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INFLUENCE OF PERIODIC CENTRIFUGATION ON CARDIOVASCULAR FUNCTIONS OF MAN DURING BED REST

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by
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FOREWORD

This study is part of a program concerned with a quantitative demonstration of the feasibility and general effectiveness of a short-radius centrifuge in an orbital laboratory. It was supported by the Crew Systems Division, Manned Spacecraft Center, Houston, Texas, with Mr. W. V. Judy, Space Medicine Branch, serving as technical monitor. Dr. W. J. White was the principal investigator for the Douglas Aircraft Company, Inc., Santa Monica, California.

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SUMMARY

A study was made of the influence of periodic centrifugation on the physiological disturbances associated with 10 days of bed rest. During bed rest the subjects were scheduled to ride the centrifuge 4 times each day; the duration of each ride was 20 min; and the magnitude of acceleration was +2.5 g_z at heart level. Subjects exercised for a 14-day period before the study. The energy cost of this exercise was approximately 1 000 kcal/day/man.

Functional and diagnostic tests conducted at regular intervals during the experiment revealed the following:

1. The prescribed regimen of +2.5 g_z for 20 min exceeded tolerance to positive acceleration. The modal conditioning regimen was +1.75 g_z for 20 min 4 times each day. When the magnitude of acceleration is referenced to foot level, the integrated g-time is 4.7 g-hours.
2. Expected deterioration produced by recumbency in the ability to tolerate 70° head-up tilt for 20 min was largely alleviated by periodic centrifugation, as judged by syncopal episodes and highest orthostatic heart rates.
3. The conditioning regimen did not appear so effective as shorter g-time integrals, as judged by highest orthostatic heart rates and plasma volumes.
4. Step-function acceleration tolerance and tolerance for sustained acceleration are more sensitive than the standard bioassay method for measuring cardiovascular changes at bed rest.
5. Tolerance to positive acceleration declines during the first 12 hours of bed rest, remains relatively constant during bed rest, and improves during ambulation.
6. Losses in body weight were progressive and ranged from 0.98 to 2.35 kg. Average weight loss during the 10-day period was 2%.
7. The condition of the experiment resulted in an average loss of 17% in total blood volume, 26% in plasma volume, and 2% in red blood cell volume.
8. No significant changes were seen in serum electrolytes, bilirubin, glucose, or blood urea nitrogen; in red blood cell, white blood cell,

or reticulocyte counts; in hemoglobin, hematocrit, or in mean corpuscular hemoglobin concentration; in hearing, or in the postural equilibrium; nor was there any change in exercise tolerance as measured by the Master's two-step test.

9. No cardiac irregularities or arrhythemias were encountered in the testing of eight subjects during a total of 135 hours of positive acceleration.

10. Application of negative pressure to the lower half of the body produces cardiovascular changes similar to those seen in 70° head-up tilt. Application of a pressure differential of 70 mm Hg to subjects after 10 days of bed rest produced presyncopal symptoms in 2 to 4 min. During the prerecumbency period, these two subjects tolerated 20 min of negative pressure without symptoms.

INTRODUCTION

Although man adapts, in time, to a null-gravity environment, a transient loss of orthostatic tolerance upon return to Earth's gravity is of major consequence to him. The greater the duration of a space mission, the greater, within limits, is the severity of this deconditioning and the possible impairment of tolerance to entry acceleration and ability to stand or move about after landing. There is, consequently, a need to study methods that will alleviate this condition and will provide more in-flight information regarding man's response to null gravity. Fig. 1 shows various cardio-protective techniques. Of these, the on-board centrifuge is especially attractive because of its potential, not only therapeutically, but also as a research and training device.

Studies of the therapeutic value of the centrifuge show that 45 min each day spent in riding it will largely prevent orthostatic intolerance during bed rest. A centrifuge with a 54-in. radius was used to provide levels of acceleration at the subject's feet of 1 or +4 g_z. The duration of the 4 rides each day was 7.5 or 11 min. Integrated g-time was systematically increased, therefore, from 0.5 and 2 g-hours to 3 g-hours (ref. 1). One goal of the present study was to increase both the magnitude (to +5 g_z) and the duration (to 20 min) of the acceleration to determine (1) if 6.7 g-hours on a longer radius centrifuge (74 in.) could be tolerated by subjects at bed rest, (2) if this conditioning regimen was more effective than the smaller g-time integrals in counteracting the effects of bed rest, and (3) the deleterious effects, if any, on man resulting from exposure to acceleration on a short-radius centrifuge. The subjects were six healthy young men.

Studies of the research uses of an on-board centrifuge show that body mass is measurable to within ±2%, and that a steep heart-to-foot acceleration gradient does not preclude a determination of blackout tolerance. A second goal of this study was to provide additional quantitative support for the uses of the centrifuge by the development and demonstration of bioassay techniques necessary for the evaluation of cardiovascular status. In this concurrent experiment, two subjects were used.

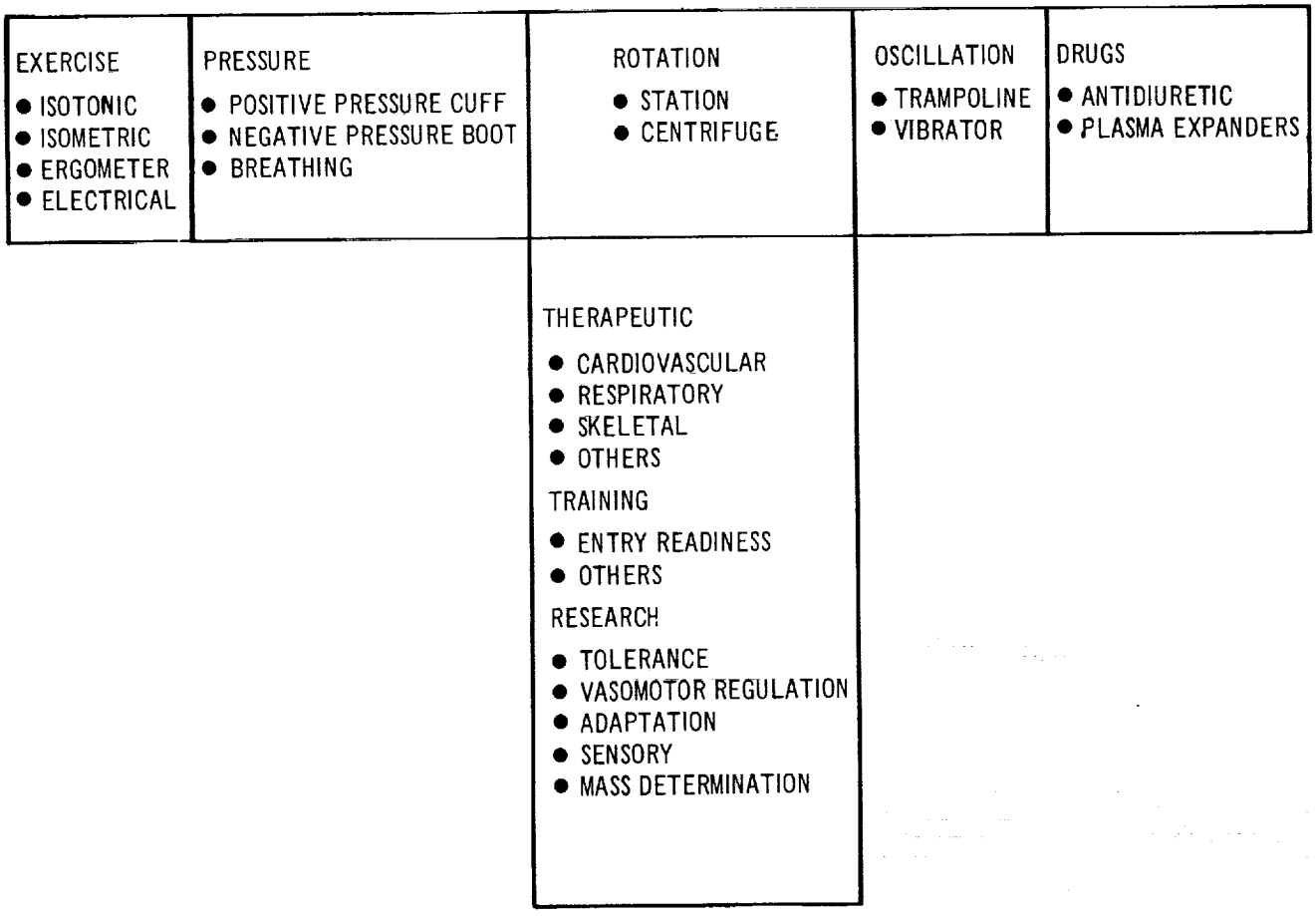

Figure 1. Cardio-Protective Techniques

METHODS

Experimental Plan

The first 12 days of the experiment included 9 days of conditioning exercise, followed by 3 days of baseline (B) measurements and exercise. A 3-day baseline-recovery (BR) period followed the 10-day testing (T) period.

The purpose of the conditioning exercise was to establish a daily level of metabolic activity at least 1 000 kcal greater than that expected during the testing period. The exercise consisted of three periods each day on the bicycle ergometer and three periods each day on the treadmill. Treadmill exercise consisted of running at 5 mph on a 10% grade for 10 min. Measured caloric value of this regimen was 150 kcal, for a total caloric expenditure of 450 kcal/day. Exercise on the bicycle ergometer consisted of a pedaling rate of 60 rpm at a power setting of 200 W. Each period lasted 17 min and resulted in caloric expenditure of 160 to 170 kcal, for a total expenditure of 480 to 510 kcal/day. Exercise on the ergometer was performed in the supine position. Thus, the caloric value of the conditioning regimen on each of the 12 days preceding the testing period was approximately 1 000 kcal/day/man.

During the 3-day baseline and baseline-recovery periods, the subjects resided in the biodynamic ward, but were not confined to their beds. Functional and biochemical tests were conducted during these periods, and monitoring procedures were started.

During the 10-day testing period, the subjects remained at strict bed rest. The only restriction placed on their movements was that the long axis of the cardiovascular system remain horizontal at all times. Emunctory functions were performed in the horizontal position. Monitoring and routine bed-fast nursing care were provided 24 hours a day during the baseline and testing periods.

The conditioning regimen followed by six of the subjects was designed to keep constant the duration, frequency, magnitude, and rate of exposure to acceleration. Duration of the ride was 20 min and the frequency of exposure was 4 times each day. The magnitude of the acceleration was +2.5 g_z, referenced to the level of the subject's heart. These were arrived at on the basis of parameterization of pressure and time (ref. 1). All rides took place between 0830 and 1600 hours. The subjects followed a ride schedule that called for 2 hours between successive rides. Fig. 2 shows the physical aspects of the conditioning. The radius of the centrifuge was 74 in. The heart-to-foot acceleration gradient was 100%. A platform with three seats was mounted on the Douglas human centrifuge. Each subject was placed on his back with his head toward the center of rotation. The legs of the subject were flexed 90° at the hips and knees. This arrangement placed the long axis of the cardiovascular system along a ray line from the center of rotation. The subjects were transported from their beds to the centrifuge and returned to bed by means of a net hammock and traveling hoist.

The protocol for two subjects in the concurrent experiment differed from that of the main experiment in that they made step-function bioassay runs periodically during the testing period. These were not intended as conditioning rides.

Subjects

Table I shows the physical characteristics of the subjects. From a population of nine subjects, Subject BI was removed prior to experimentation on B-2 for tilt-table intolerance; Subjects RM and WW were assigned to the concurrent study. All subjects were paid volunteers. They were free to withdraw from the experiment at any time. Admitting history, physical examination, Master's electrocardiogram (ECG), urinalysis, and blood analyses for each subject were normal. The subjects were placed on a diet calculated to be 2 100 kcal. Average daily calcium intake was calculated to be from 0.6 to 1.0 g. Total blood volumes were estimated from height, weight, and surface area nomographs.

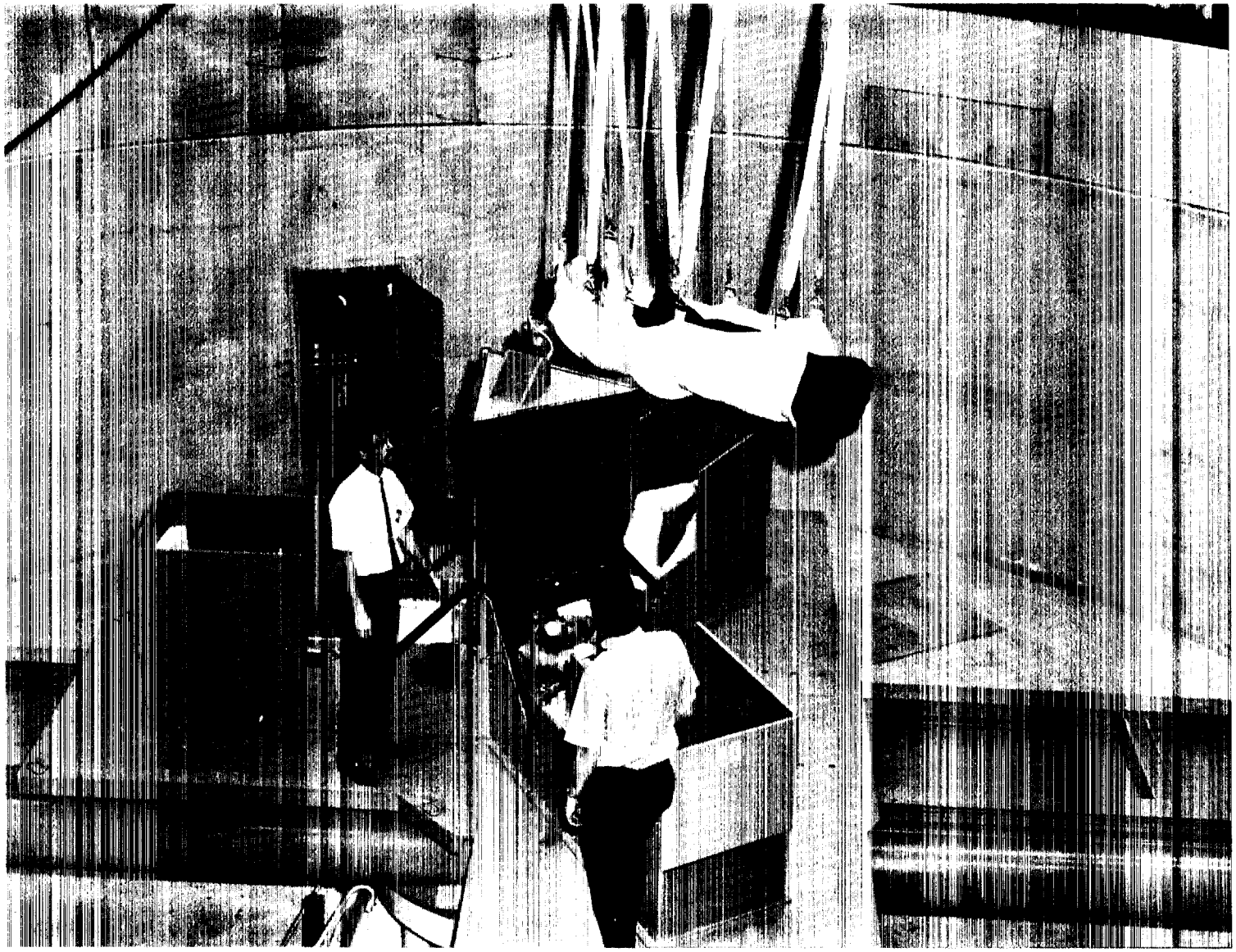

Figure 2. Triple Seating Arrangement on the Centrifuge and the Hammock Used in Transporting the Subjects

TABLE I

PHYSICAL CHARACTERISTICS OF SUBJECTS

Subject	Age	Height (cm)	Weight (kg)	Estimated Blood Volume (ml)
JA	23	184.8	89.09	6550
RE	26	168.9	71.14	5400
JH	21	167.6	72.95	5425
LH	23	179.7	79.32	5950
EH	22	180.3	67.27	5750
LL	22	176.5	77.50	5800
RM	25	188.0	85.68	6400
WW	26	180.3	73.64	5700

Before the study, the subjects were briefed thoroughly on the nature of the experiment, the probable risks, and the steps to be taken to ensure their health and welfare. During the course of the experiment, they were informed of any changes. Also, at the conclusion of the experiment they were told of the findings and given the final technical report to read.

Baseline and Intercurrent Measures

Table II lists the functional, biochemical, and monitoring tests performed during the study. These tests can be further subdivided into baseline measures made before and after the testing period, and the intercurrent measures. Table II gives the dates of each administration of the tests.

The tilt-table test was used to measure the functional reserve of the cardiovascular system. The subject, seated in a saddle, was tilted 70°, head up, for 20 min (unless syncope intervened). Heart-rate and blood-pressure readings were taken every minute before, during, and after the tilt test. The subject was allowed to rest quietly for 5 min before and after the head-up tilt. ECG were taken continuously. All tilt-table tests were conducted by the same physician.

TABLE II

BASELINE AND INTERCURRENT MEASURES

Tests	Date of Determination							
Functional								
Orthostatic tolerance	B-2*	B-3	-	-	-	-	T-10*	BR-1
Lower body negative pressure	B-2*	-	-	-	-	-	T-10*	-
Step-function acceleration tolerance	B-2*	B-3	T-2*	T-4*	T-8*	T-9*	-	BR-1, -2, -3
Sustained acceleration tolerance	B-2	-	-	-	-	-	-	BR-1, -2
Master's two step	B-1	-	-	-	-	-	-	BR-2
Postural equilibrium	-	B-3	-	-	-	-	-	BR-1
Audiometry	-	B-3	-	-	-	-	-	BR-1
Body weight	B-1	-	T-3	T-5	-	T-9	-	BR-1, -2, -3
Biochemical								
Red cell volume (Cr^{51})	B-1	-	-	T-5	-	-	T-10	-
Plasma volume (I^{125})	B-1	-	-	T-5	-	-	T-10	-
Blood--Hematocrit, hemoglobin, MCHC, RBC, WBC, and reticulocyte counts, electrolytes, bilirubin--total and direct, glucose, urea nitrogen	B-1	-	-	T-5	-	-	T-10	-
Monitoring								
Blood pressure Heart and respiration rates Temperature Fluid intake/output Conditioning regimen	Daily							

Note: *Subjects RM and WW only.

Physiological effects similar to those found with the tilt-table test are produced by the application of negative pressure to the lower part of the body. The supine subject was exposed to a pressure differential of 70 mm Hg for 20 min (unless syncope intervened). Fig. 3 shows a subject and the tank used to produce a negative pressure about the lower part of the body. The absolute pressure in the tank was approximately 690 mm Hg (760 mm Hg - 70 mm Hg). Heart-rate and blood-pressure readings were taken every minute before, during, and after the LBNP test. The subject was allowed to rest quietly for 5 min before and after the test. ECG were taken continuously. The LBNP tests were conducted by the same physician.

Tolerance to positive acceleration ($+g_z$) was measured on the centrifuge with a single, step-function run to blackout. Bioassay runs were made at a radius of 74 in. (100% heart-to-foot gradient) with a rate of onset of acceleration of 0.1 g/sec. Each step of the function was approximately 0.4 g higher than the preceding step; duration of the run at each step was 1 min. Blood-pressure and heart-rate readings were taken each minute. ECG were taken continuously, and the subjects responded to the bioassay lights by turning them off when they appeared. Tolerance was defined as the level of acceleration, referenced to heart level, at which blackout occurred.

Tolerance to sustained positive acceleration was measured by a single 20-min run at 1.75, 2.25 or +2.5 g_z. Blackout or the highest heart rate recorded during each run was chosen as the index of physiological performance. The procedure followed was that used in the step-function test of acceleration tolerance.

A routine Master's two-step test with 12-lead ECG was taken in the conventional manner. The results of this test were analyzed by a board-certified cardiologist.

The Graybiel-Fregly test was used to measure postural equilibrium (ref. 2).

Audiograms were accomplished in a conventional manner with a Bekesy-type audiometer.

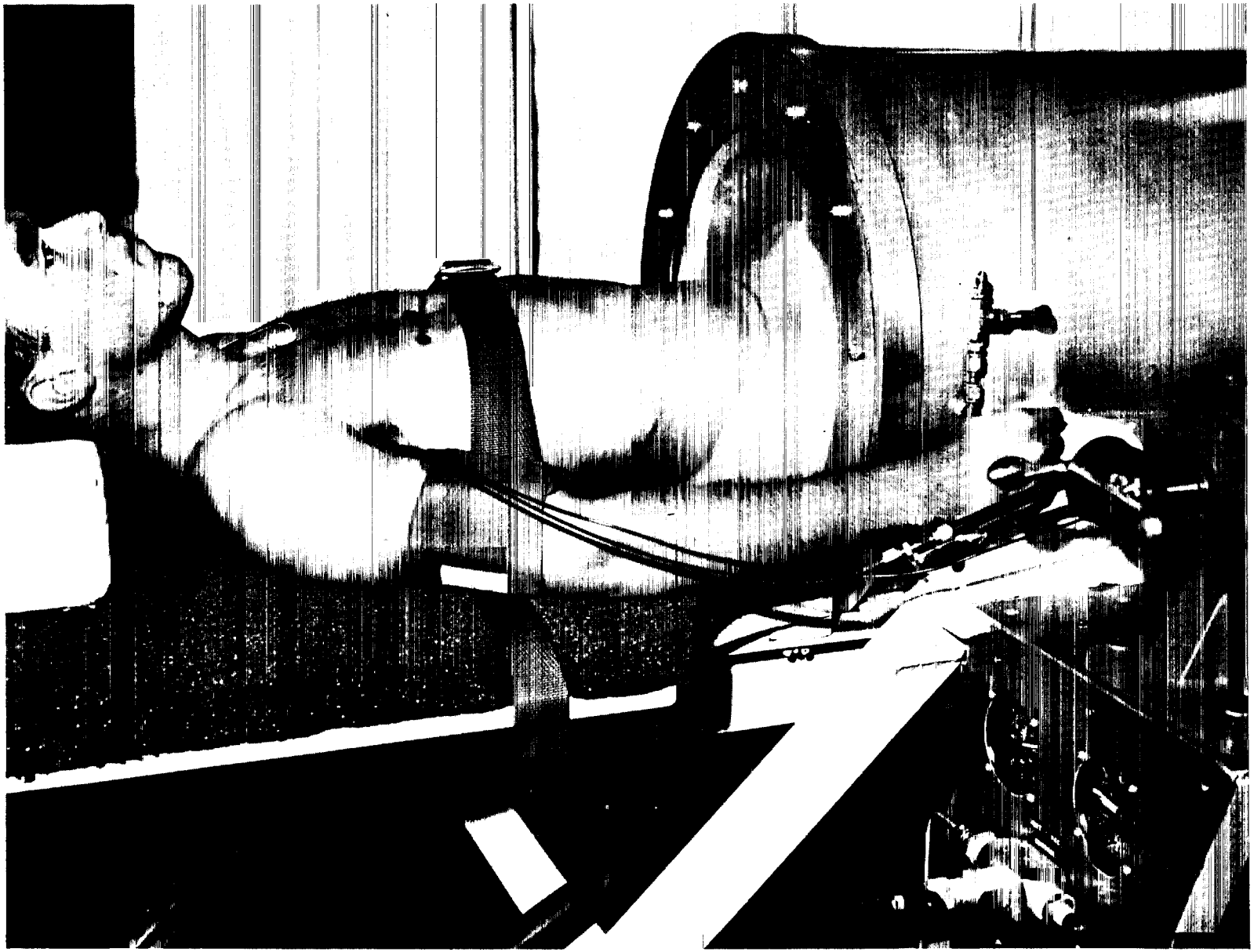

Figure 3. LBNP Test Showing the Position of the Subject, Rubber Pressure Seal, and Control Panel

The experimental plan emphasized chemical studies of the blood and determination of red blood cell (RBCV), plasma (PV), and total blood volumes (TBV). These analyses are listed in Table II. All blood-chemistry samples were drawn in the morning under fasting conditions; volume determinations were made in the afternoon.

Plasma volume was determined by the I^{125} RHISA method, and red blood cell volume by Cr^{51} labeled cells. Total blood volume was calculated directly by summing red cells and plasma volumes as determined by specific methods.* Hematocrits were performed in duplicate on the blood drawn for PV determinations. The subjects were classified as radiological workers. To maintain the radiation dose within limits specified by the Bureau of Standard Handbook 69, a direct determination of red cell volume was not possible on T-10. The volume of red cells on that date was calculated from the Cr^{51} labeled cells injected on T-5 by the assumption of a 6% elution (range 5 to 10%) of the tagged cells on T-5 and the average elution rate over the next 4 days of 1% per day. This procedure is used clinically in red blood cell survival studies where the 24-hour count is taken as the 100% value because of the variable elution during the first 24 hours. The samples were counted in duplicate with a Nuclear-Chicago scaler, pulse height analyzer, and well counter with a 2-in. thallium activated sodium iodine crystal.

*The isotope studies were conducted by Dr. Marvin B. Cohen, Bio-Nuclear Laboratories, Los Angeles, California

RESULTS

Functional Tests

Results of the tilt-table test of orthostatic tolerance are summarized numerically in Table III. During the baseline period, all subjects tolerated the test well and reported feeling alert during the entire procedure. Minimal pallor was the only symptom noted. Heart rates of all subjects were regular and remained below 100 beats/min. Blood and pulse pressures were all within a normal range. After 10 days of bed rest and periodic centrifugation, all subjects were again tilted. Except for Subject JA, the subjects showed an excellent response to tilt. They had minimal pallor, and normal blood and pulse pressures. Integrated heart rates were 20% higher than baseline rates, and the average integrated pulse pressure declined from a value of 35 mm Hg to 30 mm Hg. The average highest orthostatic heart rate recorded during tilt-table testing was 25% above that recorded during baseline. Subject JA experienced presyncopal symptoms during baseline recovery and his tilt test was terminated after 17 min.

Results of the tilt-table and LBNP tests given to the two subjects in the concurrent study are summarized in Table IV. After 10 days of bed rest, Subject RM tolerated 20 min of tilt although he reported being "on the brink of syncope" several times during the procedure. The low systolic blood pressure, narrow pulse pressure, and elevated heart rates shown in figs. 4 and 5 support the subject's observations. Subject WW tolerated 19 min of 70° head-up tilt after 10 days of bed rest. Figs. 6 and 7 are a graphic presentation of his physiological response to tilt. By comparison with the baseline tilt, these two subjects evidenced deterioration in the mechanism essential to

TABLE III

TILT-TABLE TEST--SUMMARY

Date of Determination	Number of Subjects/Syncope	Average Integrated Heart Rate		Average Integrated Pulse Pressure During Tilt	Average Highest Orthostatic Heart Rate
		Before Tilt	During Tilt		
B-3	6/0	65	83	35	89
BR-1	6/1*	64	100	30	111

Note: (1) Heart-rate entries are in beats per min, and pulse pressures in mm Hg

(2) *Time to presyncopal symptoms, 17 min

TABLE IV

TILT-TABLE AND LBNP TESTS--SUMMARY

Test Medium and Date of Determination	Number of Subjects/Syncope	Average Integrated Heart Rate		Average Integrated Pulse Pressure During Tilt	Average Highest Orthostatic Heart Rate
		Before Tilt	During Tilt		
Tilt table					
B-2	2/0	52	72	38	72
T-10	2/1	64	113	19	122
LBNP					
B-2	2/0	52	74	31	86
T-10	2/2	58	91	20	96

Note: Heart-rate entries are in beats per min, and pulse pressures in mm Hg

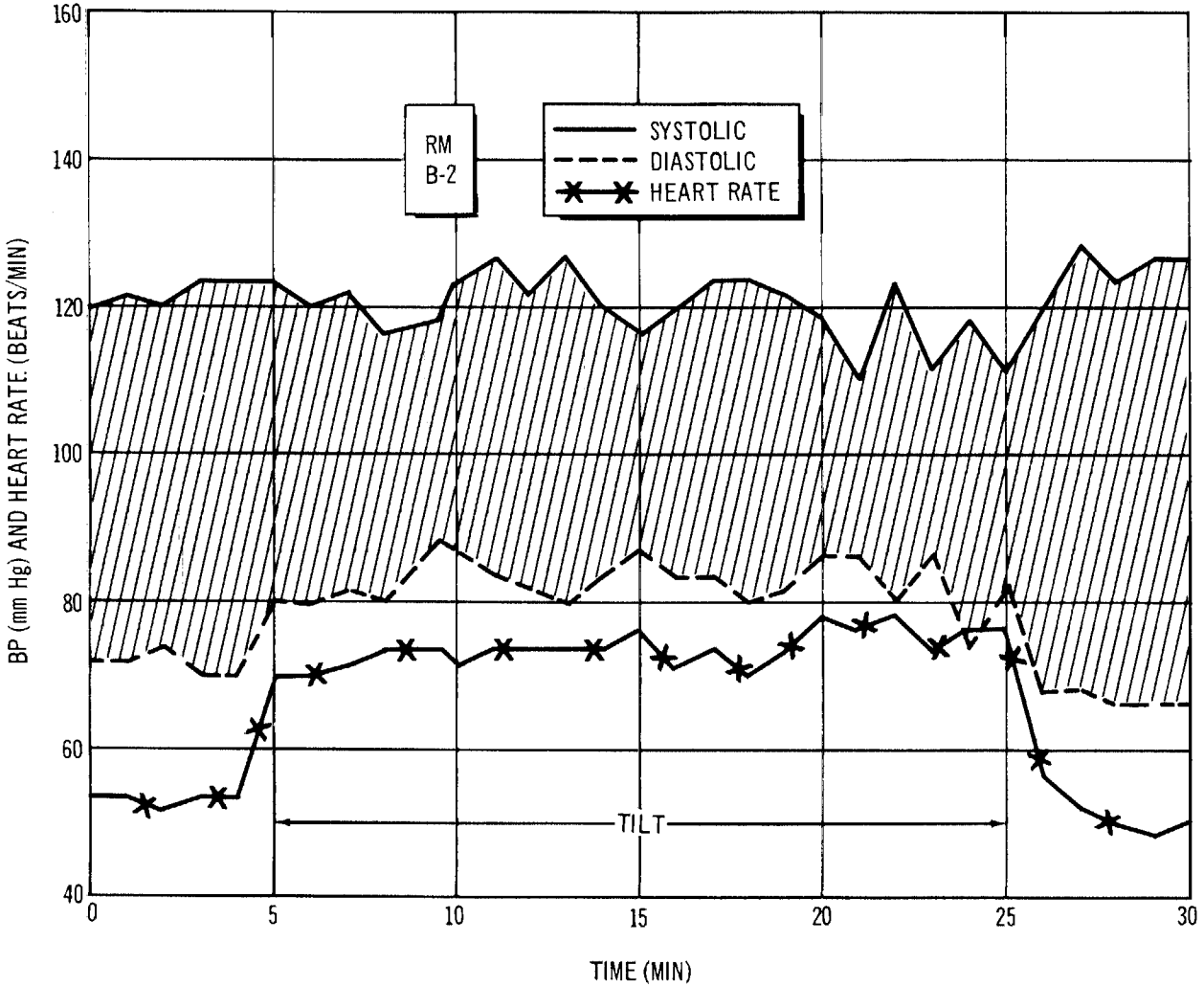

Figure 4. Orthostatic Tolerance – Subject RM on B-2

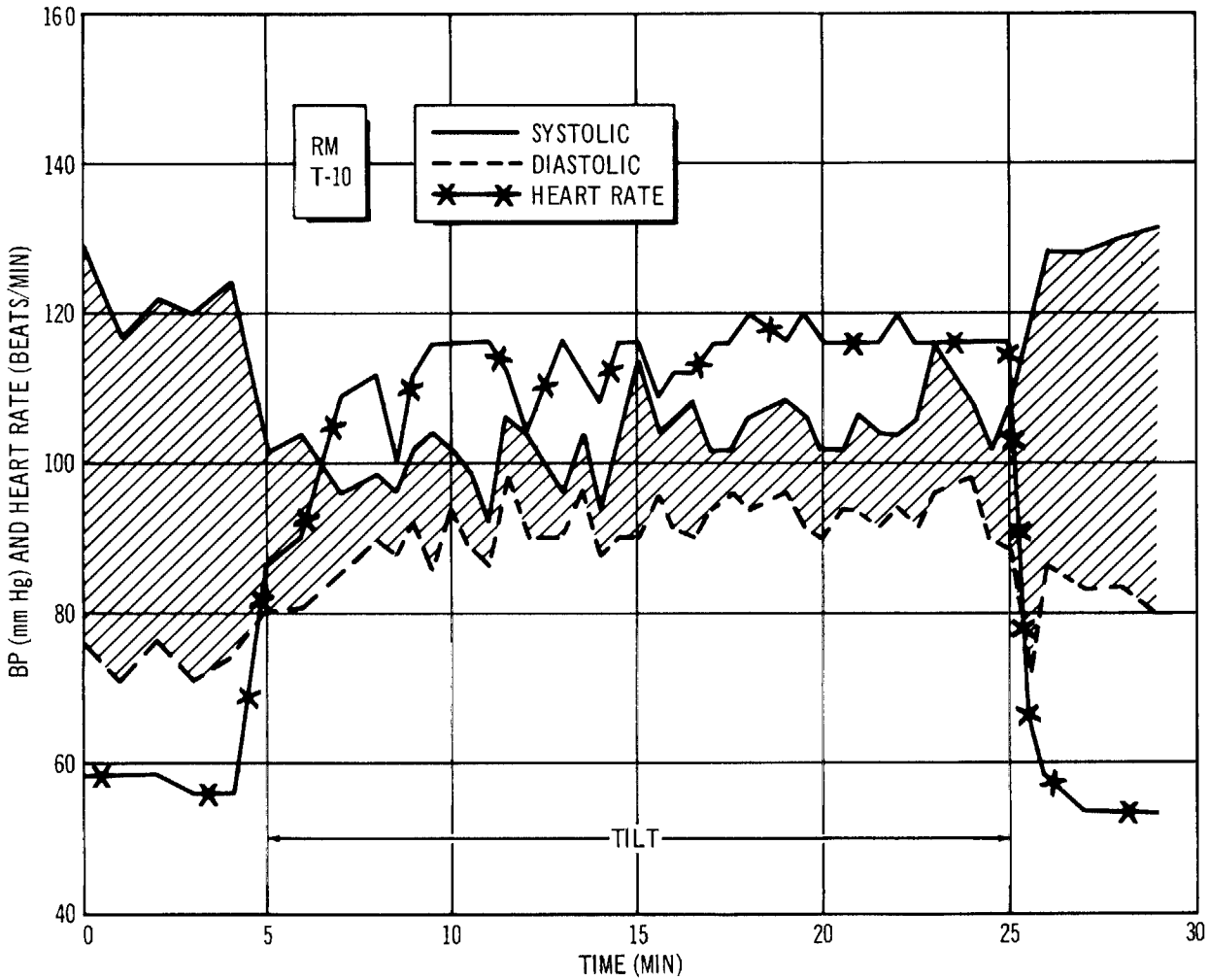

Figure 5. Orthostatic Tolerance – Subject RM on T-10

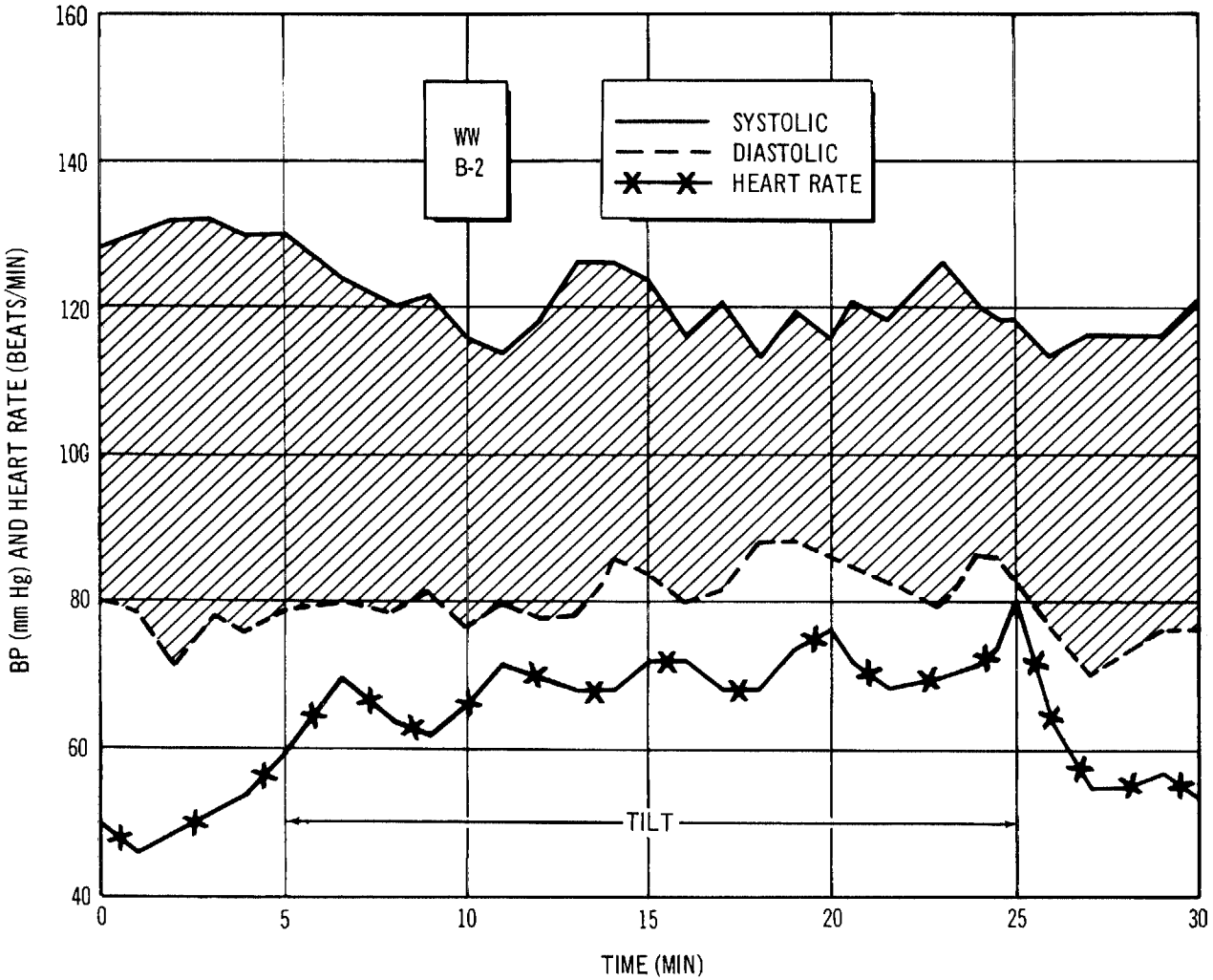

Figure 6. Orthostatic Tolerance – Subject WW on B-2

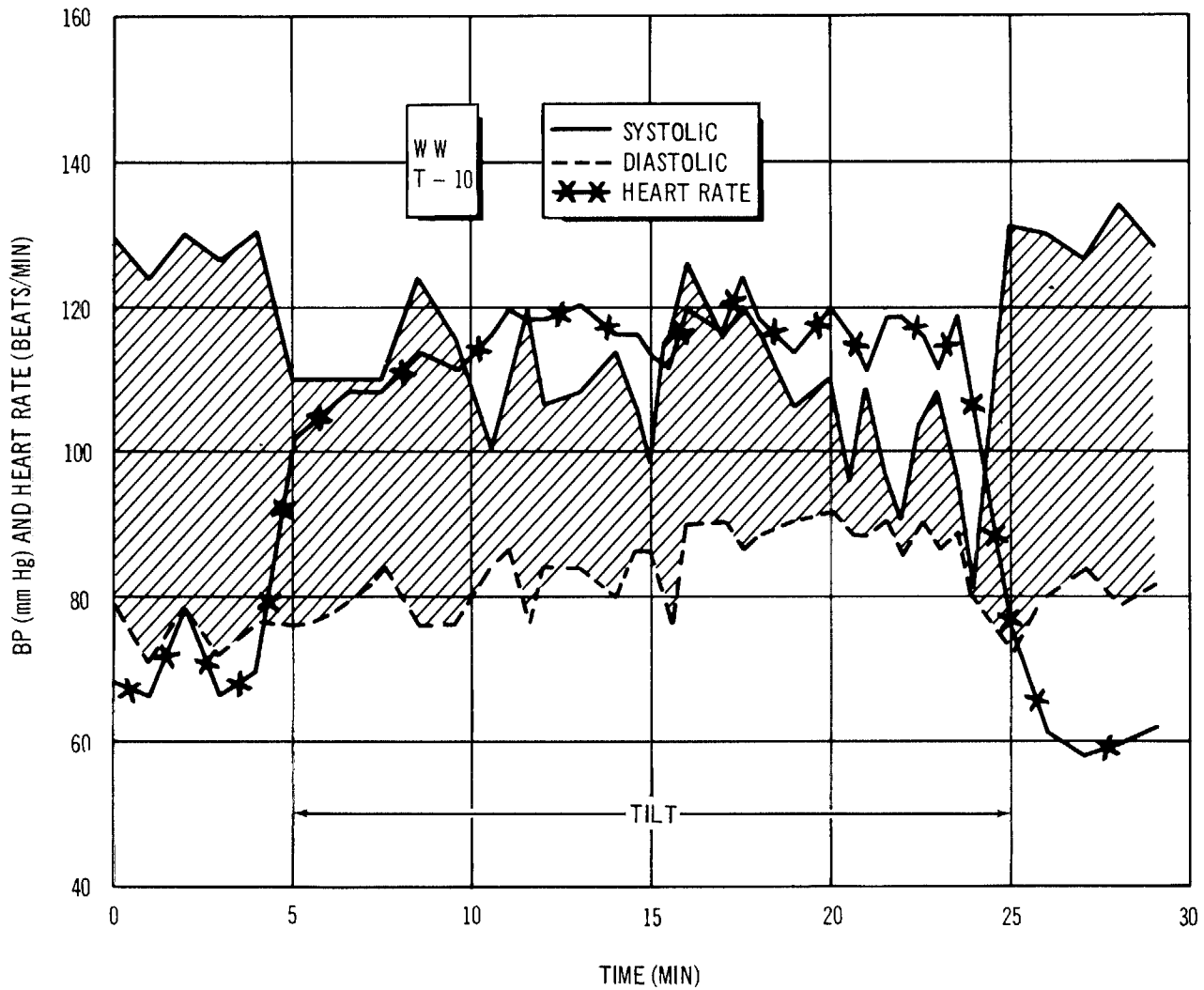

Figure 7. Orthostatic Tolerance – Subject WW on T-10

circulation in the upright position. After 10 days of bed rest, presyncopal symptoms interrupted the LBNP tests of both subjects. Subject RM tolerated 2. 5 min of negative pressure and Subject WW tolerated 4. 5 min. Figs. 8, 9, 10, and 11 are a graphic summary of their physiological responses to LBNP. Both subjects tolerated 20 min of LBNP during the baseline period before experimentation.

Tolerance to positive acceleration was measured before and, periodically, after the 10-day experimental period. A summary of the results of this test is shown in Table V. Tolerance was measured with a single, step-function run to blackout. Measurements were made at a radius of 74 in. (100% heart-to-foot gradient). Unlike the standard bioassay method, the step-function run showed that the subjects experienced a drop in acceleration tolerance on BR-1 that ranged from 12 to 38% of their baseline values. Bioassay runs conducted after ambulation on BR-2 and BR-3 showed that the tolerance of all the subjects was approaching baseline values. To differentiate the tolerance data collected during the baseline-recovery period, acceleration and time were integrated and expressed in units of $+g_z$ min. This metric shows that acceleration tolerance rapidly improves within 2 to 3 days after ambulation, although it appears to take several days to reach baseline values. This improvement, however, is achieved at a relatively high physiological price. Although the acceleration values are lower during the baseline-recovery period than during baseline, maximum heart rates remain at a high level.

Results of the step-function run to blackout for the two subjects in the concurrent experiment are summarized in Table VI. The table shows that tolerance to positive acceleration declines after 12 hours of bed rest, remains relatively constant during bed rest, and rapidly improves during ambulation. Tolerance appears to be lost much faster than it is regained.

Tolerance for sustained positive acceleration was measured before, and periodically during, the baseline-recovery period. The results of this test are summarized in Table VII. Tolerance was measured with a single 20-min run at 2. 25 or +2. 5 g_z. The highest heart rate recorded during each bioassay run was chosen as the index of physiological performance. All six subjects showed normal responses to the run on B-2. These responses were comparable with those

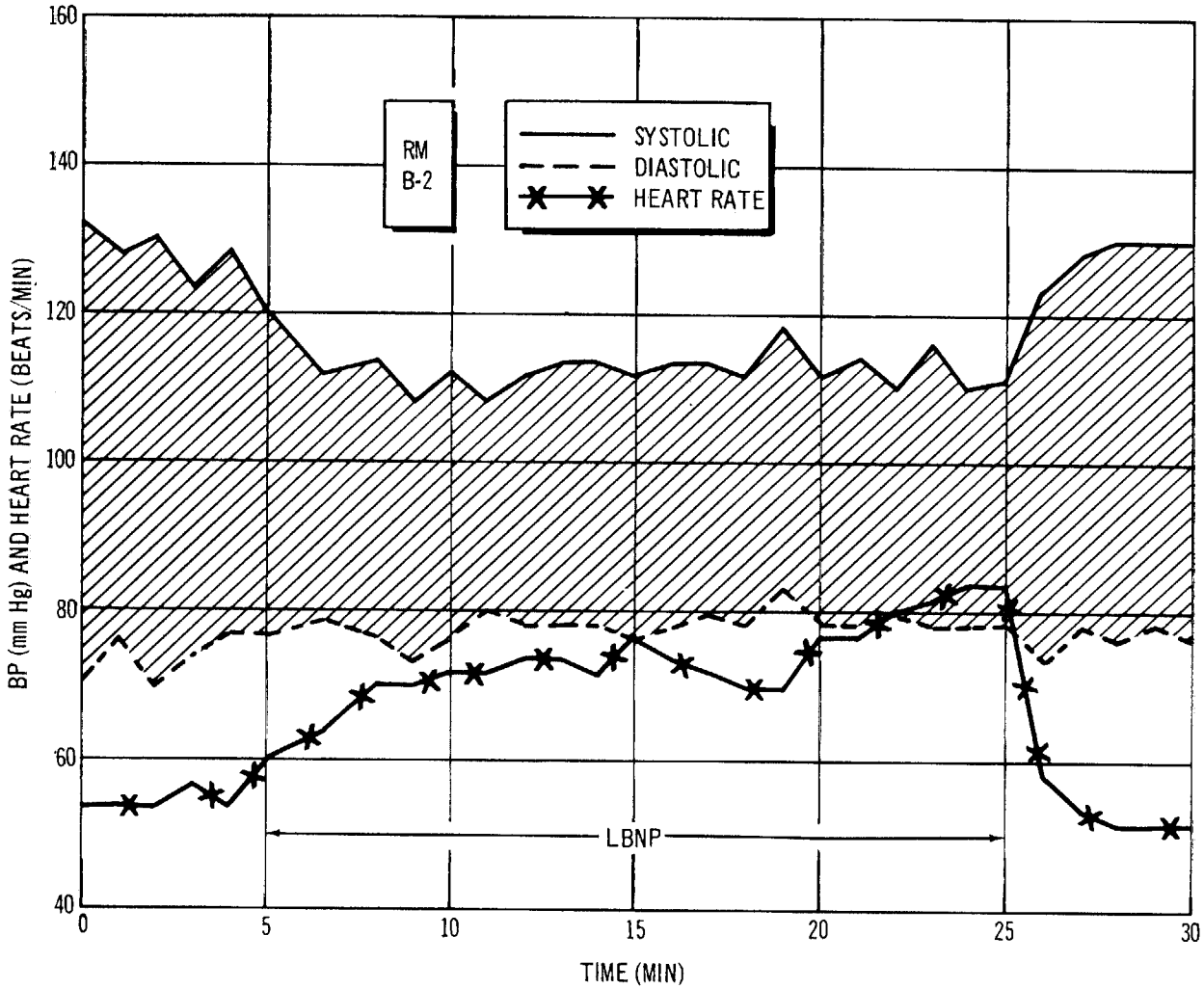

Figure 8. LBNP Test – Subject RM on B-2

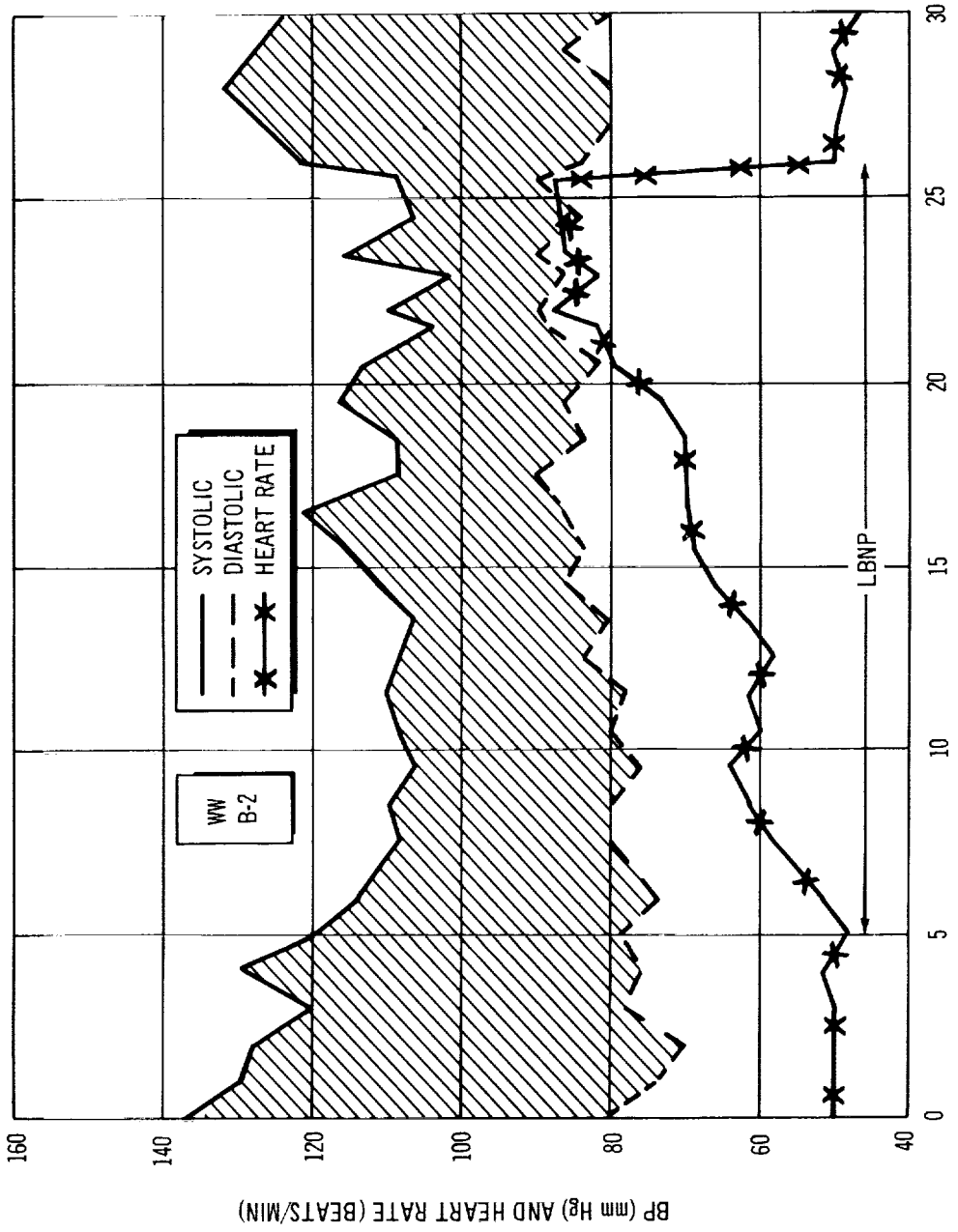

Figure 9. LBNP Test – Subject WW on B-2

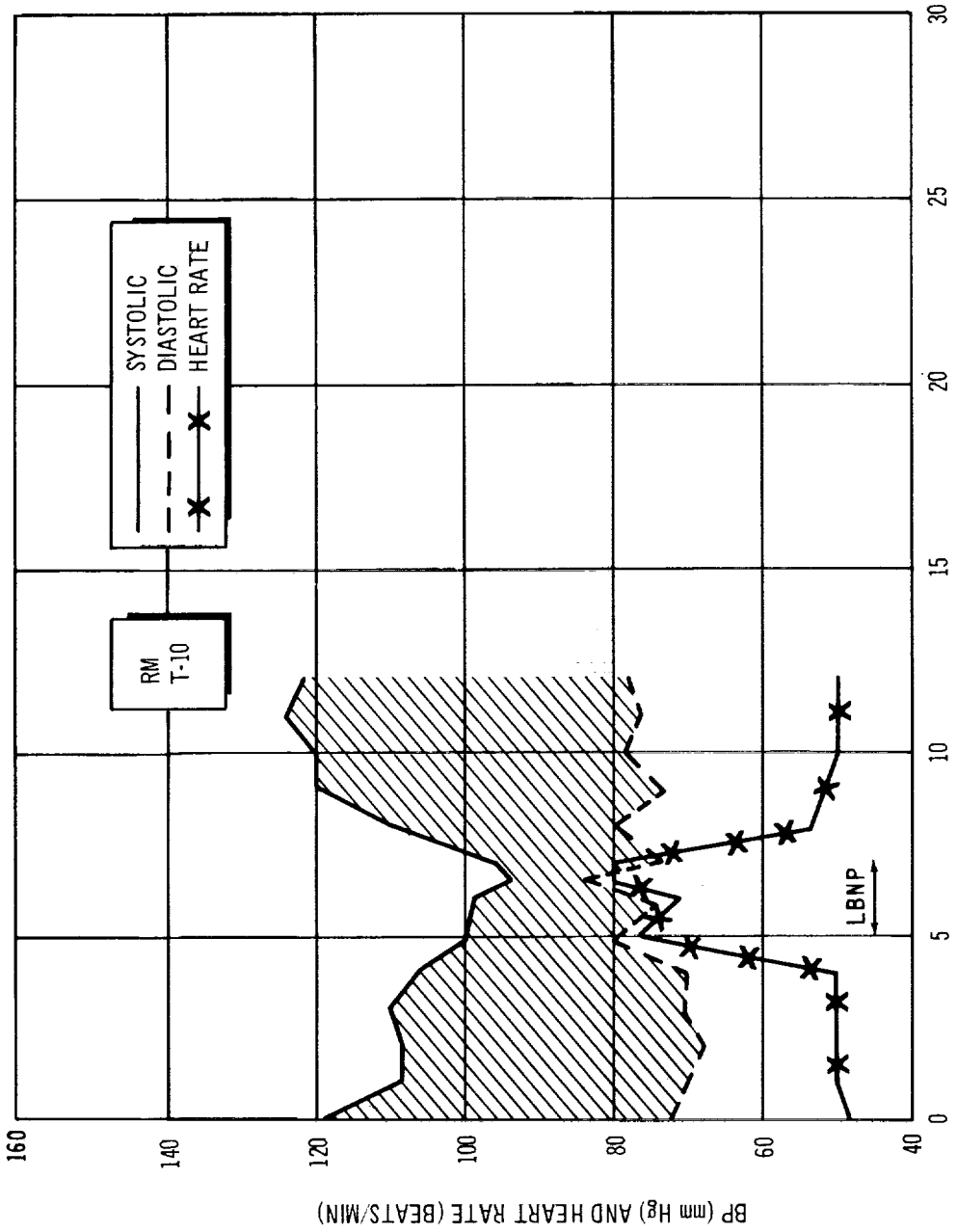

Figure 10. LBNP Test – Subject RM on T-10

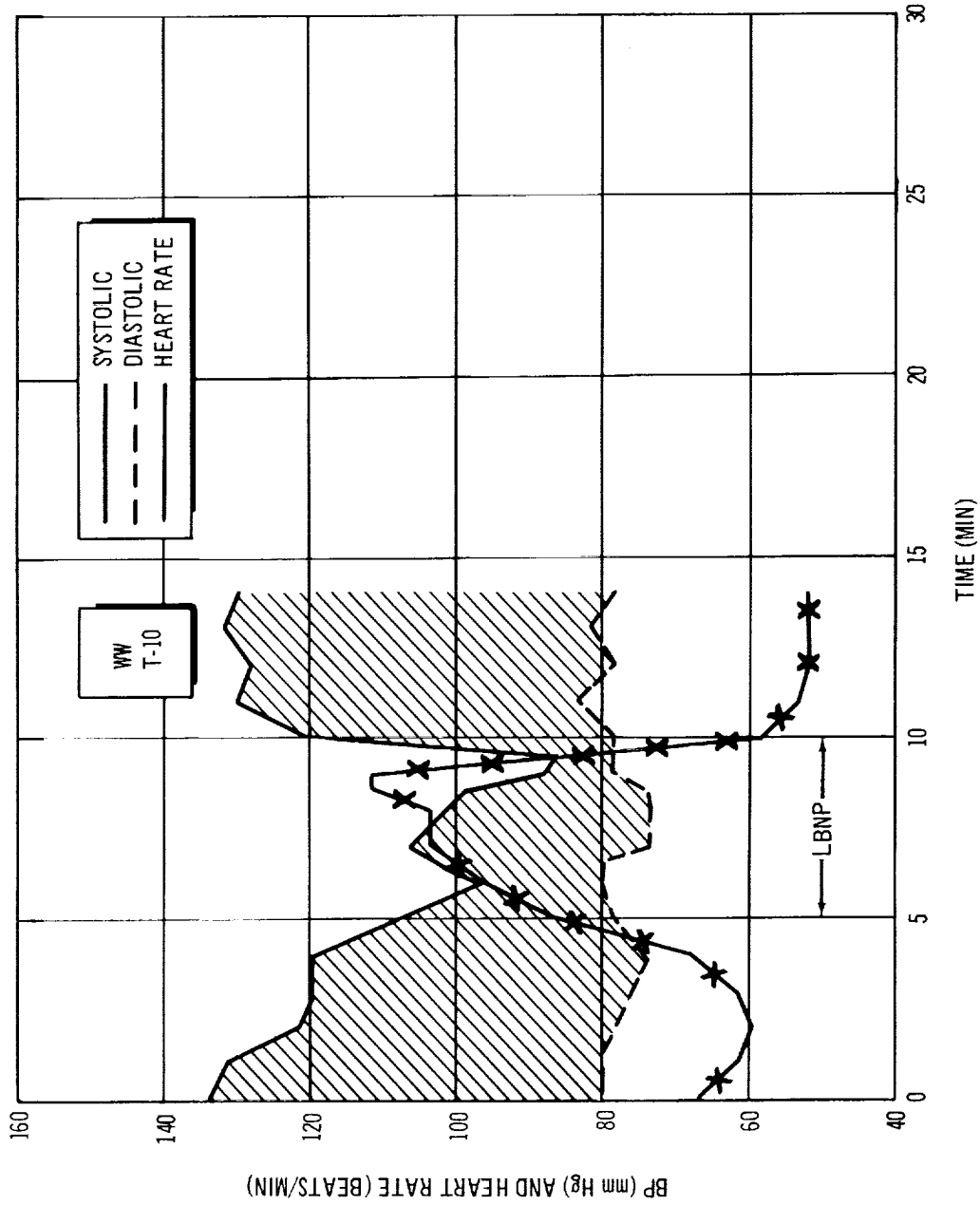

Figure 11. LBNP Test – Subject WW on T-10

TABLE V

STEP-FUNCTION ACCELERATION TOLERANCE

Subject	Date of Determination										
	B-3		BR-1			BR-2			BR-3		
	Tolerance	Highest Bioassay H. R.	Tolerance	$+g_z$ min	Highest Bioassay H. R.	Tolerance	$+g_z$ min	Highest Bioassay H. R.	Tolerance	$+g_z$ min	Highest Bioassay H. R.
JA	4.0	160	2.8	15.50	150	3.1	19.22	163	3.5	24.01	160
RE	5.0	170	3.1	18.67	150	3.5	21.45	*	3.5	24.53	170
JH	4.0	190	3.1	16.80	190	3.1	20.39	190	3.5	25.06	185
LH	4.0	150	2.8	15.40	130	3.1	21.45	150	3.5	22.75	150
EH	3.1	150	2.8	15.82	160	3.1	20.21	150	3.5	21.45	152
LL	3.5	185	2.8	12.60	181	3.1	17.51	180	3.5	21.45	180
Average	3.9	168	2.9	15.80	160	3.1	20.04	167	3.5	23.21	163

Note: (1) Entries are in $+g_z$ at heart level, time in minutes, and heart rates in beats per minute

(2) *Heart rate sample lost

TABLE VI

PERIODIC STEP-FUNCTION ACCELERATION TOLERANCE

Subject	Date of Determination																							
	B-2			T-2			T-4			T-8			T-9			BR-1			BR-2			BR-3		
	Tolerance	$+g_z$ min	Highest Bioassay H.R.	Tolerance	$+g_z$ min	Highest Bioassay H.R.	Tolerance	$+g_z$ min	Highest Bioassay H.R.	Tolerance	$+g_z$ min	Highest Bioassay H.R.	Tolerance	$+g_z$ min	Highest Bioassay H.R.	Tolerance	$+g_z$ min	Highest Bioassay H.R.	Tolerance	$+g_z$ min	Highest Bioassay H.R.	Tolerance	$+g_z$ min	Highest Bioassay H.R.
RM	3.1	13.48	149	2.4	11.44	120	2.4	10.75	125	1.6	*	*	2.0	9.00	140	2.4	10.74	170	3.1	20.12	175	2.8	16.80	168
WW	4.0	18.18	152	2.4	10.01	160	2.4	11.40	170	2.4	10.49	160	2.4	10.68	150	2.4	11.16	175	2.8	14.59	175	2.8	15.62	160

Note: (1) Entries are in $+g_z$ at heart level, time in minutes, and heart rate in beats per minute

(2) *Ride terminated because of nausea

TABLE VII

TOLERANCE TO SUSTAINED ACCELERATION

	Date of Determination								
	B-2			BR-1			BR-2		
Subject	$+g_z$	Duration	Highest Bioassay H. R.	$+g_z$	Duration	Highest Bioassay H. R.	$+g_z$	Duration	Highest Bioassay H. R.
JA	2.5	20	120	2.25	20	130	2.5	13.9	155
RE	2.5	20	100	2.25	20	135	2.5	20	120
JH	2.5	20	120	2.25	20	185	2.5	20	180
LH	2.5	20	120	2.25	20	135	2.5	20	147
EH	2.5	20	118	2.25	20	140	2.5	13.9	152
LL	2.5	20	175	2.25	20	175	2.5	20	170
Average			126			142			154
RM	2.5	20	-	1.75	3.6	140	2.25	13.9	145
WW	2.5	20	-	1.75	2.3	150	2.25	7.0	170

Note: Entries are in $+g_z$ at heart level, duration in minutes, and heart rate in beats per minute

observed during extensive testing prior to experimentation. An increase in heart rate and a rise in systolic and diastolic blood pressure with no narrowing pulse pressure were noted. There was no evidence of blackout during this type of bioassay test. Tests conducted on BR-1 at +2.25 g_z and on BR-2 at +2.5 g_z showed an increase in average heart rate and one incident of blackout (Subject JA). Because Subjects EH and JA rode the centrifuge together, the former's run was also terminated at 13.9 sec, although he did not experience blackout. Except for Subject JA, there was little difference in the pulse pressures recorded during these runs and those recorded prior to experimentation. However, the comments of the subject and observations of the staff indicated that the runs were tolerated with difficulty. Comments by the subjects revealed that neck pain, fatigue, and difficulty with breathing were the most common effects. A similar pattern of physiological responses were seen in the two subjects who participated in the concurrent experiment.

A Master's two-step ECG, taken before and after the experimentation, showed no abnormalities and no loss in exercise tolerance.

There was no significant impairment in postural equilibrium as measured with the rail walking and standing tests. Table VIII summarizes the results of the Graybiel-Fregly test.

Audiometric testing showed that hearing was unaffected by the condition of the experiment.

Changes in body weight are shown in Table IX. Losses in weight were progressive in all subjects and ranged from 0.98 to 2.35 kg. Average weight loss during bed rest was 1.72 kg or approximately 2%. Subject JH showed the most weight loss and Subject RE the least. During the baseline-recovery period, all subjects regained weight rapidly, and by BR-3 the average net loss was 0.71 kg or 1%.

TABLE VIII

POSTURE TEST--SUMMARY

Test	Date of Determination	
	B-3	BR-1
Walking	14	14
Standing--eyes open	55	93
Standing--eyes closed	56	37

Note: Walking entries are in steps; standing entries are in seconds

TABLE IX

BODY WEIGHTS

Subject	Date of Determination						
	B-3	T-3	T-5	T-9	BR-1	BR-2	BR-3
JA	89.09	89.12	87.72	87.20	86.80	86.50	87.03
RE	71.14	71.04	70.61	70.48	70.16	70.95	71.86
JH	72.95	72.05	71.52	71.55	70.60	72.14	71.93
LH	79.32	78.13	78.04	77.47	77.12	77.31	77.79
EH	67.27	66.26	66.51	65.95	66.00	66.73	66.97
LL	77.50	77.08	76.99	76.45	76.25	76.70	77.44

Note: Entries are in kg

Biochemical Tests

The effects of bed rest and periodic centrifugation on red blood cell volume (RBCV), plasma volume (PV), and total blood volume (TBV) are shown in Table X for each subject. The condition of the experiment resulted in an average loss of 13% in TBV, 18% in PV, 5% in RBCV between B-1 and T-5, and 17% in TBV, 26% in PV, and 2% in RBCV between B-1 and T-10. Subject LH consistently showed the largest losses in TBV and PV. He also showed a 2.2-kg weight loss and his fluid output was approximately 3000 ml higher than his intake during the testing period. Subject LL showed the smallest loss during the testing period in TBV and PV. Also, he showed the smallest weight loss and his fluid intake exceeded his output by 2000 ml. RBCV on T-5 showed a decrease in four of the subjects and an increase in two of the subjects. On T-10, RBCV showed a further decrease in three subjects, a slight elevation in two subjects, and a second large increase in Subject JA. Subject RE showed a decrease in RBCV and PV from B-1 to T-10 of 667 and 1169 ml, respectively. His weight loss was the smallest, 0.98 kg, as was the difference in his fluid intake-output, -5 ml/24 hour. The average net decreases in RBCV cannot be explained on the basis of overt hemolysis since bilirubins and reticulocyte counts remained within normal limits. During bed rest and periodic centrifugation, TBV decreased in all of the subjects. The predominant loss was in PV component, and this loss was generally consistent with decrease in fluid balance and body weight.

The two subjects in the concurrent study showed progressive losses in TBV, PV, and RBCV; these are shown in Table X. Subject WW showed a loss of 690 ml in RBCV between B-1 and T-10; Subject RM showed a loss of 223 ml. Losses in PV were of the same order as the other subjects in the study. The loss in TBV for Subject WW was 1567 ml, the largest shown by any of the subjects. The loss of Subject RM was 1334 ml, the third largest loss of the study between B-1 and T-10.

TABLE X

FLUID COMPARTMENT VALUES

Subject	Date of Determination								
	B-1			T-5			T-10		
	RBCV	PV	TBV	RBCV	PV	TBV	RBCV	PV	TBV
JA	2438	3717	6155	2797	3213	6010	2675	2994	5669
RE	1925	3326	5251	1460	2468	3928	1723	2157	3880
JH	2453	3476	5929	2317	2992	5309	2093	2769	4862
LH	2632	4278	6910	2193	3199	5392	2609	2809	5418
EH	2074	4205	6279	1938	3315	5253	2082	2936	5018
LL	2331	3379	5710	2429	3139	5568	2401	2849	5250
Average	2309	3730	6039	2189	3054	5243	2264	2752	5016
RM	2667	4338	7005	2393	3799	6192	2444	3233	5677
WW	2586	3738	6324	2106	2724	4830	1896	2861	4757
Average	2627	4038	6665	2250	3262	5511	2170	3047	5217

Note: Entries are in ml

There were no significant changes in blood chemistries as a result of the experiment. No trends were apparent when the two groups of subjects were compared.

Hemoglobin remained within normal limits for all subjects during the testing period; however, variations occurred within these normal limits. After 5 days, hemoglobin increased from 0.3 to 2.7 g/100 ml in all the subjects. The average increase was 1.5 g/100 ml. From T-5 to T-10, hemoglobin decreased in all but one subject. The decreases varied from 0.5 to 2.0 g/100 ml and averaged 1.2 g/100 ml.

Hematocrits also remained within normal range for all the subjects, but variations occurred. After 5 days of testing, the hematocrits of all subjects increased from 1 to 7 vol %. The average increase was 4 vol %. From T-5 to T-10, the hematocrits of all but one subject decreased. The decrease ranged from 1 to 4 vol % and averaged 3 vol %.

Mean corpuscular hemoglobin concentration varied inconsistently. Some subjects showed losses and gains or combinations of both during the testing period. Gains varied from concentrations of 0.1% to 1.5%. Decreases ranged from concentrations of 0.5 to 2.0%.

Red blood cell counts remained within normal range during the entire testing period, but variations occurred. The red blood cell counts of all subjects increased after 5 days of testing. Increases ranged from 0.1 to 0.5 million, the average being 0.3 million. From T-5 to T-10, four subjects showed a continued decrease in red blood cell counts and four subjects showed an increase.

After 5 days of testing, reticulocyte counts decreased in all subjects except one, who showed no change. Decreases varied from 0.12% to 0.62%, the average being 0.36%. From T-5 to T-10, all subjects showed an increase in reticulocyte counts.

White blood cell counts and differential counts remained essentially normal for all subjects during the testing period.

Serum sodium levels remained within normal limits during the study, although the majority of the subjects were on the high side of normal and two subjects (JA and JH) showed above normal levels on one occasion each. After 5 days of testing, all subjects showed a decrease in sodium levels, decreasing by an average of 7 meq/L. From T-5 to T-10, all subjects showed an increase in sodium, the average increase being 5.4 meq/L.

Serum potassium values for all subjects were on the high side of normal during the testing period. After 5 days of testing, six subjects showed a slight decrease in potassium levels, averaging 0.5 meq/L. From T-5 to T-10, potassium continued to decrease slightly in four subjects by an average of 0.5 meq/L. A slight increase was shown by four other subjects.

Serum chloride values remained within normal limits for all subjects, except for two occasions during the baseline period when subjects JA and LL showed elevations above normal. Subsequent chloride determinations of these subjects were normal. The majority of subjects showed chloride values in the upper range of normal during the testing period. After 5 days, seven of the subjects showed a decrease in serum chloride, the decreases ranging from 1 to 16 meq/L, or an average of 7 meq/L. From T-5 to T-10, two subjects showed a continued decrease of 1 and 5 meq/L, respectively, while five subjects showed an increase in chloride varying from 1 to 5 meq/L. One subject showed no change in serum chloride.

The carbon dioxide combining power of the serum of several subjects (JA, EH, JH, and WW) was below normal during the baseline period and, for Subject RM, on T-2. However, none of these subjects showed any clinical signs of acidosis, no gastrointestinal pathology, and all had normal fluid intake-output levels. No signs or symptoms of abnormal clinical entities were present. The carbon dioxide values of all other subjects remained within normal limits during the testing period. After 5 days of testing, seven subjects showed an increase in carbon dioxide ranging from

2.0 to 11.0 meq/L, or an average of 5.8 meq/L. After 10 days, five subjects showed a decrease in carbon dioxide from T-5 and three subjects showed an increase. At T-5 and T-10, all values remained within normal limits. Decreases in carbon dioxide varied from 0.9 to 7.0 meq/L and increases from 0.8 to 1.6 meq/L.

Although several electrolyte values were above or below normal on occasion, none of the subjects showed any clinical signs or symptoms of electrolyte imbalance or other pathology. All subjects were in good health during the study. Deviation from normal could have resulted from individual subject variation or from laboratory technique on the day the determinations were made.

Total and direct serum bilirubin values remained within a normal range for all subjects during the testing period.

Serum glucose values remained within normal limits for all subjects throughout the testing period, except for Subject EH during the baseline period and on T-5 when the glucose levels were 50 and 55 mg/100 ml, respectively. His glucose value on T-10 was normal. Glucose values for Subject LH were depressed on T-5 and T-10, at which time they were 55 and 58 mg/100 ml, respectively. Both subjects were clinically normal. The majority of subjects showed values within the lower range of normal throughout the testing period.

Blood urea nitrogen values remained within normal limits of all subjects during the entire testing period. Subject EH showed a urea nitrogen value of 22 mg/100 ml on T-10, essentially normal. Average urea nitrogen values during the baseline period, and on T-5 and T-10, were mg/100 ml on all three occasions. The subjects showed variations from 1 to 4 mg/100 ml during the study, but, as stated, all values remained within a normal range.

Table XI summarizes the results of the blood chemistry tests performed at regular intervals during the experimental period.

Table XI

BLOOD CHEMISTRIES

Test	Date of Determination and Subject*																							
	B-1								T-5								T-10							
	JA	RE	EH	JH	LH	LL	RM	WW	JA	RE	EH	JH	LH	LL	RM	WW	JA	RE	EH	JH	LH	LL	RM	WW
Hbg (g/100 ml)	16.0	13.8	13.0	14.8	15.7	15.7	14.0	15.0	17.5	16.5	15.3	15.5	16.0	17.5	15.0	17.0	15.5	15.5	14.5	15.0	15.5	15.5	15.0	15.5
Hct (vol. %)	46	40	40	44	45	45	42	44	50	47	45	45	49	50	45	48	46	45	42	45	46	45	44	46
MCHC (%)	35.5	35.0	32.5	35.0	35.0	35.0	33.5	35.0	35.0	35.5	34.0	35.0	33.0	35.0	34.0	36.0	34.0	35.0	34.5	33.5	34.0	35.0	34.0	34.0
RBC (millions)	5.2	5.2	4.6	5.0	5.2	5.1	4.7	4.8	5.5	5.5	5.1	5.1	5.3	5.6	5.0	5.3	5.4	5.3	4.9	5.2	5.4	5.2	5.1	5.4
WBC (thousands)	6.0	6.5	6.8	7.1	7.8	7.2	7.0	6.8	7.4	5.7	5.3	6.8	5.1	6.0	6.0	5.4	8.0	5.6	6.2	6.4	7.7	6.3	6.8	5.1
Reticulocyte (%)	0.75	0.25	0.25	1.00	0.75	0.50	0.50	0.25	0.25	0.13	0.25	0.50	0.13	0.25	0.10	0.13	0.60	0.60	0.40	0.70	0.40	0.50	0.50	0.40
Na^+ (meq/L)	154	147	145	149	148	148	149	150	138	145	140	144	143	144	140	140	148	147	147	153	148	146	143	145
K^+ (meq/L)	5.8	5.1	5.4	4.8	4.7	5.2	5.0	5.5	5.0	5.1	4.8	4.9	4.0	4.5	4.5	5.4	4.8	4.5	5.0	4.3	4.2	4.6	5.0	5.0
Cl^- (meq/L)	120	110	106	110	98	115	108	107	104	108	105	104	105	100	107	101	105	103	104	109	107	102	108	101
CO_2 Comb. (meq/L)	14.5	23.0	17.5	17.5	27.3	23.0	22.0	20.0	25.5	25.2	25.7	25.7	25.2	25.0	25.2	25.5	22.5	24.3	26.5	24.3	26.8	23.5	18.2	26.0
Bilirubin--total (mg/100 ml)	0.9	0.5	0.9	1.1	0.7	0.4	0.9	0.6	0.7	0.8	0.9	1.1	1.1	0.8	0.8	0.8	0.5	0.8	0.5	1.0	0.7	0.5	0.6	0.5
Bilirubin--direct (mg/100 ml)	0.3	0.4	0.4	0.3	0.2	0.2	0.4	0.3	0.2	0.3	0.4	0.3	0.6	0.3	0.2	0.3	0.2	0.3	0.3	0.3	0.3	0.2	0.2	0.2
Glucose (mg/100 ml)	62	68	50	78	60	72	76	78	66	63	55	75	55	62	60	64	64	68	70	74	58	82	67	72
BUN (mg/100 ml)		15	19	13	14	18	18	15	14	16	19	16	17	14	17	16	11	15	22	14	16	16	16	14

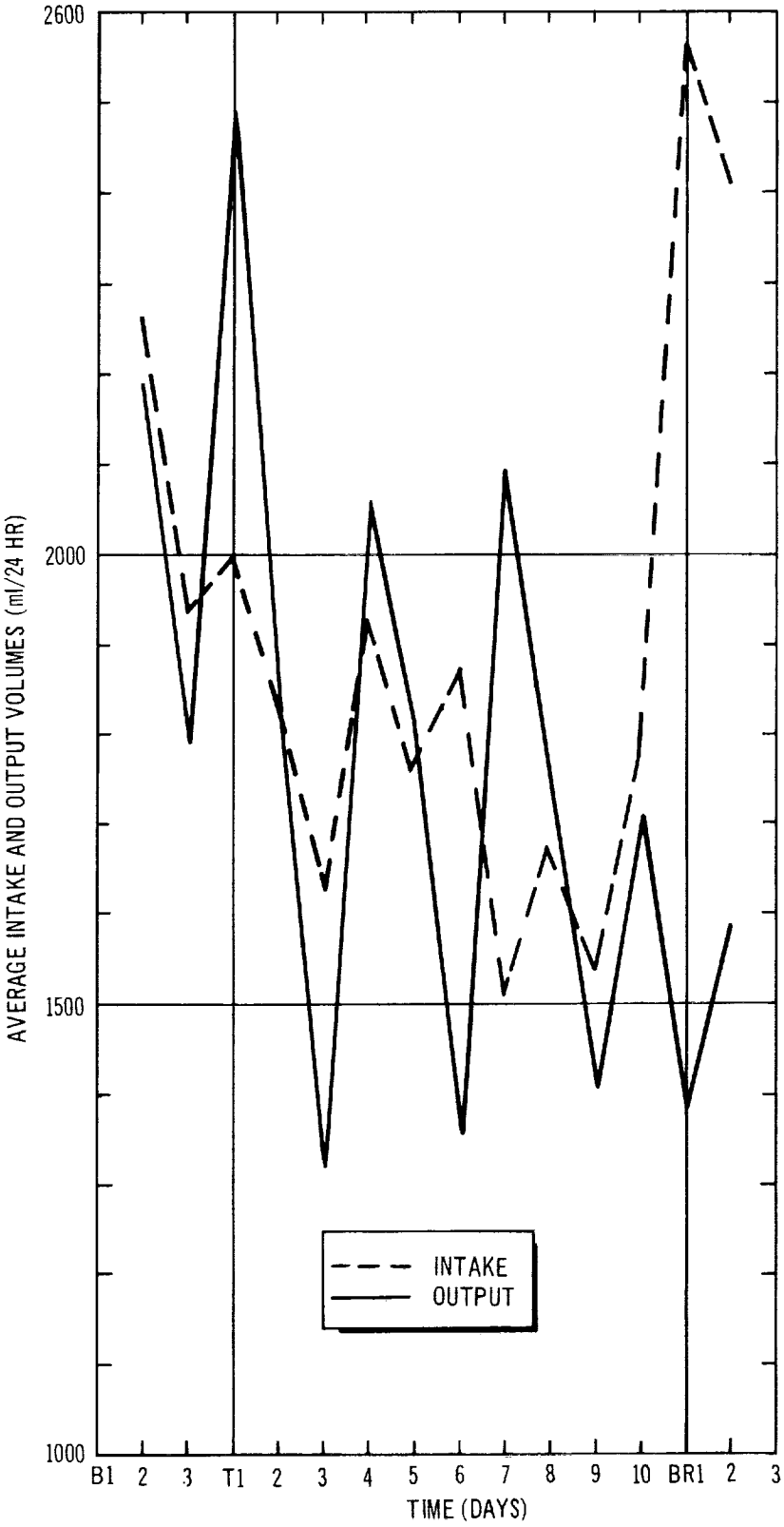

Figure 12. Fluid Intake and Output

tolerate +2.5 g_z. The most frequent reason for termination was the onset of grayout and blackout. Reports by the subjects indicated that the first run of the day was the most difficult. This table and Table VII show that tolerance to sustained, positive acceleration declines after 12 hours of bed rest, remains relatively constant during bed rest, and rapidly improves during ambulation.

TABLE XII

AVERAGE FLUID INTAKE AND OUTPUT

Subject	Total Intake	Total Output	Average Daily Intake	Average Daily Output	ΔAverage Daily Intake/ Output
JA	19 500	20 119	1950	2012	- 62
RE	15 365	15 415	1537	1542	- 5
JH	16 290	14 570	1629	1457	+172
LH	15 110	18 270	1511	1827	-316
EH	21 990	23 755	2199	2376	-177
LL	16 900	14 950	1690	1495	+195
Average			1753	1785	- 32
RM	13 840	11 010	1384	1101	+283
WW	32 890	33 910	3289	3391	-102
Average			2337	2246	+ 91

Note: Entries are in ml.

TABLE XIII (page 1 of 2)

DEVIATIONS FROM THE CONDITIONING REGIMEN

Subject	Time	Date of Determination and Subject														
		T-1			T-2			T-3			T-4			T-5		
		$+g_z$	Duration	Highest Conditioning Heart Rate	$+g_z$	Duration	Highest Conditioning Heart Rate	$+g_z$	Duration	Highest Conditioning Heart Rate	$+g_z$	Duration	Highest Conditioning Heart Rate	$+g_z$	Duration	Highest Conditioning Heart Rate
JA	0930	2.50	5.77	110	2.00	13.88	110	1.75	20.00	105	1.75	20.00	115	1.75	20.00	110
	1130	2.00	20.00	100	1.75	20.00	-	1.75	20.00	100	1.75	20.00	108	1.75	20.00	-
	1400	2.00	20.00	108	1.75	20.00	103	2.00	20.00	110	2.00	17.23	130	1.75	20.00	122
	1600	2.00	20.00	100	1.75	20.00	93	2.00	20.00	115	1.75	20.00	120	1.75	20.00	-
RE	0930	2.50	5.77	120	2.00	13.88	120	1.75	20.00	98	1.75	20.00	94	1.75	20.00	98
	1130	2.00	20.00	95	1.75	20.00	-	1.75	20.00	98	1.75	20.00	91	1.75	20.00	-
	1400	2.00	20.00	94	1.75	20.00	90	2.00	20.00	105	2.00	17.23	103	1.75	20.00	80
	1600	2.00	20.00	100	1.75	20.00	95	2.00	20.00	105	1.75	20.00	100	1.75	20.00	-
JH	0930	2.50	5.77	170	2.00	13.88	145	1.75	20.00	132	1.75	20.00	136	1.75	20.00	145
	1130	2.00	20.00	130	1.75	20.00	-	1.75	20.00	155	1.75	20.00	135	1.75	20.00	-
	1400	2.00	20.00	135	1.75	20.00	133	2.00	20.00	160	2.00	17.23	155	1.75	20.00	155
	1600	2.00	20.00	120	1.75	20.00	125	2.00	20.00	165	1.75	20.00	120	1.75	20.00	-
LH	0830	2.50	3.12	98	2.00	13.65	125	1.75	12.78	105	1.75	20.00	100	1.75	20.00	-
	1030	2.00	20.00	90	2.00	10.08	125	1.75	20.00	105	1.75	20.00	115	1.75	20.00	-
	1300	2.00	20.00	-	1.75	20.00	97	2.00	18.65	120	2.00	20.00	100	1.75	20.00	100
	1500	2.00	20.00	100	1.75	20.00	96	2.00	20.00	100	1.75	20.00	120	1.75	20.00	100
EH	0830	2.50	3.12	98	2.00	13.65	118	1.75	12.78	120	1.75	20.00	115	1.75	20.00	-
	1030	2.00	20.00	110	2.00	10.08	112	1.75	20.00	120	1.75	20.00	108	1.75	20.00	-
	1300	2.00	20.00	-	1.75	20.00	108	2.00	18.65	138	2.00	20.00	125	1.75	20.00	100
	1500	2.00	20.00	100	1.75	20.00	112	2.00	20.00	125	1.75	20.00	115	1.75	20.00	112
LL	0830	2.50	3.12	130	2.00	13.65	150	1.75	12.78	140	1.75	20.00	125	1.75	20.00	-
	1030	2.00	20.00	140	2.00	10.08	160	1.75	20.00	136	1.75	20.00	155	1.75	20.00	-
	1300	2.00	20.00	-	1.75	20.00	135	2.00	18.65	152	2.00	20.00	136	1.75	20.00	138
	1500	2.00	20.00	125	1.75	20.00	140	2.00	20.00	122	1.75	20.00	135	1.75	20.00	138
Mode		2.00	20.00		1.75	20.00		1.75-2.00	20.00		1.75	20.00		1.75	20.00	
Average				110			111			120			117			116

Note: (1) Entries are in $+g_z$ at heart level, duration in minutes, and heart rate in beats per minute
(2) * Run stopped because of failure of traveling hoist
(3) • Run stopped because of failure of bioassay lights

TABLE XIII (page 2 of 2)

Date of Determination and Subject															
T-6			T-7			T-8			T-9			T-10			
$+g_z$	Duration	Highest Conditioning Heart Rate	$+g_z$	Duration	Highest Conditioning Heart Rate	$+g_z$	Duration	Highest Conditioning Heart Rate	$+g_z$	Duration	Highest Conditioning Heart Rate	$+g_z$	Duration	Highest Conditioning Heart Rate	
1.75	20.00	102	1.75	20.00	110	•	•	•	2.00	5.19	132	1.75	20.00	110	
*	*	*	1.75	20.00	102	•	•	•	1.75	20.00	108	2.00	12.00	110	
*	*	*	2.00	20.00	132	•	•	•	1.75	20.00	-	1.75	20.00	102	
*	*	*	•	•	•	2.00	20.00	135	1.75	20.00	110	2.00	20.00	107	
1.75	20.00	100	1.75	20.00	100	•	•	•	2.00	5.19	94	1.75	20.00	90	
*	*	*	1.75	20.00	90	•	•	•	1.75	20.00	108	2.00	12.00	86	
*	*	*	2.00	20.00	119	•	•	•	1.75	20.00	-	1.75	20.00	77	
*	*	*	•	•	•	2.00	20.00	90	1.75	20.00	88	2.00	20.00	125	
1.75	20.00	128	1.75	20.00	120	•	•	•	2.00	5.19	162	1.75	20.00	125	
*	*	*	1.75	20.00	110	•	•	•	1.75	20.00	155	2.00	12.00	180	
*	*	*	2.00	20.00	130	•	•	•	1.75	20.00	-	1.75	20.00	115	
*	*	*	•	•	•	2.00	20.00	170	1.75	20.00	145	2.00	20.00	125	
1.75	20.00	94	1.75	20.00	98	•	•	•	2.00	17.17	-	1.75	20.00	88	
2.00	18.00	110	1.75	20.00	85	•	•	•	1.75	20.00	90	2.00	16.08	98	
*	*	*	2.00	20.00	115	•	•	•	1.75	20.00	-	1.75	20.00	82	
*	*	*	•	•	•	2.00	20.00	110	1.75	20.00	-	2.00	20.00	100	
1.75	20.00	112	1.75	20.00	100	•	•	•	2.00	17.17	-	1.75	20.00	122	
2.00	18.00	125	1.75	20.00	100	•	•	•	1.75	20.00	118	2.00	16.08	130	
*	*	*	2.00	20.00	118	•	•	•	1.75	20.00	-	1.75	20.00	115	
*	*	*	•	•	•	2.00	20.00	120	1.75	20.00	-	2.00	20.00	135	
1.75	20.00	140	1.75	20.00	125	•	•	•	2.00	17.17	-	1.75	20.00	140	
2.00	18.00	165	1.75	20.00	120	•	•	•	1.75	20.00	140	2.00	16.08	165	
*	*	*	2.00	20.00	138	•	•	•	1.75	20.00	-	1.75	20.00	130	
*	*	*	•	•	•	2.00	20.00	150	1.75	20.00	-	2.00	20.00	150	
1.75	20.00		1.75	20.00		2.00	20.00		1.75	20.00		1.75	20.00		
		120			112			129			118			113	

DISCUSSION

The mechanism by which periodic centrifugation serves to ameliorate the effects of bed rest is not entirely understood. It is believed that the hemodynamic alterations are similar to those seen during a change from the horizontal to vertical body position in a gravitational field. Expected alterations during centrifugation would be a decrease in cardiac output, an increase in heart rate, a narrowing of pulse pressure, an elevation in blood pressure, and a decrease in central blood volume with periodic pooling in the lower extremities. Regional distribution of blood flow is probably altered, resulting in, among other things, decreased renal blood flow and increased levels of renin-aldosterone and angiotensin. Because gravitational and accelerative forces are physically identical, centrifugation must activate many of the mechanisms that are functional during passive standing. However, periodic centrifugation with a significant heart-to-foot acceleration gradient is not equivalent to a gravitational field.

It is uncertain what the optimal daily schedule for centrifugation should be. In an earlier study in this series in which centrifugation was also begun at the start of bed rest, 3 g-hours were used; in this study, the modal run was 4.7 g-hours.* Both were found effective as judged by presyncopal symptoms and highest orthostatic heart rate on the tilt table. Three hours of daily standing (3 g-hours) has been shown to be the minimum effective duration for reversing bed rest induced tilt intolerance and hypercalciuria (ref. 3), and 8 hours (8 g-hours) of quiet sitting by the subjects at bed rest prevents orthostatic intolerance (ref. 4). Although many aspects of the conditioning regimen require further study, one generalization that can

*The g-hours integral or parameter is computed by multiplying acceleration (g) at the feet or some other point of the body by the duration of the ride (minutes) and dividing by 60.

be made with relative certainty is that 60 min a day spent in riding a centrifuge will alleviate the transient cardiovascular instability produced by bed rest. This time is in sharp contrast with the times required of other cardio-protective techniques which require a considerable portion of a 24-hour period to produce beneficial effects.

There is some suggestion that the 100% heart-to-foot gradient of this study produced a larger loss in plasma volume than the 219% gradient of the earlier study. The exact mechanism of this and the red blood cell volume events are yet to be fully examined. It is apparent, however, that the 219% gradient alters very little the vascular pressures in the head and neck, and offers less impedance to venous return than a 100% gradient. The 100% gradient, on the other hand, imposes a much larger workload on the cardiovascular system because of the larger pressure head (ref. 5). Pooling of blood in the veins of the legs, and a transfer of fluid from the intravascular space as a result of increased pressure, may result in an apparent decrease in plasma volume. This is the familiar "third space" problem, and sequestration is one of the multiple problems associated with the measurement of intravascular volumes in this type of experiment.

It is of interest to note that a significant correlation is yet to be demonstrated between losses in plasma and blood volumes and cardiovascular changes on the tilt table. Many studies show that acute blood loss produces increased heart rate and decreased pulse pressure and syncopal episodes during tilt testing (ref. 6). In the bed rest centrifuge studies, however, knowledge of plasma and blood volume losses is not helpful in predicting a subject's response to tilt. Fig. 13 summarizes the results of three studies, and shows the relation between gains or losses in plasma volume and increases and decreases in highest orthostatic rate between baseline and the end of testing. Although a casual relation is a reasonable expectation, and the cardio-protective techniques involve mechanical attempts to protect, in part, intravascular volumes, this lack of relationship is vexing.

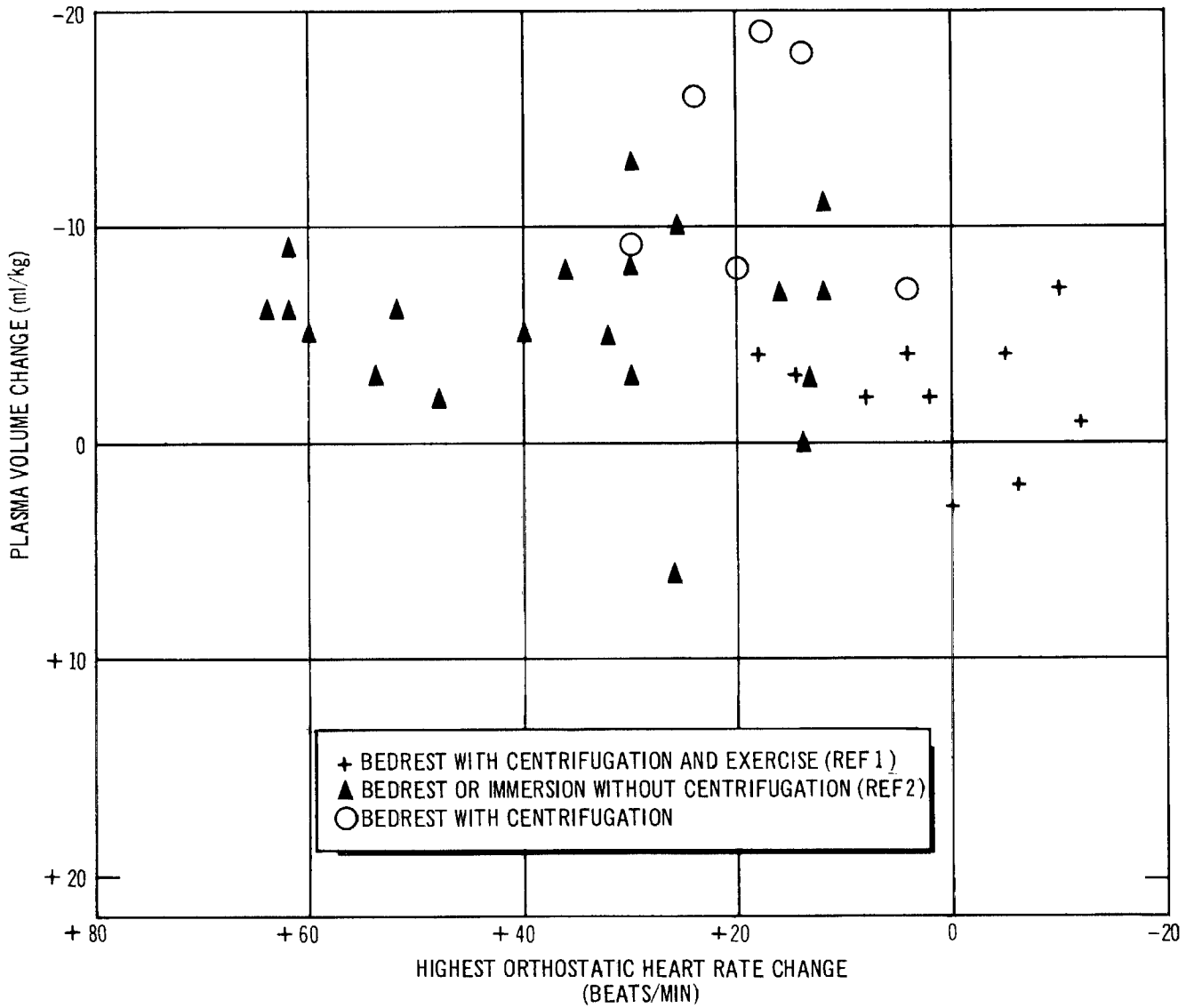

Figure 13. Relation of Changes in Plasma Volume and Highest Orthostatic Heart Rate

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DAC-59039

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P. D. White, J. W. Nyberg, L. M. Finney, and W. J. White.
June 1966. 45 pp. OTS price $3

DAC-59039

A study was made of the influence of periodic centrifugation on the physiological disturbances associated with 10 days of bed rest. Subjects rode the centrifuge 4 times each day; the duration of each ride was 20 min; the level of acceleration was +2.5 g_z, referenced to heart level. Subjects were exercised for a 14-day period before the study. Major findings of this study were that (1) the prescribed protocol of +2.5 g_z for 20 min after 12 hours of bed rest exceeded the tolerance of the subjects to positive acceleration; (2) the modal conditioning regimen was +1.75 g_z for 20 min 4 times each day; (3) the expected deterioration produced by recumbency in orthostatic tolerance was alleviated by periodic centrifugation; (4) the conditioning regimen was not quite so effective as shorter g-time integrals; (5) no cardiac irregularities or arrhythmias were encountered; (6) step-function acceleration tolerance and tolerance for sustained acceleration appear to be a sensitive method for measuring the cardiovascular status; and (7) tolerance to positive acceleration declines after 12 hours of bed rest, remains relatively constant, and rapidly improves during ambulation.

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