.E.	±0.7	±0.7	±0.9	±1.4	±2.7

[a] $p < 0.05$, bed rest or recovery vs control

[b] $p < 0.05$, bed rest vs ambulatory control

[c] $p < 0.01$, bed rest vs control

TABLE 35.— PLASMA CONCENTRATIONS

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(a) Plasma sodium, meq/liter					
Bed-rest group					
A	138	147	144	106.5	104.3
B	137	149	137	108.8	100.0
C	136	147	141	108.1	103.7
D	138	152	137	110.1	99.3
E	138	145	141	105.1	102.2
F	136	140	132	102.9	97.1
G	137	152	132	110.9	96.4
H	138	152	137	110.1	99.3
Mean	137	148[a]	138	107.8	100.3
S.D.	±1	±4	±4	±2.8	±2.9
S.E.	±1	±1	±2	±1.0	±1.0
Ambulatory control group					
I	134	147	134	109.7	100.0
J	136	154	134	113.2	98.5
K	141	152	139	107.8	98.6
L	134	147	130	109.7	97.0
Mean	136	150[b]	134	110.1	98.5
S.D.	±3	±4	±4	±2.3	±1.2
S.E.	±2	±2	±2	±1.1	±0.6
(b) Plasma calcium, meq/liter					
Bed-rest group					
A	4.20	4.39	4.25	104.5	101.2
B	4.45	4.39	4.20	98.7	94.4
C	4.55	4.39	4.35	96.5	95.6
D	4.45	4.39	4.30	98.7	96.6
E	4.50	4.55	4.40	101.1	97.8
F	4.35	4.39	4.50	100.9	103.4
G	4.25	4.55	4.30	107.1	101.2
H	4.35	4.22	4.35	97.0	100.0
Mean	4.39	4.41	4.33	100.6	98.8
S.D.	±0.12	±0.11	±0.09	±3.7	±3.2
S.E.	±0.04	±0.04	±0.03	±1.3	±1.1
Ambulatory control group					
I	4.35	4.56	4.25	104.8	97.7
J	4.20	4.22	4.20	100.5	100.0
K	4.50	4.39	4.45	97.6	98.9
L	4.15	4.22	4.30	101.7	103.6
Mean	4.30	4.35	4.30	101.2	100.1
S.D.	±0.16	±0.16	±0.11	±3.0	±2.5
S.E.	±0.08	±0.08	±0.05	±1.5	±1.3

[a] $p < 0.01$, bed rest vs control.

[b] $p < 0.005$, bed rest vs control.

TABLE 35. - CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(c) Plasma magnesium, meq/liter					
Bed-rest group					
A	1.54	1.50	1.56	97.4	101.3
B	1.54	1.65	1.60	107.1	103.9
C	1.41	1.68	1.64	119.1	116.3
D	1.38	1.62	1.46	117.4	105.8
E	1.41	1.50	1.60	106.4	113.5
F	1.41	1.56	1.50	110.6	106.4
G	1.51	1.68	1.72	111.3	113.9
H	1.41	1.56	1.56	110.6	110.6
Mean	1.45	1.59[a]	1.58[a]	110.0	109.0
S.D.	±0.07	±0.07	±0.08	±6.8	±5.4
S.E.	±0.02	±0.03	±0.03	±2.4	±1.9
Ambulatory control group					
I	1.49	1.56	1.56	104.7	104.7
J	1.51	1.62	1.58	107.3	104.6
K	1.44	1.74	1.62	120.8	112.5
L	1.45	1.62	1.66	111.7	114.5
Mean	1.47	1.63[b]	1.60[b]	111.1	109.1
S.D.	±0.03	±0.08	±0.04	±7.1	±5.2
S.E.	±0.02	±0.04	±0.02	±3.5	±2.6
(d) Plasma chloride, meq/liter					
Bed-rest group					
A	104.3	105.5	107.5	101.2	103.1
B	99.0	104.8	105.8	105.9	106.9
C	103.8	108.1	108.0	104.1	104.0
D	100.3	105.0	105.6	104.7	105.3
E	104.0	104.8	106.2	100.8	102.1
F	103.0	105.9	104.9	102.8	101.8
G	104.3	107.0	107.2	102.6	102.8
H	104.0	106.8	105.3	102.7	101.3
Mean	102.8	106.0[c]	106.3[c]	103.1	103.4
S.D.	±2.0	±1.2	±1.1	±1.7	±1.9
S.E.	±0.7	±0.4	±0.4	±0.6	±0.7
Ambulatory control group					
I	100.5	103.5	105.0	103.0	104.5
J	103.8	106.7	105.7	102.8	101.8
K	102.4	107.8	108.8	105.3	106.3
L	103.6	106.7	106.4	103.0	102.7
Mean	102.6	106.2[d]	106.5[d]	103.5	103.8
S.D.	±1.5	±1.9	±1.7	±1.2	±2.0
S.E.	±0.8	±0.9	±0.8	±0.6	±1.0

[a] $p < 0.005$, bed rest or recovery vs control.
[b] $p < 0.05$, bed rest or recovery vs control.
[c] $p < 0.001$, bed rest or recovery vs control.
[d] $p < 0.01$, recovery vs control.

TABLE 35.– CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(e) Plasma albumin, g/100 ml					
Bed-rest group					
A	3.82	3.51	3.29	91.9	86.1
B	4.03	3.49	3.84	86.6	95.3
C	3.81	3.41	3.48	89.5	91.3
D	4.25	3.50	3.32	82.4	78.1
E	4.06	3.41	4.05	84.0	99.8
F	3.66	3.62	4.24	98.9	115.8
G	3.67	3.44	3.93	93.7	107.1
H	3.59	3.30	3.46	91.9	96.4
Mean	3.86	3.46[a]	3.70	89.9	96.2
S.D.	±0.23	±0.09	±0.36	±5.4	±11.8
S.E.	±0.08	±0.03	±0.13	±1.9	±4.2
Ambulatory control group					
I	3.70	3.32	3.54	89.7	95.7
J	3.77	3.52	3.61	93.4	95.8
K	3.98	3.68	4.15	92.5	104.3
L	3.72	3.84	4.01	103.2	107.8
Mean	3.79	3.59	3.83	94.7	100.9
S.D.	±0.13	±0.22	±0.30	±5.9	±6.1
S.E.	±0.06	±0.11	±0.15	±2.9	±3.1
(f) Plasma globulin, g/100 ml					
Bed-rest group					
A	2.00	2.44	2.38	122.0	119.0
B	2.79	2.81	2.44	100.7	87.5
C	2.63	2.53	2.27	96.2	86.3
D	2.03	2.36	2.16	116.3	106.4
E	1.92	2.39	1.98	124.5	103.1
F	2.26	2.68	2.31	118.6	102.2
G	2.47	2.32	2.25	93.9	91.1
H	1.84	2.28	1.93	123.9	104.9
Mean	2.24	2.48[b]	2.22	112.0	100.1
S.D.	±0.35	±0.19	±0.18	±12.9	±11.1
S.E.	±0.12	±0.07	±0.06	±4.6	±3.9
Ambulatory control group					
I	2.81	2.55	2.20	90.7	78.3
J	2.39	2.40	2.21	100.4	92.5
K	2.22	2.42	2.01	109.0	90.5
L	2.28	2.66	2.40	116.7	105.3
Mean	2.42	2.51	2.20	104.2	91.7
S.D.	±0.27	±0.12	±0.16	±11.2	±11.1
S.E.	±0.13	±0.06	±0.08	±5.6	±5.5

[a] $p < 0.005$, bed rest vs control.

[b] $p < 0.05$ bed rest vs control.

TABLE 35.– CONCLUDED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(g) Plasma fibrinogen, g/100 ml					
Bed-rest group					
A	0.44	0.63	0.45	143.2	102.3
B	.49	.75	.46	153.1	93.9
C	.53	.64	.56	120.8	105.7
D	.44	.72	.53	163.6	120.5
E	.40	.75	.53	187.5	132.5
F	.43	.75	.46	174.4	107.0
G	.53	.79	.53	149.1	100.0
H	.50	.70	.49	140.0	98.0
Mean	0.47	0.72[a]	0.50	154.0	107.5
S.D.	±0.05	±0.06	±0.04	±20.9	±12.9
S.E.	±0.02	±0.02	±0.01	±7.4	±4.5
Ambulatory control group					
I	0.59	0.83	0.67	140.7	113.6
J	.42	.68	.52	161.9	123.8
K	.29	.52	.28	179.3	96.6
L	.38	.65	.40	171.1	105.3
Mean	0.42	0.67[a]	0.47	163.3	109.8
S.D.	±0.13	±0.13	±0.17	±16.6	±11.6
S.E.	±0.06	±0.06	±0.08	±8.3	±5.8
(h) Plasma albumin/globulin rates					
Bed-rest group					
A	1.91	1.44	1.38	75.4	72.3
B	1.44	1.24	1.57	86.1	109.0
C	1.45	1.35	1.53	93.1	105.5
D	2.09	1.48	1.54	70.8	73.7
E	2.11	1.43	2.05	67.8	97.2
F	1.62	1.35	1.84	83.3	113.6
G	1.49	1.48	1.75	99.3	117.4
H	1.95	1.45	1.79	74.4	91.8
Mean	1.76	1.40[b]	1.68	81.3	97.6
S.D.	±0.29	±0.08	±0.22	±11.1	±17.3
S.E.	±0.10	±0.03	±0.08	±3.9	±6.1
Ambulatory control group					
I	1.32	1.30	1.61	98.5	122.0
J	1.58	1.47	1.63	93.0	103.2
K	1.79	1.52	2.06	84.9	115.1
L	1.63	1.44	1.67	88.3	102.5
Mean	1.58	1.43	1.74	91.2	110.7
S.D.	±0.20	±0.09	±0.21	±5.9	±9.5
S.E.	±0.10	±0.05	±0.11	±3.0	±4.7

[a] $p < 0.001$, bed rest vs control.

[b] $p < 0.01$, bed rest vs control.

TABLE 36.– CIRCULATING PLASMA

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(a) Circulating plasma protein, g					
Bed-rest group					
A	171	147	173	86.0	101.2
B	194	153	185	78.9	95.4
C	194	161	175	83.0	90.2
D	172	153	154	89.0	89.5
E	184	162	190	88.0	103.3
F	146	141	162	96.6	111.0
G	152	135	158	88.8	103.9
H	166	163	178	98.2	107.2
Mean	172	152[a]	172	88.6	100.2
S.D.	±18	±10	±13	±6.4	±7.8
S.E.	±6	±4	±5	±2.3	±2.8
Ambulatory control group					
I	165	172	181	104.2	110.0
J	180	185	179	102.8	99.4
K	171	179	178	104.7	104.1
L	167	192	185	115.0	110.8
Mean	171	182	181	106.7[b]	106.1
S.D.	±7	±9	±3	±5.6	±5.4
S.E.	±3	±4	±2	±2.8	±2.7
(b) Circulating plasma albumin, g					
Bed-rest group					
A	104	79	93	76.0	89.4
B	107	76	105	71.0	98.1
C	106	84	96	79.2	90.6
D	109	82	85	75.2	78.0
E	117	84	117	71.8	100.0
F	84	72	98	85.7	116.7
G	84	71	92	84.5	109.5
H	101	86	104	85.1	103.0
Mean	102	79[c]	99	78.6	98.2
S.D.	±12	±6	±10	±6.0	±12.2
S.E.	±4	±2	±3	±2.1	±4.3
Ambulatory control group					
I	86	85	100	98.8	116.3
J	103	99	102	96.1	99.0
K	105	100	115	95.2	109.5
L	97	103	109	106.2	112.4
Mean	98	97	107	99.1[b]	109.3
S.D.	±9	±8	±7	±5.0	±7.4
S.E.	±4	±4	±3	±2.5	±3.7

[a] $p < 0.005$, bed rest vs control.

[b] $p < 0.001$, bed rest vs ambulatory control.

[c] $p < 0.001$, bed rest vs control.

TABLE 36.– CONCLUDED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(c) Circulating plasma globulin, g					
Bed-rest group					
A	54.6	54.7	67.4	100.2	123.4
B	73.9	61.0	66.9	82.5	90.5
C	73.1	62.0	62.9	84.8	86.0
D	52.0	55.0	55.3	105.8	106.3
E	55.5	59.0	57.4	106.3	103.4
F	52.0	53.6	53.4	103.1	102.7
G	56.3	47.8	52.9	84.9	94.0
H	51.5	59.3	58.3	115.1	113.2
Mean	58.6	56.6	59.3	97.8	102.4
S.D.	±9.4	±4.7	±5.8	±12.2	±12.3
S.E.	±3.3	±1.7	±2.0	±4.3	±4.3
Ambulatory control group					
I	65.2	65.3	62.0	100.2	95.1
J	65.5	67.2	62.3	102.6	95.1
K	58.4	65.6	55.5	112.3	95.0
L	59.5	71.3	65.3	119.8	109.7
Mean	62.2	67.4	61.3	108.7	98.7
S.D.	±3.7	±2.8	±4.1	±9.0	±7.3
S.E.	±1.9	±1.4	±2.1	±4.5	±3.7
(d) Circulating plasma fibrinogen, g					
Bed-rest group					
A	12.0	14.1	12.7	117.5	105.8
B	13.0	16.3	12.6	125.4	96.9
C	14.7	15.7	15.5	106.8	105.4
D	11.3	16.8	13.6	148.7	120.4
E	11.6	18.5	15.4	159.5	132.8
F	9.9	15.0	10.6	151.5	107.1
G	12.1	16.3	12.5	134.7	103.3
H	14.0	18.2	14.8	130.0	105.7
Mean	12.3	16.4[a]	13.5[b]	134.3	109.7
S.D.	±1.5	±1.5	±1.7	±18.0	±11.4
S.E.	±0.5	±0.5	±0.6	±6.4	±4.0
Ambulatory control group					
I	13.7	21.2	18.9	154.7	138.0
J	11.5	19.0	14.7	165.2	127.8
K	7.6	14.1	7.7	185.5	101.3
L	9.9	17.4	10.9	175.8	110.1
Mean	10.7	17.9[a]	13.1	170.3[c]	119.3
S.D.	±2.6	±3.0	±4.8	±13.3	±16.6
S.E.	±1.3	±1.5	±2.4	±6.6	±8.3

[a] $p < 0.001$, bed rest vs control.

[b] $p < 0.05$, recovery vs control.

[c] $p < 0.01$, bed rest vs ambulatory control.

TABLE 37. - PLASMA GLOBULIN CONCENTRATION

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(a) Plasma α-1-globulin concentration, g/100 ml					
Bed-rest group					
A	0.14	0.20	0.23	142.9	164.3
B	.20	.24	.25	120.0	125.0
C	.22	.18	.23	81.8	104.5
D	.16	.21	.16	131.3	100.0
E	.18	.19	.18	105.6	100.0
F	.24	.23	.23	95.8	95.8
G	.24	.22	.23	91.7	95.8
H	.11	.21	.17	190.9	154.5
Mean	0.19	0.21	0.21	120.0	117.5
S.D.	±0.05	±0.02	±0.03	±35.3	±27.6
S.E.	±0.02	±0.01	±0.01	±12.5	±9.8
Ambulatory control group					
I	0.21	0.15	0.17	71.4	81.0
J	.21	.20	.17	95.2	90.5
K	.25	.21	.18	84.0	72.0
L	.16	.19	.18	118.8	112.5
Mean	0.21	0.19	0.18	92.4	89.0
S.D.	±0.04	±0.03	±0.01	±20.1	±17.4
S.E.	±0.02	±0.01	±0.01	±10.1	±8.7
(b) Plasma α-2-globulin concentration, g/100 ml					
Bed-rest group					
A	0.54	0.68	0.65	125.9	120.4
B	.62	.64	.61	103.2	98.4
C	.65	.57	.56	87.7	86.2
D	.57	.65	.66	114.0	115.8
E	.41	.57	.44	139.0	107.3
F	.49	.52	.53	106.1	108.2
G	.64	.61	.57	95.3	89.1
H	.45	.56	.48	124.4	106.7
Mean	0.55	0.60	0.56	112.0	104.0
S.D.	±0.09	±0.05	±0.08	±17.2	±12.0
S.E.	±0.03	±0.02	±0.03	±6.1	±4.3
Ambulatory control group					
I	0.65	0.52	0.50	80.0	76.9
J	.50	.48	.46	96.0	92.0
K	.57	.59	.53	103.5	93.0
L	.58	.61	.62	105.2	106.9
Mean	0.57	0.55	0.53	96.2	92.2
S.D.	±0.06	±0.06	±0.07	±11.5	±12.3
S.E.	±0.03	±0.03	±0.03	±5.8	±6.1

TABLE 37.– CONCLUDED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(c) Plasma β-globulin concentration, g/100 ml					
Bed-rest group					
A	0.51	0.64	0.59	125.5	115.7
B	.79	.81	.75	102.5	94.9
C	.77	.89	.69	115.6	89.6
D	.65	.75	.62	115.4	95.4
E	.59	.72	.66	122.0	111.9
F	.66	.89	.72	134.8	109.1
G	.81	.80	.84	98.8	103.7
H	.60	.74	.66	123.3	110.0
Mean	0.67	0.78[a]	0.69	117.2	103.8
S.D.	±0.11	±0.09	±0.08	±11.9	±9.5
S.E.	±0.04	±0.03	±0.03	±4.2	±3.3
Ambulatory control group					
I	0.71	0.83	0.63	116.9	88.7
J	.75	.72	.72	96.0	96.0
K	.68	.81	.70	119.1	102.9
L	.58	.68	.62	117.2	106.9
Mean	0.68	0.76	0.67	112.3	98.6
S.D.	±0.07	±0.07	±0.05	±10.9	±8.0
S.E.	±0.04	±0.04	±0.02	±5.5	±4.0
(d) Plasma γ-globulin concentration, g/100 ml					
Bed-rest group					
A	0.81	0.92	0.91	113.6	112.3
B	1.18	1.12	0.83	94.9	70.3
C	.99	.89	.79	89.9	79.8
D	.65	.75	.72	115.4	110.8
E	.74	.91	.70	123.0	94.6
F	.87	1.04	.83	119.5	95.4
G	.78	.69	.61	88.5	78.2
H	.68	.77	.62	113.2	91.2
Mean	0.84	0.89	0.75	107.3	91.6
S.D.	±0.18	±0.15	±0.11	±13.9	±15.1
S.E.	±0.06	±0.05	±0.04	±4.9	±5.3
Ambulatory control group					
I	1.24	1.05	0.90	84.7	72.6
J	.93	1.00	.84	107.5	90.3
K	.72	.81	.60	112.5	83.3
L	.96	1.18	.98	122.9	102.1
Mean	0.96	1.01	0.83	106.9	87.1
S.D.	±0.21	±0.15	±0.16	±16.1	±12.4
S.E.	±0.11	±0.08	±0.08	±8.1	±6.2

[a] $p < 0.01$, bed rest vs control.

TABLE 38. CIRCULATING GLOBULIN

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(a) Circulating α-1-globulin, g					
Bed-rest group					
A	3.8	4.5	6.5	118.4	171.1
B	5.3	5.2	6.9	98.1	130.2
C	6.1	4.4	6.4	72.1	104.9
D	4.1	4.9	4.1	119.5	100.0
E	5.2	4.7	5.2	90.4	100.0
F	5.5	4.6	5.3	83.6	96.4
G	5.5	4.5	5.4	81.8	98.2
H	3.1	5.5	5.2	177.4	167.7
Mean	4.8	4.8	5.6	105.2	121.1
S.D.	±1.0	±0.4	±0.9	±33.7	±31.7
S.E.	±0.4	±0.1	±0.3	±11.9	±11.2
Ambulatory control group					
I	4.9	3.8	4.8	77.6	98.0
J	5.8	5.6	5.3	96.6	91.4
K	6.6	5.7	5.0	86.4	75.8
L	4.2	5.1	4.9	121.4	116.7
Mean	5.4	5.1	5.0	95.5	95.5
S.D.	±1.0	±0.9	±0.2	±18.9	±16.9
S.E.	±0.5	±0.4	±0.1	±9.5	±8.5
(b) Circulating α-2-globulin, g					
Bed-rest group					
A	14.8	15.2	18.4	102.7	124.3
B	16.4	13.9	16.7	84.8	101.8
C	18.1	14.0	15.5	77.3	85.6
D	14.6	15.1	16.9	103.4	115.8
E	11.8	14.1	12.8	119.5	108.5
F	11.3	10.4	12.3	92.0	108.8
G	14.6	12.6	13.4	86.3	91.8
H	12.6	14.6	14.5	115.9	115.1
Mean	14.3	13.7	15.1	97.7	106.5
S.D.	±2.3	±1.6	±2.2	±15.2	±12.9
S.E.	±0.8	±0.6	±0.8	±5.4	±4.6
Ambulatory control group					
I	15.1	13.3	14.1	88.1	93.4
J	13.7	13.4	13.0	97.8	94.9
K	15.0	16.0	14.6	106.7	97.3
L	15.1	16.4	16.9	108.6	111.9
Mean	14.7	14.8	14.6	100.3	99.4
S.D.	±0.7	±1.7	±1.6	±9.4	±8.5
S.E.	±0.3	±0.8	±0.8	±4.7	±4.3

TABLE 38. - CONCLUDED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(c) Circulating β-globulin, g					
Bed-rest group					
A	13.9	14.4	16.7	103.6	120.1
B	20.9	17.6	20.6	84.2	98.6
C	21.4	21.8	19.1	101.9	89.3
D	16.6	17.5	15.9	105.4	95.8
E	17.1	17.8	19.1	104.1	111.7
F	15.2	17.8	16.6	117.1	109.2
G	18.4	16.5	19.8	89.7	107.6
H	16.8	19.2	19.9	114.3	118.5
Mean	17.5	17.8	18.5	102.5	106.4
S.D.	±2.6	±2.1	±1.8	±11.1	±10.9
S.E.	±0.9	±0.7	±0.6	±3.9	±3.9
Ambulatory control group					
I	16.4	21.3	17.7	129.9	107.9
J	20.5	20.2	20.3	98.5	99.0
K	17.9	21.9	19.3	122.3	107.8
L	15.1	18.2	16.9	120.5	111.9
Mean	17.5	20.4	18.6	117.8	106.7
S.D.	±2.3	±1.6	±1.5	±13.5	±5.4
S.E.	±1.2	±0.8	±0.8	±6.7	±2.7
(d) Circulating γ-globulin, g					
Bed-rest group					
A	22.1	20.6	25.8	93.2	116.7
B	31.3	24.3	22.7	77.6	72.5
C	27.5	21.8	21.9	79.3	79.6
D	16.7	17.5	18.4	104.8	110.2
E	21.4	22.4	20.3	104.7	94.9
F	20.0	20.8	19.2	104.0	96.0
G	17.8	14.2	14.3	79.8	80.3
H	19.0	20.0	18.7	105.3	105.1
Mean	22.0	20.2	20.2	93.6	94.4
S.D.	±5.0	±3.1	±3.4	±12.8	±15.9
S.E.	±1.8	±1.1	±1.2	±4.5	±5.6
Ambulatory control group					
I	28.8	26.9	25.4	93.4	88.2
J	25.5	28.0	23.7	109.8	92.9
K	18.9	22.0	16.6	116.4	87.8
L	25.1	31.6	26.6	125.9	106.0
Mean	24.6	27.1	23.1	111.4	93.7
S.D.	±4.1	±4.0	±4.5	±13.7	±8.5
S.E.	±2.1	±2.0	±2.2	±6.8	±4.3

TABLE 39. PLASMA ALKALINE PHOSPHATASE CONCENTRATION

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(a) Plasma alkaline phosphatase concentration, units/liter					
Bed-rest group					
A	14.5	17.2	17.3	118.6	119.3
B	23.3	24.3	30.0	104.3	128.8
C	19.2	21.9	23.6	114.1	122.9
D	12.6	14.7	15.8	116.7	125.4
E	11.8	14.6	16.4	123.7	139.0
F	23.3	27.8	29.7	119.3	127.5
G	17.0	18.6	20.4	109.4	120.0
H	14.0	18.0	17.9	128.6	127.9
Mean	17.0	19.6[a]	21.4[a]	116.8	126.4
S.D.	±4.6	±4.7	±5.8	±7.7	±6.2
S.E.	±1.6	±1.7	±2.0	±2.7	±2.2
Ambulatory control group					
I	19.2	21.4	20.3	111.5	105.7
J	12.9	18.6	19.4	144.2	150.4
K	21.6	25.7	26.1	119.0	120.8
L	17.3	21.4	20.3	123.7	117.3
Mean	17.8	21.8[b]	21.5[c]	124.6	123.6
S.D.	±3.7	±2.9	±3.1	±14.0	±19.0
S.E.	±1.8	±1.5	±1.5	±7.0	±9.5
(b) Plasma glutamate-oxaloacetate transaminase concentration, units/ml					
Bed-rest group					
A	37.4	29.3	30.4	78.3	81.3
B	48.0	30.2	30.2	62.9	62.9
C	38.8	29.5	31.2	76.0	80.4
D	39.0	33.7	30.4	86.4	77.9
E	40.1	29.5	30.6	73.6	76.3
F	53.8	35.5	33.3	66.0	61.9
G	39.8	30.8	31.5	77.4	79.1
H	42.7	30.1	30.1	70.5	70.5
Mean	42.5	31.1[a]	31.0[a]	73.9	73.8
S.D.	±5.6	±2.3	±1.1	±7.4	±7.8
S.E.	±2.0	±0.8	±0.4	±2.6	±2.7
Ambulatory control group					
I	38.8	30.2	31.0	77.8	79.9
J	36.9	30.6	31.0	82.9	84.0
K	39.0	30.6	30.0	78.5	76.9
L	38.0	30.5	29.7	80.3	78.2
Mean	38.2	30.5[a]	30.4[c]	79.9	79.8
S.D.	±1.0	±0.2	±0.7	±2.3	±3.1
S.E.	±0.5	±0.1	±0.3	±1.1	±1.5

[a] $p < 0.001$, bed rest or recovery vs control.

[b] $p < 0.05$, bed rest or recovery vs control.

[c] $p < 0.005$, recovery vs control.

TABLE 39.– CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(c) Plasma glutamate-pyruvate transaminase concentration, units/ml					
Bed-rest group					
A	21.3	19.7	19.2	92.5	90.1
B	29.7	19.5	20.4	65.7	68.7
C	22.2	20.9	20.5	94.1	92.3
D	22.5	26.4	22.7	117.3	100.9
E	22.0	21.4	20.5	97.3	93.2
F	34.0	29.8	25.8	87.6	75.9
G	21.6	21.1	21.7	97.7	100.5
H	24.0	20.9	21.4	87.1	89.2
Mean	24.7	22.5	21.5[a]	92.4	88.9
S.D.	±4.7	±3.7	±2.0	±14.3	±11.3
S.E.	±1.6	±1.3	±0.7	±5.1	±4.0
Ambulatory control group					
I	21.3	19.1	19.4	89.7	91.1
J	23.2	20.5	20.4	88.4	87.9
K	22.4	22.1	21.1	98.7	94.2
L	21.6	21.3	20.5	98.6	94.9
Mean	22.1	20.8	20.4[a]	93.9	92.0
S.D.	±0.9	±1.3	±0.7	±5.6	±3.2
S.E.	±0.4	±0.6	±0.4	±2.8	±1.6
(d) Plasma total lactate dehydrogenase concentration, units/ml					
Bed-rest group					
A	301	251	264	83.4	87.7
B	274	245	260	89.4	94.9
C	287	253	272	88.2	94.8
D	291	248	263	85.2	90.4
E	285	252	280	88.4	98.2
F	281	242	277	86.1	98.6
G	287	261	278	90.9	96.9
H	279	268	284	96.1	101.8
Mean	286	252[b]	272[a]	88.5	95.4
S.D.	±8	±8	±9	±3.9	±4.6
S.E.	±3	±3	±3	±1.4	±1.6
Ambulatory control group					
I	277	244	256	88.1	92.4
J	285	264	249	92.6	87.4
K	290	278	272	95.9	93.8
L	279	249	263	89.2	94.3
Mean	283	259[a]	260[a]	91.5	92.0
S.D.	±6	±15	±10	±3.5	±3.2
S.E.	±3	±8	±5	±1.8	±1.6

[a] $p < 0.05$, bed rest or recovery vs control.

[b] $p < 0.001$, bed rest or recovery vs control.

TABLE 39.– CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(e) Plasma LDH-1 isoenzyme concentration, units/ml					
Bed-rest group					
A	127.0	76.9	112.4	60.6	88.5
B	122.0	68.8	107.1	56.4	87.8
C	106.5	75.5	108.2	70.9	101.6
D	100.8	70.4	98.0	69.8	97.2
E	113.0	57.6	98.9	51.0	87.5
F	108.1	49.9	102.1	46.2	94.4
G	112.5	65.3	109.5	58.0	97.3
H	116.7	72.3	114.1	62.0	97.8
Mean	113.3	67.1[a]	106.3[b]	59.4	94.0
S.D.	±8.5	±9.2	±6.0	±8.5	±5.4
S.E.	±3.0	±3.3	±2.1	±3.0	±1.9
Ambulatory control group					
I	122.3	66.4	118.8	54.3	97.1
J	119.0	66.5	102.2	55.9	85.9
K	127.0	69.4	101.7	54.6	80.1
L	106.4	64.4	103.8	60.5	97.6
Mean	118.7	66.7[a]	106.6	56.3	90.2
S.D.	±8.8	±2.1	±8.2	±2.9	±8.6
S.E.	±4.4	±1.0	±4.1	±1.4	±4.3
(f) Plasma LDH-2 isoenzyme concentration, units/ml					
Bed-rest group					
A	122.6	88.7	86.6	72.3	70.6
B	98.2	76.9	80.6	78.3	82.1
C	97.0	98.2	93.7	101.2	96.6
D	145.9	88.5	76.9	60.7	52.7
E	96.0	94.2	92.2	98.1	96.0
F	80.3	92.3	85.3	114.9	106.2
G	87.8	91.7	80.7	104.4	91.9
H	81.1	99.8	89.0	123.1	109.7
Mean	101.1	91.3	85.6	94.1	88.2
S.D.	±22.5	±7.1	±5.9	±21.7	±19.0
S.E.	±7.9	±2.5	±2.1	±7.7	±6.7
Ambulatory control group					
I	80.1	73.1	71.6	91.3	89.4
J	97.0	82.4	72.6	84.9	74.8
K	96.0	114.5	73.0	119.3	76.0
L	96.3	102.8	87.4	106.7	90.8
Mean	92.4	93.2	76.2[b]	100.6	82.8
S.D.	±8.2	±18.9	±7.5	±15.5	±8.5
S.E.	±4.1	±9.4	±3.8	±7.7	±4.3

[a] $p < 0.001$, bed rest or recovery vs control.

[b] $p < 0.05$, bed rest or recovery vs control.

TABLE 39.– CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(g) Plasma LDH-3 isoenzyme concentration, units/ml					
Bed-rest group					
A	39.3	51.6	41.3	131.3	105.1
B	38.0	60.5	44.9	159.2	118.2
C	46.9	59.7	43.4	127.3	92.5
D	32.8	62.6	53.5	190.9	163.1
E	52.8	64.5	59.5	122.2	112.7
F	36.0	68.3	57.4	189.7	159.4
G	47.5	53.4	50.4	112.4	106.1
H	47.5	60.7	51.0	127.8	107.4
Mean	42.6	60.2[a]	50.2[b]	145.1	120.6
S.D.	±7.0	±5.5	±6.6	±30.9	±26.2
S.E.	±2.5	±1.9	±2.3	±10.9	±9.3
Ambulatory control group					
I	44.4	60.4	41.1	136.0	92.6
J	45.5	71.8	41.5	157.8	91.2
K	40.7	70.8	56.5	174.0	138.8
L	45.0	61.0	46.8	135.6	104.0
Mean	43.9	66.0[c]	46.5	150.9	106.7
S.D.	±2.2	±6.1	±7.2	±18.6	±22.2
S.E.	±1.1	±3.1	±3.6	±9.3	±11.1
(h) Plasma LDH-4 isoenzyme concentration, units/ml					
Bed-rest group					
A	3.0	15.6	12.4	520.0	413.3
B	3.2	19.4	14.9	606.3	465.6
C	15.9	9.1	14.5	57.2	91.2
D	6.6	10.4	18.1	157.6	274.2
E	16.9	14.9	17.6	88.2	104.1
F	12.4	12.0	18.2	96.8	146.8
G	18.6	31.7	20.9	170.4	112.4
H	20.8	15.0	17.8	72.1	85.6
Mean	12.2	16.0	16.8	221.1	211.7
S.D.	±7.0	±7.1	±2.7	±216.0	±153.6
S.E.	±2.5	±2.5	±0.9	±76.4	±54.3
Ambulatory control group					
I	15.1	21.8	13.1	144.4	86.8
J	11.8	23.6	17.6	200.0	149.2
K	14.6	9.3	23.6	63.7	161.6
L	12.5	13.2	13.3	105.6	106.4
Mean	13.5	17.0	16.9	128.4	126.0
S.D.	±1.6	±6.8	±4.9	±58.0	±35.2
S.E.	±0.8	±3.4	±2.5	±29.0	±17.6

[a] $p < 0.001$, bed rest or recovery vs control.

[b] $p < 0.05$, bed rest or recovery vs control.

[c] $p < 0.01$, bed rest vs control.

TABLE 39.– CONCLUDED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(i) Plasma LDH-5 isoenzyme concentration, units/ml					
Bed-rest group					
A	9.1	18.2	11.3	200.0	124.2
B	12.6	19.4	12.5	154.0	99.2
C	20.7	10.5	12.2	50.7	58.9
D	4.9	16.1	16.5	328.6	336.7
E	6.3	20.8	11.8	330.2	187.3
F	44.2	19.5	14.0	44.1	31.7
G	20.6	18.9	16.5	91.7	80.1
H	12.9	20.2	12.1	156.6	93.8
Mean	16.4	18.0	13.4	169.5	126.5
S.D.	±12.7	±3.3	±2.1	±112.4	±96.7
S.E.	±4.5	±1.2	±0.7	±39.7	±34.2
Ambulatory control group					
I	15.1	22.3	11.4	147.7	75.5
J	11.7	19.7	15.1	168.4	129.1
K	11.7	14.0	17.2	119.7	147.0
L	18.8	7.6	11.7	40.4	62.2
Mean	14.3	15.9	13.9	119.1	103.5
S.D.	±3.4	±6.5	±2.8	±56.1	±41.0
S.E.	±1.7	±3.3	±1.4	±28.1	±20.5

TABLE 40.– URINE DATA

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(a) Urine volume, liters/24 hr					
Bed-rest group					
A	1.35	0.36	0.44	26.7	32.6
B	1.00	0.41	---	41.0	---
C	1.74	0.93	1.16	53.4	66.7
D	1.74	1.04	1.72	59.8	98.9
E	2.55	1.98	2.90	77.6	113.7
F	2.33	2.20	2.77	94.4	118.9
G	.90	.43	.67	47.8	74.4
H	1.20	.32	1.24	26.7	103.3
Mean	1.60	0.96[a]	1.56	53.4	86.9
S.D.	±0.60	±0.75	±0.97	±23.7	±30.7
S.E.	±0.21	±0.27	±0.36	±8.4	±11.6
Ambulatory control group					
I	1.22	1.48	1.32	121.3	108.2
J	1.30	.92	.99	70.8	76.2
K	1.02	.80	1.35	78.4	132.4
L	1.93	.60	1.62	31.1	83.9
Mean	1.37	0.95	1.32	75.4	100.2
S.D.	±0.39	±0.38	±0.26	±37.0	±25.4
S.E.	±0.20	±0.19	±0.13	±18.5	±12.7
(b) Urine specific gravity (24 hr)					
Bed-rest group					
A	1.013	1.022	1.015	169.2	115.4
B	1.013	1.018	---	138.5	---
C	1.012	1.020	1.012	166.7	100.0
D	1.015	1.016	1.008	106.7	53.3
E	1.009	1.007	1.008	77.8	88.9
F	1.008	1.007	1.004	87.5	50.0
G	1.015	1.017	1.016	113.3	106.7
H	1.018	1.020	1.018	111.1	100.0
Mean	1.013	1.016	1.012	121.4	87.8
S.D.	±0.003	±0.006	±0.005	±33.9	±25.9
S.E.	±0.001	±0.002	±0.002	±12.0	±9.8
Ambulatory control group					
I	1.015	1.014	1.016	93.3	106.7
J	1.017	1.019	1.009	111.8	52.9
K	1.017	1.016	1.014	94.1	82.4
L	1.011	1.015	1.017	136.4	154.5
Mean	1.015	1.016	1.014	108.9	99.1
S.D.	±0.003	±0.002	±0.004	±20.2	±43.0
S.E.	±0.001	±0.001	±0.002	±10.1	±21.5

[a] $p < 0.001$, bed rest vs control.

TABLE 40. CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(c) Urine pH (24 hr)					
Bed-rest group					
A	6.51	5.93	5.92	91.1	90.9
B	7.01	5.69	---	81.2	---
C	6.78	6.16	7.30	90.9	107.7
D	7.16	6.26	5.71	87.4	79.7
E	6.66	6.34	6.28	95.2	94.3
F	7.11	5.78	6.35	81.3	89.3
G	6.41	6.32	6.75	98.6	105.3
H	6.89	5.71	6.82	82.9	99.0
Mean	6.82	6.02[a]	6.45	88.6	95.2
S.D.	±0.28	±0.28	±0.55	±6.5	±9.7
S.E.	±0.10	±0.10	±0.21	±2.3	±3.7
Ambulatory control group					
I	6.42	6.37	7.46	99.2	116.2
J	7.17	5.21	6.08	72.7	84.8
K	5.56	6.66	5.90	119.8	106.1
L	6.78	6.32	6.64	93.2	97.9
Mean	6.48	6.14	6.52	96.2	101.3
S.D.	±0.69	±0.64	±0.70	±19.4	±13.3
S.E.	±0.34	±0.32	±0.35	±9.7	±6.6
(d) Urine Na/K ratio (24 hr)					
Bed-rest group					
A	3.45	1.58	2.49	45.8	72.2
B	4.83	3.86	---	79.9	---
C	3.07	2.46	1.81	80.1	59.0
D	2.98	3.50	4.51	117.4	151.3
E	3.27	2.72	2.70	83.2	82.6
F	4.41	3.03	4.68	68.7	106.1
G	2.89	3.40	6.83	117.6	236.3
H	2.80	3.27	4.37	116.8	156.1
Mean	3.46	2.94	3.91	88.7	123.4
S.D.	±0.75	±0.76	±1.71	±28.4	±62.4
S.E.	±0.27	±0.29	±0.65	±9.3	±23.6
Ambulatory control group					
I	3.19	3.55	2.04	111.3	63.9
J	4.53	2.08	4.96	45.9	109.5
K	2.65	4.72	4.16	178.1	157.0
L	4.45	2.72	6.22	61.1	139.8
Mean	3.71	3.27	4.35	99.1	117.6
S.D.	±0.93	±1.14	±1.76	±59.6	±40.8
S.E.	±0.47	±0.57	±0.88	±29.8	±20.4

[a] $p < 0.005$, bed rest vs control.

TABLE 40. CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(e) Urine total nitrogen excretion rate, g/24 hr					
Bed-rest group					
A	8.84	4.67	3.03	52.8	34.3
B	6.32	3.36	---	53.2	---
C	12.61	12.61	7.36	100.0	58.4
D	16.88	10.22	6.09	60.5	36.1
E	12.74	7.77	11.94	61.0	93.7
F	6.96	9.04	4.34	129.9	62.4
G	7.60	3.50	5.28	46.1	69.5
H	12.95	3.26	11.00	25.2	84.9
Mean	10.61	6.80[a]	7.01[a]	66.1	62.8
S.D.	±3.72	±3.61	±3.35	±33.2	±22.5
S.E.	±1.32	±1.28	±1.26	±11.7	±8.5
Ambulatory control group					
I	10.36	9.89	8.94	95.5	86.3
J	13.45	13.35	3.90	99.3	29.0
K	10.63	4.88	9.38	45.9	88.2
L	7.06	7.87	13.28	111.5	188.1
Mean	10.38	9.00	8.88	88.1	97.9
S.D.	±2.61	±3.56	±3.85	±28.9	±66.1
S.E.	±1.31	±1.78	±1.92	±14.5	±33.1
(f) Urine ammonia excretion rate, mmol/24 hr					
Bed-rest group					
A	25.0	14.9	11.8	59.6	47.2
B	18.2	24.7	---	135.7	---
C	30.7	36.2	22.1	117.9	72.0
D	29.5	26.2	25.7	88.8	87.1
E	34.3	26.6	50.6	77.6	147.5
F	23.0	36.7	26.6	159.6	115.7
G	21.8	12.2	13.4	56.0	61.5
H	24.0	12.7	17.3	52.9	72.1
Mean	25.8	23.8	23.9	93.5	86.2
S.D.	±5.3	±9.8	±13.1	±40.0	±34.5
S.E.	±1.9	±3.5	±4.9	±14.2	±13.1
Ambulatory control group					
I	30.5	40.1	11.3	131.5	37.0
J	22.3	32.6	11.5	146.2	51.6
K	39.8	15.8	36.0	39.7	90.5
L	23.5	19.4	25.0	82.6	106.4
Mean	29.0	27.0	21.0	100.0	71.4
S.D.	±8.0	±11.3	±11.9	±48.5	±32.5
S.E.	±4.0	±5.7	±6.0	±24.3	±16.2

[a] $p < 0.05$, bed rest or recovery vs control.

TABLE 40.- CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(g) Urine creatinine excretion rate, mmol/24 hr					
Bed-rest group					
A	10.32	7.56	6.02	73.3	58.3
B	8.66	5.40	---	62.4	---
C	9.31	8.30	5.76	89.2	61.9
D	10.49	7.44	6.72	70.9	64.1
E	10.22	7.42	11.16	72.6	109.2
F	8.23	8.62	7.73	104.7	93.9
G	8.50	5.02	5.66	59.1	66.6
H	10.27	4.22	9.55	41.1	93.0
Mean	9.50	6.75[a]	7.51[b]	71.7	78.1
S.D.	±0.93	±1.63	±2.12	±19.2	±20.1
S.E.	±0.33	±0.58	±0.80	±6.8	±7.6
Ambulatory control group					
I	9.10	8.59	9.10	94.4	100.0
J	10.08	9.10	4.80	90.3	47.6
K	9.26	6.82	10.82	73.7	116.8
L	8.06	4.97	8.88	61.7	110.2
Mean	9.13	7.37	8.40	80.0	93.7
S.D.	±0.83	±1.87	±2.55	±15.1	±31.5
S.E.	±0.41	±0.94	±1.28	±7.6	±15.7
(h) Urine creatine excretion rate, mmol/24 hr					
Bed-rest group					
A	0.85	1.24	0.51	145.9	60.0
B	1.34	0.95	---	70.9	---
C	2.50	2.90	3.28	116.0	131.2
D	3.66	3.62	1.46	98.9	39.9
E	3.63	1.60	1.21	44.1	33.3
F	2.56	2.87	1.57	112.1	61.3
G	1.80	2.52	1.16	140.0	64.4
H	1.30	1.30	1.48	100.0	113.8
Mean	2.21	2.13	1.52	103.5	72.0
S.D.	±1.06	±0.98	±0.85	±33.8	±36.7
S.E.	±0.38	±0.35	±0.32	±11.9	±13.9
Ambulatory control group					
I	1.54	1.78	0.66	115.6	42.9
J	4.03	1.82	2.95	45.2	73.2
K	2.37	2.68	1.41	113.1	59.5
L	2.06	.96	1.00	46.6	48.5
Mean	2.50	1.81	1.51[c]	80.1	56.0
S.D.	±1.08	±0.70	±1.01	±39.5	±13.4
S.E.	±0.54	±0.35	±0.51	±19.8	±6.7

[a] $p < 0.005$, bed rest vs control.

[b] $p < 0.05$, recovery vs control.

[c] $p < 0.001$, recovery vs control.

TABLE 40.-- CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(i) Urine hydroxyproline excretion rate, mmol/24 hr					
Bed-rest group					
A	0.332	0.253	0.117	76.2	35.2
B	---	---	---	---	---
C	0.433	0.330	.186	76.2	43.0
D	.425	.416	.198	97.9	46.6
E	.455	.227	.380	49.9	83.5
F	.469	.325	.303	69.3	64.6
G	.356	.157	.191	44.1	53.7
H	.396	.124	.292	31.3	73.7
Mean	0.409	0.262[a]	0.238[b]	63.6	57.2
S.D.	±0.051	±0.103	±0.090	±22.9	±17.5
S.E.	±0.019	±0.039	±0.034	±8.6	±6.6
Ambulatory control group					
I	0.241	0.436	0.193	180.9	80.1
J	0.415	.280	.029	67.5	7.0
K	.338	.153	.208	45.3	61.5
L	.074	.136	.286	183.8	386.5
Mean	0.267	0.251	0.179	119.4	133.8
S.D.	±0.147	±0.139	±0.108	±73.3	±171.3
S.E.	±0.074	±0.069	±0.054	±36.6	±85.7
(j) Urine 17-OH corticosteroid excretion rate, mmol/24 hr					
Bed-rest group					
A	1.93	0.94	1.24	48.7	64.2
B	1.53	4.63	---	302.6	---
C	3.51	2.27	5.13	64.7	146.2
D	3.51	1.27	.97	36.2	27.6
E	4.55	2.32	1.69	51.0	37.1
F	---	---	---	---	---
G	3.65	.94	.24	25.8	6.6
H	2.15	.20	1.45	9.3	67.4
Mean	2.98	1.80	1.79	76.9	58.2
S.D.	±1.11	±1.46	±1.71	±101.2	±48.8
S.E.	±0.42	±0.55	±0.70	±38.2	±19.9
Ambulatory control group					
I	2.09	0.86	1.12	41.1	53.6
J	2.77	1.14	1.16	41.2	41.9
K	4.85	.59	.98	12.2	20.2
L	1.11	.56	1.89	50.5	170.3
Mean	2.71	0.79	1.29	36.3	71.5
S.D.	±1.58	±0.27	±0.41	±16.6	±67.3
S.E.	±0.79	±0.14	±0.20	±8.3	±33.7

[a] $p < 0.005$, bed rest vs control.

[b] $p < 0.001$, recovery vs control.

TABLE 40.– CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(k) Urine epinephrine excretion rate, nmol/24 hr					
Bed-rest group					
A	23.5	8.1	10.7	34.5	45.5
B	9.8	7.1		72.4	---
C	9.3	5.9	20.8	63.4	223.7
D	5.5	12.5	21.1	227.3	383.6
E	17.7	12.3	24.4	69.5	137.9
F	8.4	14.3	24.0	170.2	285.7
G	8.5	2.8	8.9	32.9	104.7
H	11.7	1.2	14.4	10.3	123.1
Mean	11.8	8.0	17.8	85.1	186.3
S.D.	±5.9	±4.7	±6.4	±74.9	±117.6
Ambulatory control group					
I	17.8	13.0	11.5	73.0	64.6
J	10.8	11.1	4.7	102.8	43.5
K	9.2	5.4	11.0	58.7	119.6
L	13.3	2.4	13.9	18.0	104.5
Mean	12.8	8.0	10.3	63.1	83.1
S.D.	±3.8	±4.9	±3.9	±35.2	±35.1
S.E.	±1.9	±2.5	±2.0	±17.6	±17.6
(l) Urine norepinephrine/epinephrine excretion (24 hr)					
Bed-rest group					
A	8.6	13.6	24.4	158.1	283.7
B	10.5	7.6		72.4	---
C	14.4	18.0	20.2	125.0	140.3
D	24.4	8.3	9.0	34.0	36.9
E	12.8	7.2	15.9	56.3	124.2
F	15.0	4.8	9.5	32.0	63.3
G	15.6	12.9	13.6	82.7	87.2
H	14.3	41.7	19.9	291.6	139.2
Mean	14.5	14.3	16.1	106.5	125.0
S.D.	±4.7	±11.9	±5.8	±86.5	±80.2
S.E.	±1.7	±4.2	±2.2	±30.6	±30.3
Ambulatory control group					
I	6.5	11.2	23.2	172.3	356.9
J	8.3	10.9	22.6	131.3	272.3
K	15.4	12.6	22.1	81.8	143.5
L	8.4	25.8	12.9	307.1	153.6
Mean	9.7	15.1	20.2[a]	173.1	231.6
S.D.	±3.9	±7.2	±4.9	±96.7	±102.0
S.E.	±2.0	±3.6	±2.4	±48.3	±51.0

[a] $p < 0.05$, recovery vs control.

TABLE 40.– CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(m) Urine cyclic-AMP excretion rate, μmol/24 hr					
Bed-rest group					
A	1.91	1.05	1.59	55.0	83.2
B	1.17	1.40	----	119.7	----
C	1.48	3.28	1.93	221.6	130.4
D	1.62	1.22	1.26	75.3	77.8
E	2.80	2.97	2.55	106.1	91.1
F	1.74	2.29	1.56	131.6	89.7
G	1.61	.96	1.81	59.6	112.4
H	2.54	1.02	1.38	40.2	54.3
Mean	1.86	1.77	1.73	101.1	91.3
S.D.	±0.55	±0.94	±0.43	±58.6	±24.5
S.E.	±0.19	±0.33	±0.16	±20.7	±9.2
Ambulatory control group					
I	0.87	2.74	1.64	314.9	188.5
J	1.40	3.01	1.32	215.0	94.3
K	1.82	2.01	2.34	110.4	128.6
L	2.13	1.89	1.82	88.7	85.4
Mean	1.56	2.41	1.78	182.3	124.2
S.D.	±0.55	±0.55	±0.43	±104.2	±46.7
S.E.	±0.27	±0.27	±0.21	±52.1	±23.4
(n) Urine osmotic activity, mosm/mol creatinine					
Bed-rest group					
A	72.1	39.0	40.2	54.1	55.8
B	65.9	43.1	----	65.4	----
C	88.7	85.3	93.4	96.2	105.3
D	77.6	76.5	89.3	98.6	115.1
E	93.4	62.8	82.8	67.2	88.7
F	97.1	57.1	70.1	58.8	72.2
G	41.5	62.2	63.9	149.9	202.2
H	97.0	68.2	88.7	70.3	91.4
Mean	79.2	61.8[a]	78.3	82.6	104.4
S.D.	±19.2	±15.6	±18.4	±31.7	±47.4
S.E.	±6.8	±5.5	±6.9	±11.2	±17.9
Ambulatory control group					
I	87.0	87.4	89.1	100.5	102.4
J	104.3	83.6	91.5	80.2	87.7
K	102.6	76.7	72.6	74.8	70.8
L	104.2	69.0	104.6	66.2	100.4
Mean	99.5	79.2	89.5	80.4	90.3
S.D.	±8.4	±8.1	±13.1	±14.6	±14.6
S.E.	±4.2	±4.1	±6.6	±7.3	±7.3

[a] $p < 0.05$, bed rest vs control.

TABLE 40.—CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(o) Urine chloride excretion, mol/mol creatinine					
Bed-rest group					
A	15.8	5.6	8.0	35.4	50.6
B	17.6	6.9	—	39.2	—
C	22.7	13.0	15.8	57.3	69.6
D	23.0	12.9	21.0	56.1	91.3
E	23.6	11.5	13.8	48.7	58.5
F	28.6	10.8	18.6	37.8	65.0
G	14.6	11.2	21.2	76.7	145.2
H	21.9	10.2	21.2	46.6	96.8
Mean	21.0	10.3[a]	17.1	49.7	82.4
S.D.	±4.7	±2.7	±4.9	±13.6	±32.4
S.E.	±1.6	±0.9	±1.9	±4.8	±12.2
Ambulatory control group					
I	20.0	18.2	19.6	91.0	98.0
J	23.9	13.7	26.3	57.3	110.0
K	15.6	15.7	15.4	100.6	98.7
L	29.7	12.7	28.3	42.8	95.3
Mean	22.3	15.1	22.4	72.9	100.5
S.D.	±6.0	±2.4	±6.0	±27.4	±6.5
S.E.	±3.0	±1.2	±3.0	±13.7	±3.3
(p) Urine sodium excretion, mol/mol creatinine					
Bed-rest group					
A	15.4	5.2	7.6	33.8	49.4
B	18.4	9.1	—	49.5	—
C	22.1	15.7	16.5	71.0	74.7
D	24.4	19.8	21.7	81.1	88.9
E	25.3	17.0	16.4	67.2	64.8
F	35.0	13.9	21.0	39.7	60.0
G	14.2	13.1	24.4	92.3	171.8
H	21.1	12.1	24.7	57.3	117.1
Mean	22.0	13.2[b]	18.9	61.5	89.5
S.D.	±6.6	±4.6	±6.0	±20.2	±42.5
S.E.	±2.3	±1.6	±2.3	±7.1	±16.1
Ambulatory control group					
I	18.7	20.8	20.3	111.2	108.6
J	26.5	13.3	26.3	50.2	99.2
K	13.7	21.3	17.5	155.5	82.2
L	33.1	16.3	31.0	49.2	93.7
Mean	23.0	17.9	23.8	91.5	95.9
S.D.	±8.5	±3.8	±6.1	±51.6	±11.0
S.E.	±4.3	±1.9	±3.0	±25.8	±5.5

[a] $p < 0.001$, bed rest vs control.

[b] $p < 0.005$, bed rest vs control.

TABLE 40.– CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(q) Urine potassium excretion, mol/mol creatinine					
Bed-rest group					
A	4.47	3.27	3.07	73.1	68.7
B	3.80	2.35	---	61.8	---
C	7.22	6.36	10.63	88.1	147.2
D	8.19	5.65	4.82	69.0	58.9
E	7.75	6.24	6.07	80.5	78.3
F	7.93	4.59	4.48	57.9	56.5
G	4.92	3.86	3.57	78.5	72.6
H	7.55	3.70	5.65	49.0	74.8
Mean	6.48	4.50[a]	5.47	69.7	79.6
S.D.	±1.77	±1.46	±2.51	±13.0	±30.9
S.E.	±0.63	±0.52	±0.95	±4.6	±11.7
Ambulatory control group					
I	5.86	5.87	9.95	100.2	169.8
J	5.85	6.38	5.29	109.1	90.4
K	5.18	4.50	4.20	86.9	81.1
L	7.44	6.00	4.98	80.6	66.9
Mean	6.08	5.69	6.11	94.2[b]	102.1
S.D.	±0.96	±0.82	±2.60	±12.9	±46.2
S.E.	±0.48	±0.41	±1.30	±6.4	±23.1
(r) Urine magnesium excretion, mol/mol creatinine					
Bed-rest group					
A	250	275	141	110.0	56.4
B	307	441	---	143.6	---
C	299	677	330	226.4	110.4
D	400	945	359	236.3	89.8
E	395	592	470	149.9	119.0
F	344	636	283	184.9	82.3
G	267	343	369	128.5	138.2
H	424	457	413	107.8	97.4
Mean	336	546[c]	338	160.9	99.1
S.D.	±65	±214	±105	±49.9	±26.6
S.E.	±23	±76	±40	±17.6	±10.1
Ambulatory control group					
I	411	683	315	166.2	76.6
J	280	458	342	163.6	122.1
K	253	526	333	207.9	131.6
L	695	620	525	89.2	75.5
Mean	410	572	379	156.7	101.5
S.D.	±202	±100	±98	±49.4	±29.6
S.E.	±101	±50	±49	±24.7	±14.8

[a] $p < 0.005$, bed rest vs control.

[b] $p < 0.05$, bed rest vs ambulatory control.

[c] $p < 0.05$, bed rest vs control.

TABLE 40. CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(s) Urine calcium excretion rate, mol/mol creatinine					
Bed-rest group					
A	372	357	264	96.0	71.0
B	319	611	---	191.5	---
C	559	741	361	132.6	64.6
D	550	798	618	145.1	112.4
E	520	722	597	138.8	114.8
F	548	626	471	114.2	85.9
G	276	273	431	98.9	156.2
H	544	493	557	90.6	102.4
Mean	461	578[a]	471	126.0	101.0
S.D.	±118	±188	±130	±33.6	±31.2
S.E.	±42	±67	±49	±11.9	±11.8
Ambulatory control group					
I	457	619	416	135.4	91.0
J	461	548	533	118.9	115.6
K	503	567	434	112.7	86.3
L	452	451	517	99.8	114.4
Mean	468	546	475	116.7	101.8
S.D.	±23	±70	±59	±14.8	±15.3
S.E.	±12	±35	±29	±7.4	±7.7
(t) Urine phosphate excretion, mol/mol creatinine					
Bed-rest group					
A	1.65	1.80	1.46	109.1	88.5
B	1.94	2.80	---	144.3	---
C	3.08	3.72	4.01	120.8	130.2
D	3.28	3.84	3.02	117.1	92.1
E	2.27	3.48	3.24	153.3	142.7
F	2.28	2.89	2.41	126.8	105.7
G	2.09	2.27	2.42	108.6	115.8
H	2.39	2.77	3.60	115.9	150.6
Mean	2.37	2.95[a]	2.88	124.5	117.9
S.D.	±0.55	±0.71	±0.86	±16.3	±24.2
S.E.	±0.20	±0.25	±0.32	±5.8	±9.2
Ambulatory control group					
I	2.56	3.75	2.64	146.5	103.1
J	2.66	3.24	2.40	121.8	90.2
K	2.05	3.08	2.68	150.2	130.7
L	2.70	2.15	3.63	79.6	134.4
Mean	2.49	3.06	2.84	124.5	114.6
S.D.	±0.30	±0.67	±0.54	±32.5	±21.4
S.E.	±0.15	±0.33	±0.27	±16.2	±10.7

[a] $p < 0.05$, bed rest vs control.

TABLE 40. CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(u) Urine total nitrogen excretion, g/mmol creatinine					
Bed-rest group					
A	0.86	0.62	0.50	72.1	58.1
B	.73	.62	---	84.9	---
C	1.35	1.52	1.28	112.6	94.8
D	1.61	1.37	.91	85.1	56.5
E	1.25	1.05	1.07	84.0	85.6
F	.85	1.05	.77	123.5	90.6
G	.89	.70	.93	78.7	104.5
H	1.26	.77	1.15	61.1	91.3
Mean	1.10	0.96	0.94	87.8	83.1
S.D.	±0.31	±0.34	±0.26	±20.6	±18.5
S.E.	±0.11	±0.12	±0.10	±7.3	±7.0
Ambulatory group					
I	1.14	1.15	0.98	100.9	86.0
J	1.33	1.47	.81	110.5	60.9
K	1.15	.72	.87	62.6	75.7
L	.88	1.58	1.50	179.5	170.5
Mean	1.13	1.23	1.04	113.4	98.3
S.D.	±0.19	±0.39	±0.31	±48.7	±49.2
S.E.	±0.09	±0.19	±0.16	±24.3	±24.6
(v) Urine ammonia excretion, mol/mol creatinine					
Bed-rest group					
A	2.42	1.97	1.96	81.4	81.0
B	2.10	4.57	---	217.6	---
C	3.30	4.36	3.84	132.1	116.4
D	2.81	3.52	3.82	125.3	135.9
E	3.36	3.58	4.53	106.5	134.8
F	2.79	4.26	3.44	152.7	123.3
G	2.56	2.43	2.37	94.9	92.6
H	2.34	3.01	1.81	128.6	77.4
Mean	2.71	3.46	3.11	129.9	108.8
S.D.	±0.45	±0.94	±1.06	±42.0	±24.8
S.E.	±0.16	±0.33	±0.40	±14.9	±9.4
Ambulatory control group					
I	3.35	4.67	1.24	139.4	37.0
J	2.21	3.58	2.40	162.0	108.6
K	4.30	2.32	3.33	54.0	77.4
L	2.92	3.90	2.82	133.6	96.6
Mean	3.20	3.62	2.45	122.3	79.9
S.D.	±0.87	±0.98	±0.89	±47.1	±31.4
S.E.	±0.44	±0.49	±0.45	±23.6	±15.7

TABLE 40.-- CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(w) Urine urea excretion, mol/mol creatinine					
Bed-rest group					
A	44.2	20.4	16.4	46.2	37.1
B	31.5	20.6	.....	65.4	.....
C	57.5	48.1	44.6	83.7	77.6
D	59.5	40.3	40.0	67.7	67.2
E	66.2	50.1	42.4	75.7	64.0
F	40.2	33.9	38.7	84.3	96.3
G	30.6	26.1	31.3	85.3	102.3
H	41.5	29.1	35.0	70.1	84.3
Mean	46.4	33.6[a]	35.5[b]	72.3	75.5
S.D.	±13.2	±11.6	±9.5	±13.1	±22.0
S.E.	±4.7	±4.1	±3.6	±4.6	±8.3
Ambulatory control group					
I	43.2	38.6	34.6	89.4	80.1
J	54.5	46.3	34.6	85.0	63.5
K	38.8	28.4	29.9	73.2	77.1
L	38.7	27.4	41.4	70.8	107.0
Mean	43.8	35.2[c]	35.1	79.6	81.9
S.D.	±7.4	±9.0	±4.7	±9.0	±18.2
S.E.	±3.7	±4.5	±2.4	±4.5	±9.1
(x) Urine creatine excretion, mmol/mol creatinine					
Bed-rest group					
A	82	164	85	200.0	103.6
B	155	176	.....	113.5	.....
C	269	349	569	129.7	211.5
D	349	487	217	139.5	62.2
E	355	216	108	60.8	30.4
F	311	333	203	107.1	65.3
G	212	502	205	236.8	96.7
H	127	308	155	242.5	122.0
Mean	233	317	220	153.7	98.8
S.D.	±104	±130	±162	±65.6	±58.3
S.E.	±37	±46	±61	±23.2	±22.0
Ambulatory control group					
I	169	207	73	122.5	43.2
J	400	200	615	50.0	153.8
K	256	393	130	153.5	50.8
L	256	193	113	75.4	44.1
Mean	270	248	233	100.4	73.0
S.D.	±96	±97	±256	±46.5	±54.0
S.E.	±48	±48	±128	±23.2	±27.0

[a] $p < 0.001$, bed rest vs control.

[b] $p < 0.05$, recovery vs control.

[c] $p < 0.01$, bed rest vs control.

TABLE 40.– CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(y) Urine hydroxyproline excretion rate, mmol/mol creatinine					
Bed-rest group					
A	32.2	33.5	19.4	104.0	60.2
B	---	---	---	---	---
C	46.5	39.8	32.3	85.6	69.5
D	40.5	55.9	29.5	138.0	72.8
E	44.5	30.6	34.1	68.8	76.6
F	57.0	37.7	39.2	66.1	68.8
G	41.9	31.3	33.7	74.7	80.4
H	38.6	29.4	30.6	76.2	79.3
Mean	43.0	36.9	31.3[a]	87.6	72.5
S.D.	±7.7	±9.2	±6.1	±25.6	±7.1
S.E.	±2.9	±3.5	±2.3	±9.7	±2.7
Ambulatory control group					
I	26.5	50.8	21.2	191.7	80.0
J	41.2	30.8	6.0	74.8	14.6
K	36.5	22.4	19.2	61.4	52.6
L	9.2	27.4	32.2	297.8	350.0
Mean	28.4	32.9	19.7	156.4	124.3
S.D.	±14.2	±12.5	±10.7	±110.9	±152.8
S.E.	±7.1	±6.2	±5.4	±55.5	±76.4
(z) Urine glucose excretion, mmol/mol creatinine					
Bed-rest group					
A	38.9	11.1	23.1	28.5	59.4
B	60.7	27.6	---	45.5	---
C	55.6	54.3	---	97.7	---
D	6.59	44.2	74.7	67.1	113.4
E	57.5	60.5	104.1	105.2	181.0
F	112.0	54.9	121.1	49.0	108.1
G	35.5	39.2	41.2	110.4	116.1
H	37.6	25.6	45.8	68.1	121.8
Mean	58.0	39.7[b]	68.3	71.4	116.6
S.D.	±24.7	±17.2	±38.5	±30.2	±38.8
S.E.	±8.7	±6.1	±15.7	±10.7	±15.8
Ambulatory control group					
I	52.7	44.9	42.4	85.2	80.5
J	49.0	34.8	60.0	71.0	122.4
K	43.8	30.9	32.8	70.5	74.9
L	65.3	37.2	57.3	57.0	87.7
Mean	52.7	37.0[b]	48.1	70.9	91.4
S.D.	±9.2	±5.9	±12.8	±11.5	±21.3
S.E.	±4.6	±3.0	±6.4	±5.8	±10.7

[a] $p < 0.001$, recovery vs control.

[b] $p < 0.05$, bed rest vs control.

TABLE 40.– CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(aa) Urine citrate excretion, mol/mol creatinine					
Bed-rest group					
A	104	130	128	125.0	123.1
B	281	263	---	93.6	---
C	226	419	601	185.4	265.9
D	208	341	485	163.9	233.2
E	416	736	690	176.9	165.9
F	425	667	375	156.9	88.2
G	226	428	521	189.4	230.5
H	278	415	402	149.3	144.6
Mean	271	425[a]	457[b]	155.1	178.8
S.D.	±107	±198	±182	±32.5	±65.7
S.E.	±38	±70	±69	±11.5	±24.8
Ambulatory control group					
I	287	411	702	143.2	244.6
J	310	365	565	117.7	182.3
K	258	601	339	232.9	131.4
L	574	736	518	128.2	90.2
Mean	357	528	531	155.5	162.1
S.D.	±146	±172	±150	±52.7	±66.6
S.E.	±73	±86	±75	±26.3	±33.3
(bb) Urine 17-OH corticosteroid excretion, μmol/mol creatinine					
Bed-rest group					
A	187	124	206	66.3	110.2
B	177	857	---	484.2	---
C	377	273	891	72.4	236.3
D	335	171	144	51.0	43.0
E	445	313	151	70.3	33.9
F	---	---	---	---	---
G	429	187	42	43.6	9.8
H	209	47	152	22.5	72.7
Mean	308	282	264	115.8	84.3
S.D.	±116	±269	±312	±163.4	±82.1
S.E.	±44	±102	±127	±61.8	±33.5
Ambulatory control group					
I	230	100	123	43.5	53.5
J	275	125	242	45.5	88.0
K	524	87	91	16.6	17.4
L	138	113	213	81.9	154.3
Mean	292	106	167	46.9	78.3
S.D.	±165	±16	±72	±26.8	±58.3
S.E.	±82	±8	±36	±13.4	±29.1

[a] $p < 0.01$, bed rest vs control.

[b] $p < 0.05$, recovery vs control.

TABLE 40. CONTINUED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(cc) Urine epinephrine excretion, μmol/mol creatinine					
Bed-rest group					
A	2.28	1.07	1.78	46.9	78.1
B	1.13	1.31	---	115.9	---
C	1.00	.71	3.61	71.0	361.0
D	.52	1.68	3.14	323.1	603.8
E	1.73	1.66	2.19	96.0	126.6
F	1.02	1.66	3.10	162.7	186.7
G	1.00	.56	1.57	56.0	157.0
H	1.14	.28	1.51	24.6	132.5
Mean	1.23	1.12	2.41[a]	112.0	235.1
S.D.	±0.54	±0.55	±0.85	±95.7	±185.8
S.E.	±0.19	±0.19	±0.32	±33.8	±70.2
Ambulatory control group					
I	1.96	1.51	1.26	77.0	64.3
J	1.07	1.22	.98	114.0	91.6
K	.99	.79	1.02	79.8	103.0
L	1.65	.48	1.57	29.1	95.2
Mean	1.42	1.00	1.21	75.0	88.5
S.D.	±0.47	±0.46	±0.27	±34.9	±16.8
S.E.	±0.23	±0.23	±0.14	±17.5	±8.4
(dd) Urine norepinephrine excretion, μmol/mol creatinine					
Bed-rest group					
A	19.7	14.6	43.4	74.1	220.3
B	11.9	10.0	---	84.0	---
C	14.4	12.8	73.1	88.9	507.6
D	12.8	14.0	28.1	109.4	219.5
E	22.1	11.9	34.7	53.8	157.0
F	15.3	7.9	29.6	51.6	193.5
G	15.6	7.2	21.4	46.2	137.2
H	16.3	11.8	30.1	72.4	184.7
Mean	16.0	11.3[b]	37.2[a]	72.6	231.4
S.D.	±3.4	±2.7	±17.2	±21.5	±125.6
S.E.	±1.2	±1.0	±6.5	±7.6	±47.5
Ambulatory control group					
I	12.7	17.0	29.3	133.9	230.7
J	8.9	13.3	22.1	149.4	248.3
K	15.3	10.0	22.5	65.4	147.1
L	13.9	12.5	20.3	89.9	146.0
Mean	12.7	13.2	23.6[a]	109.7	193.0
S.D.	±2.7	±2.9	±4.0	±38.8	±54.1
S.E.	±1.4	±1.4	±2.0	±19.4	±27.1

[a] $p < 0.05$, recovery vs control.

[b] $p < 0.01$, bed rest vs control.

TABLE 40.- CONCLUDED.

Subject	Control (Day 7)	Bed rest (Day 17)	Recovery (Day 6)	%Δ from control	
				Bed rest	Recovery
(ee) Urine cyclic-AMP excretion, μmol/mol creatinine					
Bed-rest group					
A	185	139	264	75.1	142.7
B	135	259	---	191.9	---
C	159	395	335	248.4	210.7
D	154	164	188	106.5	122.1
E	274	400	228	146.0	83.2
F	211	266	202	126.1	95.7
G	189	191	320	101.1	169.3
H	247	242	145	98.0	58.7
Mean	194	257	240	136.6	126.1
S.D.	±48	±98	±70	±57.6	±52.6
S.E.	±17	±35	±26	±20.4	±19.9
Ambulatory control group					
I	96	319	180	332.3	187.5
J	139	331	275	238.1	197.8
K	197	295	216	149.7	109.6
L	264	380	205	143.9	77.7
Mean	174	331[a]	219	216.0	143.2
S.D.	±73	±36	±40	±88.7	±58.8
S.E.	±36	±18	±20	±44.4	±29.4

[a] $p < 0.05$, bed rest vs control.

APPENDIX B

SUPPORTING GYNECOLOGICAL DATA ON FEMALE BED REST SUBJECTS

The tables in this section present detailed data on the daily fluid intake and outtake values for each subject as well as daily weights; time and duration of onset of each subject's menstrual period is indicated.

TABLE 41.– FEMALE BODY WEIGHT

Experimental parameter, day		Bed-rest group											Ambulatory group						
		A[a]	B[a]	C[b]	D[b]	E[b]	F[b]	G[b]	H[b]	Mean	S.D.	S.E.	I[a]	J[a]	K[b]	L[c]	Mean	S.D.	S.E.
Control	1	62.1	55.91	62.27	53.41	60.50	49.09	52.39	65.45	57.64	5.76	2.04	47.50	58.75	62.70	50.45	54.85	7.08	3.54
	2	62.52	51.42	61.70	54.45	59.50	49.89	53.50	65.68	57.33	5.78	2.04	49.10	59.12	63.50	49.77	55.37	7.09	3.55
	3	60.40	51.20	62.00	54.94	55.30	50.91	52.73	65.68	56.65	5.44	1.92	48.30	59.12	65.70	50.91	56.01	7.94	3.97
	4	61.40	51.45	63.40	55.16	54.40	50.40	53.42	65.52	56.89	5.73	2.03	48.60	60.00	63.70	50.90	55.80	7.21	3.60
	5	60.90	55.50	63.45	55.00	52.30	50.10	52.86	66.43	57.07	5.84	2.06	50.90	61.70	64.90	50.40	56.98	7.42	3.71
	6	60.40	55.50	63.00	54.83	52.40	50.50	53.90	66.90	57.18	5.67	2.01	47.45	60.50	64.10	51.00	55.76	7.83	3.91
	7	60.75	55.30	63.35	53.10	53.20	50.38	53.00	66.47	56.94	5.81	2.05	47.65	61.50	64.10	51.00	56.06	7.97	3.99
	8	61.30	55.00	63.50	56.10	54.00	50.88	53.74	66.67	57.65	5.51	1.95	48.20	61.00	64.80	51.67	56.42	7.77	3.89
	9	60.30	55.41	62.80	56.90	59.40	50.40	53.34	65.53	58.01	4.99	1.76	47.12	60.90	65.10	50.65	55.94	8.45	4.23
	10	59.80	55.89	62.50	58.38	59.50	50.37	53.68	66.70	58.35	5.10	1.80	47.90	60.40	64.70	50.37	55.84	8.01	4.00
	11	59.80	55.24	62.50	58.60	61.36	50.21	53.71	66.78	58.53	5.30	1.87	48.50	60.40	64.75	50.74	55.10	7.74	3.87
	12	59.60	55.55	63.00	56.80	61.00	52.02	53.80	66.64	58.55	4.92	1.74	47.80	59.50	64.03	50.09	55.36	7.69	3.84
	13	60.10	55.36	62.70	56.00	61.40	51.98	52.80	66.50	58.36	5.12	1.80	47.50	59.80	65.22	51.10	55.91	8.08	4.04
	14	59.75	55.00	62.48	56.52	61.00	51.80	52.65	66.24	58.18	5.04	1.78	47.00	60.20	64.24	50.88	55.71	8.18	4.09
Bed rest	15	58.66	55.00	62.01	55.10	59.61	47.70	52.49	65.60	57.02	5.65	2.00	48.39	60.33	64.41	50.66	55.95	7.66	3.83
	16	58.10	55.10	61.90	54.00	59.88	47.80	52.43	64.32	56.69	5.40	1.90	48.18	60.28	64.46	51.06	56.00	7.65	3.82
	17	57.60	54.74	62.15	55.00	60.30	46.20	52.48	64.94	56.68	5.93	2.10	48.36	60.06	64.82	50.26	55.88	7.86	3.93
	18	57.57	54.53	62.10	55.00	60.63	46.60	52.48	65.90	56.85	6.06	2.14	47.94	60.30	64.76	50.32	55.83	8.01	4.00
	19	57.30	54.36	61.70	56.40	60.79	46.60	53.10	65.60	56.98	5.87	2.08	48.46	59.60	64.54	50.64	55.81	7.56	3.78
	20	57.30	54.24	62.75	55.75	60.43	47.62	52.80	67.40	57.29	6.18	2.18	48.50	60.30	64.97	50.80	56.14	7.79	3.90
	21	56.40	54.08	63.68	56.90	60.19	47.35	52.84	65.10	57.07	5.85	2.07	48.10	60.60	64.80	51.45	56.24	7.78	3.89
	22	57.03	54.20	62.58	56.50	60.14	46.95	52.10	65.42	56.87	5.91	2.09	47.77	60.50	64.57	51.35	56.05	7.81	3.91
	23	56.30	54.21	62.75	56.60	60.25	46.85	52.35	65.40	56.84	5.94	2.10	48.90	60.00	64.47	51.45	56.21	7.27	3.64
	24	56.30	54.17	62.70	56.50	60.49	46.85	52.78	64.80	56.82	5.79	2.05	48.10	60.56	64.47	49.86	55.75	8.01	4.00
	25	56.36	53.68	61.95	55.90	59.76	46.90	52.40	65.74	56.59	5.89	2.08	48.10	60.56	64.72	49.62	55.75	8.16	4.08
	26	56.10	53.56	62.70	55.50	59.89	46.70	52.30	64.45	56.40	5.81	2.06	47.60	60.60	64.04	50.15	55.60	7.96	3.98
	27	56.20	53.56	62.75	56.00	60.00	47.22	52.55	65.78	56.76	5.95	2.10	47.96	60.67	64.12	49.54	55.57	8.00	4.00
	28	56.10	53.52	62.44	55.62	60.00	47.06	51.95	66.00	56.59	6.06	2.14	48.01	60.60	64.10	49.50	55.55	8.00	4.00
	29	56.30	53.38	62.70	55.50	59.87	46.50	52.35	65.35	56.49	6.05	2.14	48.00	60.00	64.05	49.52	55.39	7.86	3.92
	30	55.70	53.12	62.80	55.50	59.55	46.36	52.40	65.45	56.36	6.11	2.16	48.44	60.53	64.00	49.64	55.65	7.78	3.89
	31	55.20	53.44	62.00	55.70	59.84	47.50	52.40	65.45	56.44	5.74	2.03	48.67	60.23	64.34	50.39	55.91	7.59	3.79
Recovery	32	55.20	53.84	62.00	55.00	60.62	47.20	53.40	66.11	56.67	5.93	2.10	48.00	60.05	64.34	50.39	55.70	7.77	3.88
	33	56.20	54.11	63.50	56.50	60.62	47.30	53.58	66.30	57.26	6.05	2.14	48.50	60.40	63.86	51.49	56.06	7.25	3.63
	34	56.28	54.42	63.75	55.85	60.70	47.82	53.20	66.90	57.37	6.13	2.17	48.00	60.50	64.00	51.40	55.98	7.51	3.76
	35	56.85	54.72	63.48	55.72	60.33	47.72	53.30	65.82	57.24	5.82	2.06	48.14	61.00	63.95	50.80	55.97	7.68	3.84

[a] Day 14 September 30.

[b] Day 15 October 1.

[c] No menses during study.

menses

spotting

TABLE 42.– FLUID INTAKE – URINE OUTPUT

Experimental parameter, day		Fluid intake-output, ml — Bed-rest group subjects																								
		A			B			C			D			E			F			G			H			
		In	Out	Δ	In	Out	Δ	In	Out	Δ	In	Out	Δ	In	Out	Δ	In	Out	Δ	In	Out	Δ	In	Out	Δ	
Control	1	---	1176		715	1255	-540	2060	1495	+565	2065	1489	+576	3255	3087	+168	1605	1914	-309	2225	2343	-118	1235	2211	-987	
	2	1260	1941	-681	1020	888	+132	1290	1018	+272	1825	1595	+230	2835	3164	-329	1845	2011	-166	1455	1335	+121	1400	1164	+236	
	3	1635	922	+713	1050	911	+139	1930	1781	+149	1585	2187	-602	3180	2513	+667	1480	2277	-797	1050	1068	-18		1527		
	4	1200	1507	-307	800	805	-5	1395	1700	-305	2075	2834	-759	2990	3397	-407	2460	3303	-843	1475	1228	+247	1375	1791	-416	
	5	1655	1168	+487	1215	988	+227	1620	1240	+380	1560	3230	-1670	3525	3406	+119	2375	2533	-158	950	1624	-674	2175	1766	+409	
	6	1825	1199	+626	1135	830	+305	1270	1263	+7	2360	2338	+22	3680	3543	+137	1260	2173	-913	2540	2038	+502	1800	1899	-99	
	7	1835	1350	+485	1155	1000	+155	1895	1027	+868	2620	2822	-202	3090	2910	+180	2165	2330	-165	1460	1276	+184	1265	1526	-522	
	8	1430	---	---	1005	1000	+5	1700	1740	-40	2610	1740	+870	2770	2550	+220	2150	---	---	690	900	-210	1575	1200	+370	
	9	1150	1214	-64	1735	1931	-196	2590	1800	+790	2515	1750	+760	3015	1957	+1058	1660	2552	-892	1205	1492	-287	1535	---	---	
	10	1065	1845	-780	995	1175	-180	1740	1708	+32	2345	1908	+437	3570	2820	+750	2255	2637	-382	1230	765	+465	1960	1306	+654	
	11	1260	916	+344	1315	1651	-336	1715	1290	+425	1840	2715	-875	2965	3745	-780	2070	3585	-1515	2260	2440	-180	1475	1014	+461	
	12	1460	843	+617	975	1145	-170	1345	1036	+309	1835	3437	-1602	3725	4110	-385	3210	3430	-220	1885	2283	-398	1535	1373	+162	
	13	1425	731	+694	900	641	+259	1200	1421	-221	1870	1558	+312	3300	3322	-22	3780	3072	+708	730	1238	-508	1525	1079	+446	
	14	1020	1617	-597	1430	1867	-437	1645	1487	+158	1868	3305	-1497	3160	4643	-1483	2400	2256	+144	1085	884	+201	1555	1147	+408	
Bed rest	15	955	---	---	1240	1271	-31	1505	1195	+310	1970	2675	-705	3045	4083	-1038	2730	2542	+188	2062	2235	-173	1800	2428	-628	
	16	1815	1534	+281	850	1372	-522	1565	884	+681	1400	1620	-220	2890	3028	-138	2480	2449	+31	2935	3372	-437	1305	1197	+108	
	17	1660	1212	+448	1480	1190	+290	1765	1420	+345	1765	2387	-622	3015	2413	+602	2040	1762	+278	3060	3119	-59	1665	1426	+239	
	18	1510	1132	+378	1070	755	+315	1420	1022	+398	1160	1255	-95	3115	2062	+1053	2115	2353	-238	1990	2445	-455	1940	1240	+700	
	19	1290	905	+385	925	668	+257	1550	1165	+385	1720	2294	-574	3180	2623	+557	1310	1336	-26	1115	957	+158	1760	1090	+670	
	20	1220	893	+327	1795	1641	+154	2045	998	+1047	1868	975	+893	3025	2924	+101	2045	1536	+509	1420	1569	-149	1535	1292	+243	
	21	895	754	+141	1045	870	+175	2055	1655	+400	1745	1765	-20	3260	3679	-419	2340	2321	+19	1222	1298	-76	2126	1227	+899	
	22	735	872	-137	1375	1079	+296	1745	1661	+84	1855	2590	-735	2730	2347	+383	1480	3059	-1589	1195	1030	+165	1610	1650	-40	
	23	1115	752	+363	1395	1349	+46	1400	1265	+135	1930	2490	-560	3260	3201	+59	2530	2575	-45	2640	2392	+248	1500	913	+587	
	24	1145	1157	-12	985	1181	-196	2065	1957	+108	1870	3059	-1189	3015	2205	+810	2155	1835	+320	1510	1661	-151	1830	1125	+705	
	25	860	615	+245	1075	1138	-63	1300	1127	+173	1655	1972	-317	3525	3845	-320	2905	3206	-301	900	792	+108	2165	1056	+1109	
	26	1250	1573	-323	1085	645	+440	1740	1220	+520	1670	1986	-316	2670	2762	-92	2580	2745	-165	900	852	+48	1980	1904	+76	
	27	1105	664	+441	1285	1298	-13	2085	1185	+900	1643	2205	-562	3515	2885	+630	2515			1020	670	+341	1630	1165	+465	
	28	1015	475	+540	1380	914	+466	1745	1830	-85	1340	1966	-626	3555	4451	-896	2935	3438	-503	815	921	-106	2090	1483	+607	
	29	915	960	-45	915	950	-35	1535	1213	+322	1915	2524	-609	4040	3974	+66	3240	3498	-258	1085	1089	-4	1490	1118	+372	
	30	800	360	+440	1215	410	+805	1590	930	+660	1755	1040	+715	3640	3510	+130	2700	2875	-175	1150	602	+548	1690	1186	+504	
	31	1065	307	+758	1145	930	+215	2120	843	+1277	1795	1085	+710	3685	1980	+1700	3730	2200	+1530	1100	430	+670	1525	355	+1170	
Recovery	32	1290	373	+917	1175	775	+400	1360	1130	+230	1503	1555	-52	3855	2662	+1193	3610	2020	+1590	1090	315	+775	1790	875	+915	
	33	1030	203	+827	790	514	+276	1840	1188	+652	1635	1385	+250	3640	3628	+12	3421	2654	+767	1655	1121	+534	1679	1780	-101	
	34	1395	247	+1148	1705	869	+836	1995	1640	+355	925	1393	-468	4555	4106	+449	4060	4738	-678	1190	826	+364	1875	1800	+75	
	35	1235	243	+992	1540	---	---	2310	1160	+1150	2070	1720	+300	4720	4004	+716	4570	4296	+274	1470	1450	+20	1440	1860	-420	

NOTE: IN = total fluid intake
OUT = collected urine volume
Δ = difference between intake vs output
( ) = menstrual days

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