Modification of the Effects of Two Weeks of Bed Rest Upon Circulatory Functions in Man

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ABSTRACT

The effects of 2 weeks of bed rest on circulatory functions were studied in 72 healthy subjects, utilizing two different intervals of 2 weeks' bed rest. The value of various procedures in maintaining normal cardiovascular reflex regulatory mechanisms during bed rest was evaluated.

A 15-fold increase in syncopal reactions and a significant increase in orthostatic heart rate occurred after 2 weeks of bed rest.

Physical activity and tilt table training for 4 weeks between the two bed rest periods resulted in a decrease of the resting heart rate and an improvement in orthostatic tolerance.

An improvement in orthostatic tolerance after bed rest was noted with the various prophylactic procedures utilized in this study. A program consisting of exercise and tilt table training before bed rest and intermittent venous occlusion in the extremities during bed rest in a 10-degree head-up bed resulted in almost complete preservation of normal orthostatic tolerance. Various in-bed procedures tended to prevent hematological changes previously noted with simple bed rest. An antigravity suit proved very effective in preventing postural syncope after bed rest.

INTEREST IN man's response to a prolonged gravity-free environment has been stimulated by manned space flights—both those accomplished and those proposed. Gauer and Haber[3] called attention to the possibility of circulatory collapse due to "chronic elimination of pressoreceptor tonus similar to that observed after a prolonged confinement to bed." Other investigators[4, 5] have emphasized the importance of the effects of prolonged space flight upon the circulatory and metabolic functions. A previous publication discussed experimental studies directed toward immobilization and simulated weightlessness.[7] The report emphasized that the cardiovascular reflex mechanisms were not "pressoreceptors" but "stretch" receptors responding to stretching of the vessel wall independent of pressure. Only when pressure changes are associated with stretching are reflex mechanisms activated. Additional studies have demonstrated significant alterations in cardiovascular dynamics for subjects exposed to space cabin simulator conditions and for subjects exposed to chair rest in a normal g environment.[8, 9] The experiments demonstrated that physical inactivity does produce adverse changes in circulatory dynamics. This report deals with the influence of 2 weeks of bed rest upon circulatory functions in 72 healthy subjects. It describes the value of various procedures in maintaining normal cardiovascular reflex regulatory mechanisms during bed rest.

METHODS AND MATERIALS

Subjects were male volunteers, 17 to 23 years old, who had just completed 8 weeks of basic training in the United States Air Force. During a control period of 2 weeks of bed rest the subjects remained flat in bed with the following exceptions: they were allowed to sit in bed during meals and urination and to leave the bed for bowel movements.

A 4-week period of ambulation followed, during which a control group of 12 subjects pursued normal activities on the ward and the remaining 60 subjects underwent preconditioning consisting of daily tilt table training and physical exercise. The tilt table training, performed for 30 minutes twice daily, consisted of 45-degree head-down and 90-degree head-up tilting alternated every 30 seconds. The physical exercise included running, sit-ups, push-ups, straight leg raising, somersaults, and head stands.

During a subsequent 2 weeks of bed rest the subjects were divided into 6 groups of 12: Groups A, B, C, D, E, and F. Group A, the control group, and group B, who had received preconditioning, underwent bed rest only. In group C intermittent venous occlusion in the extremities was accomplished by inflation of blood pressure cuffs to 60 mm Hg for 1 minute every 5 minutes from 7:00 AM to 10:00 PM daily except during meals and defecation. Group D occupied a bed on which the head was elevated 10 degrees to simulate the hydrostatic effects of standing on the moon. In group E a combination of intermittent venous occlusion and a tilted bed was used. Group F performed in-bed exercises. The exercise program was one that could be performed by an astronaut confined to a seat in a space vehicle. Straps were passed tightly across the forehead, the chest, the thighs, and the legs. The subject alternated lifting against the strap with pushing against the bed. Fixed handgrips, attached to the side of the bed, were used for push-pull and side-to-side, and hand-gripping exercises. A fixed foot-halter allowed push-pull and side-to-side leg exercises. Foot and ankle exercises consisted of dorsiflexion, extension, and side-to-side rotation of the feet. Abdominal muscle tensing and quadriceps muscle tensing completed the exercise program. Each exercise was performed 15 times on the hour for 8 hours daily.

Because of psychosomatic problems 2 subjects did not complete the second period of bed rest.

Cardiovascular responses to gravity were evaluated by a standard tilt table procedure. On a motorized tilt table without a foot board, the subject was supported in a parachute harness. The sequence of events was as follows:

1. Horizontal baseline values.
2. 90° feet-down tilt — 1 minute
3. 45° head-down tilt — 1 minute
4. 90° feet-down tilt — 12 minutes
   followed by:
   - Breath holding— 45 seconds
   - Recovery—feet down— 3 minutes
   - Hyperventilation— 15 seconds
   - Breath holding— 45 seconds
   - Recovery—feet down— 3 minutes—20th minute
5. 45° head-down tilt — 1 minute
6. Horizontal

Breath holding without straining was prescribed. The respiratory maneuvers were added to the protocol to stress cardiovascular dynamics. Blood pressures and electrocardiograms were recorded at 1-minute intervals throughout the test and during and after the breathing maneuvers.

Baseline tilt table tests were performed on each subject before each period of bed rest. In 48 of the subjects an additional tilt table test was obtained at the beginning of the study during which an Air Force antigravity garment (type CSU-3/P) was worn with the leg, thigh, and abdominal bladders inflated to 60 mm. Hg. After each period of bed rest on 2 successive days tilt table tests with and without the use of the antigravity suit were performed. In the first 12 subjects tested, the antigravity suit was inflated to 30 mm. Hg.; in the remaining 60 subjects it was inflated to 60 mm. Hg. The subjects remained in bed between the tilt table tests, and the order of testing was reversed throughout the study to nullify any possible effect from previous testing.

In 42 consecutive subjects consisting of 7 subjects from each of the 6 groups (A, B, C, D, E, and F) hemoglobin and hematocrit determinations were obtained before and after each bed rest period. Body weight was also tabulated.

All subjects received a diet of approximately 2,400 calories throughout the period of the study. This was a calculated diet for metabolic balance studies which comprise another portion of the study.

RESULTS

Body Weight:—There was a progressive weight loss throughout the study, during bed rest and during activity. Changes in body weight in 42 subjects are given in Table I.

Hematological Changes:—The hemoglobin value before the first bed rest study was considered as the baseline value for each subject. After 2 weeks of bed rest 74 per cent of the subjects showed a slight increase in hemoglobin. After 4 weeks of ambulatory training following the bed rest period, 75 per cent showed a decrease in hemoglobin below the baseline value. During the second bed rest period control groups A and B, without activity or prophylactic procedures, again showed an increase in hemoglobin value. In test sub-

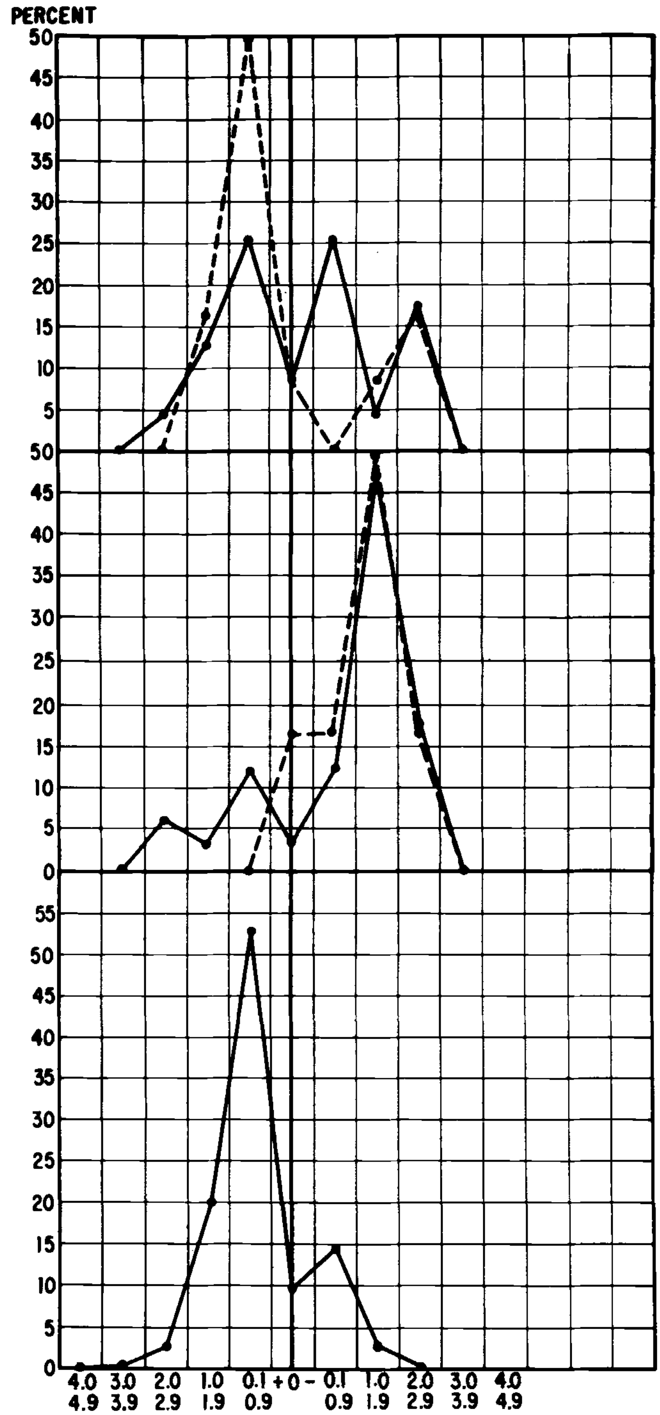

Fig. 1. Percentage distribution curves of changes in hemoglobin. Bottom curve: After first bed rest. Middle curve: After 4 weeks of ambulation. Top curve: After second bed rest. Bottom curve: All subjects. Middle and top curves: Broken line—groups A and B; solid line—groups C-F.

TABLE I. FREQUENCY DISTRIBUTION OF CHANGE IN BODY WEIGHT COMPARED TO PRE-TEST BASELINE VALUE

Change in body weight in kilograms		After 2 wks bed rest	Followed by 2 wks activity	After 4 wks activity	Followed by 2 wks bed rest
-6.01	-8.00	1			6
-4.01	-6.00	0	3	14	21
-2.01	-4.00	15	24	21	9
-0.01	-2.00	26	14	6	3
+0.01	+2.00	0	0	0	1

jects, groups C, D, E, and F, there was a random variation, with 43.5 per cent showing an increased value and 47.8 per cent, a decreased value. The percentage distribution curve of the controls during the second bed rest period is quite similar to that noted during the first bed rest study (Fig. 1). The distribution of hemoglobin changes and mean values are given in Table II.

TABLE II. FREQUENCY DISTRIBUTION OF CHANGE IN GRAMS OF HEMOGLOBIN COMPARED TO PRE-TEST BASELINE VALUE

Change in grams of hemoglobin	After 2 weeks bed rest	Followed by 4 wks ambulation		Followed by 2 more weeks of bed rest	
		Controls	Training	Without maneuvers (controls)	With maneuvers
+3.0 +3.9	0	0	0	0	0
+2.0 +2.9	·1 2.4%	0	2 6.0%	0	1 4.3%
+1.0 +1.9	8 19.2%	0	1 3.0%	2 16.3%	3 12.9%
+0.1 +0.9	22 52.8%	0	4 12.0%	6 49.8%	6 25.8%
0	4 9.6%	1 16.6%	1 3.0%	1 8.3%	2 8.6%
-0.1 -0.9	6 14.4%	1 16.6%	4 12.0%	0 0%	6 25.8%
-1.0 -1.9	1 2.4%	3 49.8%	16 48.0%	1 8.3%	1 4.3%
-2.0 -2.9	0	1 16.6%	6 18.0%	2 16.6%	4 17.2%
-3.0 -3.9	0	0	0	0	0
-4.0 -4.9	0	0	0	0	0
Number with increased value	31 74.0%	0	7 21.9%	8 66.6%	10 43.5%
Number with unchanged value	4 9.5%	1 16.6%	1 3.1%	1 8.3%	2 8.7%
Number with decreased value	7 16.6%	5 83.4%	24 75.0%	3 25.0%	11 47.8%
Mean change	+0.55	-1.16	-0.90	+.017	-0.291

The changes noted in the hematocrit values were similar to those noted in the hemoglobin value (Fig. 2). The hematocrit increased in 81 per cent of the subjects during the first bed rest period. The hematocrit decreased during the 4 weeks of activity and the controls again showed an increase during the second bed rest period. The values are given in Table III.

TABLE III. FREQUENCY DISTRIBUTION OF CHANGE IN HEMATOCRIT COMPARED TO PRE-TEST BASELINE VALUE

Change in hematocrit	After 2 weeks bed rest	Followed by 4 wks ambulation		Followed by 2 more weeks of bed rest	
		Controls	Training	Without maneuvers	With maneuvers
+7 +8					1 3.8%
+5 +6	9 21.6%	0 0	0 0	0	1 3.8%
+3 +4	11 26.4%	0 0	2 6.0%	4 28.4%	0 0
+1 +2	14 33.6%	0 0	6 18.0%	4 28.4%	10 38.0%
0	4 9.6%	1 14.3%	3 9.0%	3 21.3%	1 3.8%
-1 -2	1 2.4%	2 28.6%	6 18.0%	0 0	8 30.4%
-3 -4	2 4.8%	4 57.0%	9 27.0%	0 0	3 11.4%
-5 -6	0 0	0 0	6 18.0%	3 21.3%	1 3.8%
-7 -8	1 2.4%	0 0	2 6.0%	0 0	1 3.8%
-9 -10	0 0	0 0	0 0	0 0	0 0
Number with increased value	34 81.0%	0	8 23.5%	8 57.1%	12 46.2%
Number with unchanged value	4 9.5%	1 14.3%	3 8.9%	3 21.4%	1 3.8%
Number with decreased value	4 9.5%	6 85.7%	23 67.6%	3 21.4%	13 50.0%
Mean value	+2.6	-2.43	-2.06	0.15	-0.32

Orthostatic Tolerance:—At the beginning of the study the difference in the heart rate obtained in the horizontal position and after 12 minutes of orthostasis was commonly increased 22 to 26 beats per minute for all subjects. The increased heart rate with orthostasis appeared to have little relation to the baseline heart rate. The average increase was approximately the same. After bed rest the heart rate at 12 minutes of orthostasis was markedly increased over the baseline value. Usually the increase was at least 40 beats per minute

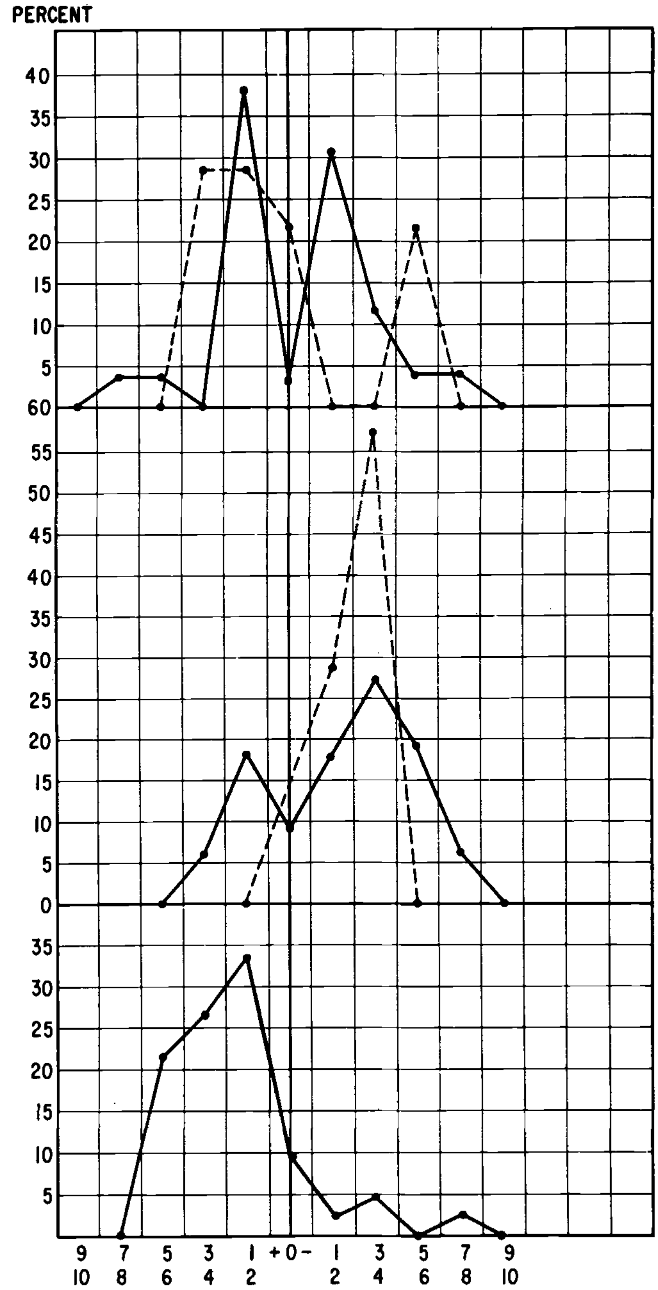

Fig. 2. Percentage distribution curves of changes in hematocrit. Bottom curve: After first bed rest. Middle curve: After 4 weeks of ambulation. Top curve: After second best rest. Bottom curve: All subjects. Middle and top curves: Broken line—groups A and B; solid line—groups C-F.

during 12 minutes of orthostasis after a 2-week bed rest period.

Four weeks of ambulatory activity generally caused a decrease in baseline heart rate. (Table IV) The mean heart rate at the beginning of the study for the 72 subjects was 75 beats per minute. After 4 weeks of ambulation, it was 67 beats per minute for the 12 subjects in group A. For the subjects undergoing the exercise and training program, it was 62.2 beats per minute.

The effects of physical exercise and tilt table training on orthostatic heart rate in ambulatory subjects was evaluated by comparing heart rates after 12 minutes of orthostasis in the tilt table tests performed before each period of bed rest. Before the second period of bed rest 7 subjects in group A showed an increase in heart rate and 5, a decrease; a mean decrease of 1.9 beats per minute occurred. In the remaining groups, who all had ambulatory training, 41 subjects (70.5 per cent), had a decrease in heart rate before the second bed rest; the mean decrease was 9.9 beats per minute. (See Table V and Figure 3)

TABLE IV. RESTING HEART RATE BEFORE STUDY AND AFTER 4 WEEKS OF AMBULATION

Heart rate	Before Experiment		After 2 weeks bed rest followed by 4 weeks ambulation		After 2 weeks bed rest followed by 4 weeks training	
			Group A		Groups B-F	
	No.	%	No.	%	No.	%
110 - 119						
100 - 109	2	2.8			0	
90 - 99	5	6.9			3	5.2
80 - 89	16	22.2	2	16.6	5	8.6
70 - 79	25	34.6	2	16.6	6	10.3
60 - 69	20	27.8	5	41.5	20	34.5
50 - 59	3	4.3	3	25.0	13	22.4
40 - 49	1	1.4	0		7	12.1
30 - 39	0	0	0		4	7.0
Mean heart rate	75		67		62.2	

TABLE V. THE DIFFERENCE IN THE 12TH MINUTE ORTHOSTATIC HEART RATE IN TILT TABLE RESTING PERFORMED BEFORE THE SECOND AND FIRST BED REST PERIOD

Change in heart rate		Control group		Training group	
		No.	%	No.	%
+70	+79				
+60	+69				
+50	+59				
+40	+49				
+30	+39			3	5.1
+20	+29			3	5.1
+10	+19	3	25.0	3	5.1
+ 1	+ 9	4	33.3	6	10.2
0		0	0	2	3.4
- 1	- 9	1	8.3	14	23.8
-10	-19	3	25.0	12	20.4
-20	-29	1	8.3	8	13.6
-30	-39			1	1.7
-40	-49			4	6.8
-50	-59			0	0
-60	-69			2	3.4
Subjects with increased heart rate		7	58.3	15	25.9
Subjects with unchanged heart rate		0	0	2	3.4
Subjects with decreased heart rate		5	41.7	41	70.5
Mean		-1.9		-9.9	

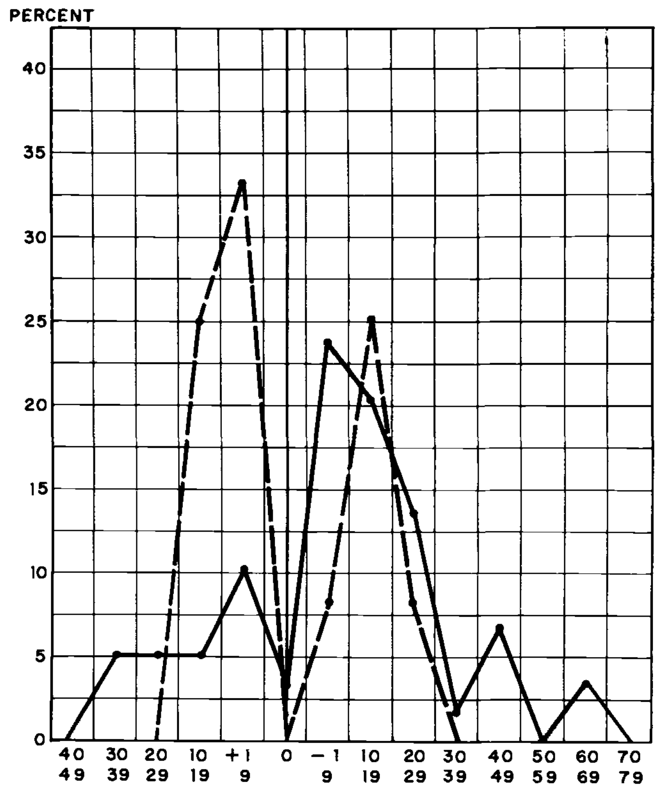

Fig. 3. Percentage distribution curves of differences in 12th minute orthostatic heart rate in tilt table testing performed before the second and first bed rest periods. Broken line: Group A; solid line: Groups B-F.

As indicated above, in a high percentage of subjects there was a decrease in the resting heart rate following the ambulatory training period. The opposite effect was seen with bed rest. The control group A had a mean

TABLE VI. DIFFERENCE IN BASELINE HEART RATE FOR EACH GROUP BEFORE AND AFTER THE 2ND BED REST PERIOD

Difference in heart rate		Group A		Group B		Group C		Group D		Group E		Group F	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
+40	+49	1	8.3										
+30	+39	0	0					1	8.3			1	9.1
+20	+29	1	8.3	4	33.3	3	27.3	2	16.6			1	9.1
+10	+19	6	50.5	5	41.5	3	27.3	2	16.6	3	25.0	6	54.6
+ 1	+ 9	2	16.6	1	8.3	4	36.4	4	33.3	2	16.6	1	9.1
0		0	0	0	0	0	0	0		1	8.3	0	0
- 1	- 9	1	8.3	1	8.3	1	9.1	3	25.0	5	41.5	1	9.1
-10	-19	1	8.3	0	0					1	8.3	1	9.1
-20	-29			0	0								
-30	-39			1	8.3								
Mean		+12.33		+9.5		+11.36		+10.83		+1.75		+12.55	

increase in resting heart rate of 12.33 beats per minute after the second bed rest period. (See Table VI) It will be noted that group E showed an increase only of 1.75 beats per minute following the second bed rest period. This group manifested better orthostatic tolerance after the second period of bed rest than other groups in the study.

In order to study the influence of the procedures performed during bed rest for the second 2-week period, a comparison of the orthostatic heart rate was made for each group. The heart rate was obtained at the end of two bed rest periods following 12 minutes of orthostasis. The value for the orthostatic heart rate after the second bed rest period was subtracted from the value obtained after the first bed rest period. A positive value indicated improved orthostatic tolerance. (Table VII) In the control group A the ortho-

TABLE VII. THE DIFFERENCE IN THE 12TH MINUTE ORTHOSTATIC HEART RATE BETWEEN THE END OF THE 1ST AND 2ND BED REST PERIODS

Change in heart rate	Group A		Group B		Group C		Group D		Group E		Group F	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
+70 +79											1	10.0
+60 +69					1	10			1	8.3	0	
+50 +59			1	8.3			2	16.6	2	16.6	0	
+40 +49			1	8.3			1	8.3	1	8.3	0	
+30 +39	1	8.3	0	0	1	10.0			2	16.6	0	
+20 +29	1	8.3	1	8.3			4	33.2	2	16.6	1	10.0
+10 +19	0	0	1	8.3	4	40.0	3	24.9	3	24.9	3	30.0
+ 1 + 9	3	25.0	3	25.0	2	20.0	1	8.3	0		2	20.0
0	0	0	1	8.3	0		0		0		0	
- 1 - 9	3	25.0	3	25.0	0		0		0		2	20.0
-10 -19	1	8.3	1	8.3	0		0		1	8.3	1	10.0
-20 -29	2	16.6	0	0	2	20.0	1	8.3				
-30 -39	0	0	0	0								
-40 -49	1	8.3	0	0								
Subjects with increased heart rate	5	41.7	7	58.3	8	80.0	11	91.7	11	91.7	7	70
Subjects with unchanged heart rate	0		1	8.3	0		0		0		0	
Subjects with decreased heart rate	7	58.3	4	33.3	2	20.0	1	8.3	1	8.3	3	30
Mean	-1.2		+10.0		+12.5		+22.6*		+31.00*		+14.2	

*Significant difference in mean orthostatic heart rate: P < .01

static heart rate was not materially different at the end of the two bed rest periods. Variations for the most part were small. Judged by heart rates, subjects in group B demonstrated an improved orthostatic tolerance over group A. The mean value for the increased heart rate at the end of the first bed rest period as compared to the end of the second bed rest period for group B was 10 beats per minute. Even though these subjects had no in-bed prophylactic procedures, they showed improvement in orthostatic tolerance at the end of the second bed rest period when compared to control subjects in group A. In group C, 80 per cent of the subjects had a higher heart rate during orthostasis at the end of the first bed rest period as compared to the second bed rest period with a mean difference of 12.5 beats per minute. In group D, 91.7 per cent of the subjects had a higher orthostatic heart rate after the first bed rest period compared to testing after the

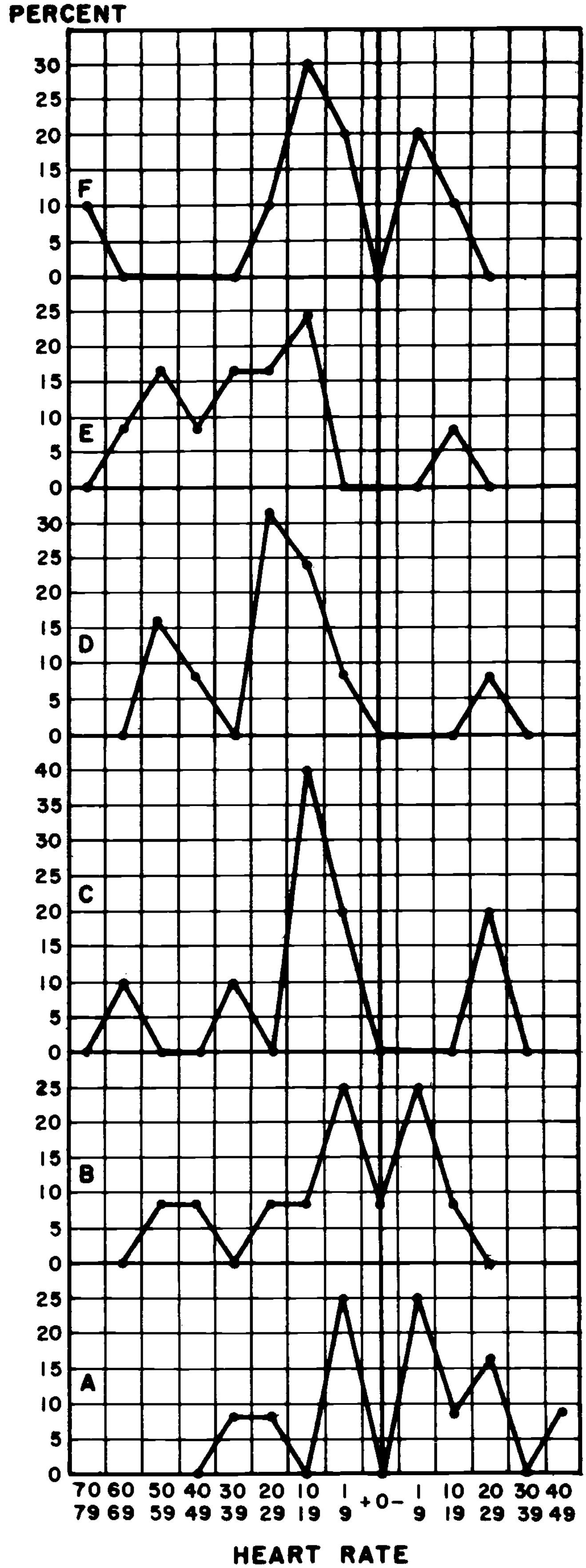

Fig. 4. Percentage distribution curves of differences in 12th minute orthostatic heart rate in tilt table testing performed at the end of the first and second bed rest periods. Letters refer to groups.

second bed rest period with a mean difference of 22.6 beats per minute. In group E, 91.7 per cent of the subjects had a higher heart rate during orthostatic testing at the end of the first bed rest period as compared to the end of the second bed rest period. The mean increase was 31 beats per minute. In group F, 70 per cent of the subjects showed a higher orthostatic heart rate during tests after the first bed rest period as compared to tests at the end of the second bed rest period, with a mean increase of 14.2 beats per minute. Only the control subjects in group A had a mean heart rate which was higher during orthostatic testing at the end of the second bed rest period as compared to the first bed rest period. All other test groups showed a mean decrease in heart rate by comparison at the end of the second bed rest period. The percentage distribution of changes in heart rate is seen in Figure 4.

The heart rates after 12 minutes of orthostasis for each subject in group E before the first bed rest and after the first and second periods of bed rest are shown in Table VIII. Little difference is seen between orthostatic heart rates before the first bed rest and after the second bed rest. One-half the subjects had lower heart rates after the second bed rest than before the first bed rest. When orthostatic heart rates after the 2 periods of bed rest are compared 11 of the 12 subjects showed marked reductions after the second bed rest.

TABLE VIII. HEART RATES: 12TH MINUTE OF ORTHOSTASIS GROUP E. PRECOND., CUFFS, & 10° TILT

Subject	Before Bed Rest	Post Bed Rest 1	Post Bed Rest 2
1.	129	148	93
2.	99	156	98
3.	129	156	127
4.	91	156	118
5.	87	110	79
6.	100	136	125
7.	100	134	93
8.	93	120	103
9.	83	103	113
10.	115	114	98
11.	97	140	117
12.	90	145	92
Mean heart rate	101	135	104

The use of the antigravity suit decreased the orthostatic heart rate compared to testing without the antigravity suit. After the first period of bed rest the mean orthostatic heart rate for the 12th minute of orthostasis for all subjects was 24 beats per minute lower when an antigravity suit was worn.

Syncopal episodes were markedly increased after bed rest. There were no syncopal episodes before or after the first bed rest period during the first 12 minutes of orthostasis. Only 2 subjects had syncopal episodes before the first bed rest period between the 13th and 20th minutes of orthostasis combined with respiratory maneuvers. There were 29 subjects that had a syncopal reaction during the 13th to 20th minute of orthostasis following the first 2-week bed rest period without an antigravity suit. Fewer episodes of syncope occurred after the second bed rest period when preventive procedures were used in certain groups as compared to those occurring after the first bed rest period without protective mechanisms. Before the second bed rest period 5 subjects had syncopal episodes; after the second bed rest period 20 subjects experienced syncopal episodes without an antigravity suit. (Table IX) A comparison of the change in incidence of syncopal episodes can be made by identifying the group and subject number. Of particular interest is group E in which circulatory collapse occurred in 4 subjects after the first bed rest and in one subject after the second bed rest.

Using the antigravity suit there was a marked decrease in syncopal episodes. Before the first bed rest study there were no syncopal episodes when the suit was used. After the first bed rest period 7 subjects experienced syncope while using the antigravity suit. Only 3 subjects had syncopal episodes after the second 2-week bed rest period while using the suit during orthostasis.

TABLE IX. SYNCOPAL EPISODES

	Without Antigravity Suit			
	Before 1st Bed Rest	Before 2nd Bed Rest	After 1st Bed Rest	After 2nd Bed Rest
12 minutes of orthostasis				C_6 F_5
13th to 20th minutes of orthostasis plus respiratory maneuvers	A_2 F_1	A_7 C_2 C_4 D_1 F_1	A_3 A_4 A_7 A_8 B_1 B_3 B_5 B_6 B_8 B_{10} B_{12} C_2 C_3 C_6 D_2 D_5 D_6 D_7 D_{10} E_2 E_3 E_6 E_{11} F_2 F_3 F_8 F_9 F_{11} F_{12}	A_4 A_8 A_7 B_2 B_3 B_6 B_8 C_8 C_{12} C_4 D_2 D_6 D_7 E_9 F_4 F_{11} F_{12} F_1
Total	2	5	29	20
	With Antigravity Suit			
12 minutes of orthostasis			A_1	
13th to 20th minutes of orthostasis plus respiratory maneuvers		No test performed.	A_7 C_{10} D_2 D_6 D_{10} F_5	A_7 D_5 F_1
Total	0		7	3

DISCUSSION

The diet of approximately 2,400 calories was apparently not adequate to maintain body weight since loss in body weight was progressive throughout the study. The loss in body weight did not appear to affect orthostatic tolerance.

Though the variations are small, the incidence of hemoconcentration after 2 weeks of bed rest is sufficiently high to suggest a change in blood volume. The most likely explanation is a decrease in plasma volume rather than an increase in red cell mass. Several workers have reported a decrease in plasma volume during bed rest.[2, 10, 12]

The decrease in hemoglobin and hematocrit after 4 weeks of ambulation to levels below baseline values is compatible with a decrease in red cell mass and increase in plasma volume similar to that observed by Taylor et al.[12] during physical training following bed rest. In dogs, an increased destruction of red cells has been demonstrated during physical exercise following inactivity.[1] The results suggested a reduced activity of the bone marrow of dogs during confinement and an increased blood forming activity during physical training.

The present study does not permit a conclusion concerning the persistence of hemoconcentration during bed rest. It is possible that a relative decrease in red cell production would ultimately lead to a more baseline concentration of hemoglobin with a smaller blood volume.

During the second bed rest period the 24 subjects that were inactive in bed again demonstrated a pattern similar to that noted during the first bed rest period. This would suggest that the mechanism that was operating initially was again manifested. The reproducibility of the percentage distribution curves speaks well for the probable accuracy of the laboratory procedures. This trend was not noted in the test subjects carrying out prophylactic procedures while at bed rest. These studies were sufficiently different to fall within the range of random laboratory variation or to suggest that, if a plasma volume factor were implicated, the procedures were successful in maintaining normal plasma volume or volumes not appreciably different from the preceding baseline values. This evidence suggests that prophylactic procedures of the type employed with this study are capable of preventing hematological variations noted during the 2-week bed rest period.

It is of further interest that the evidence for hemoconcentration noted in this study was not seen in the previous study of subjects exposed to space cabin simulator environment. Those subjects tended to show decreased hemoglobin and hematocrit with decreased blood volume and plasma volume. It is possible that the altered environment of the space cabin simulator over and above the physical inactivity may have had significant hematological influences. Since hematological variations can be seen with physical inactivity, a true assessment of their value in the space cabin simulator must be made in conjunction with studies of the influence of physical inactivity. If physical inactivity tends to induce hemoconcentration, such an effect could mask any inhibition of hemopoietic action induced by hyperoxia.

This study has demonstrated in a large number of subjects the expected decrease in orthostatic tolerance manifested by syncopal episodes following a 2-week period of bed rest. During orthostatic testing syncopal episodes were 15 times more common after the first 2-week bed rest period than before the first bed rest period.

The decrease in resting heart rate after various forms of physical activity observed in this study is not a new observation. It is commonly accepted that increased physical activity tends to decrease the resting heart rate in the average healthy individual engaging in usual daily activities. Well-trained athletes are known to develop bradycardia with increased training. The resting heart rate is an important indication of the level of physical fitness. The subsequent demonstration in group B that the level of physical fitness tends to provide some protection against manifestations of decreased orthostatic tolerance suggests that this is an index of some importance in estimating an individual's orthostatic tolerance and of considerable value in assessing problems of cardiovascular deconditioning. Raab et al.[11] have emphasized that individuals during bed rest and physical inactivity tend to develop a rapid resting heart rate with an inefficient myocardium owing to the storage to catecholamine products within the myocardial cell. Raab states that the catecholamines decrease the myocardial cell's ability to utilize oxygen, increase myocardial irritability, and predispose the heart to arrhythmias.

The opposite spectrum of physical activity was seen during the bed rest periods. During bed rest there was a tendency for the heart rate to increase. During the second bed rest group E showed the least change in heart rate following the second 2-week bed rest period. The resting heart rate may provide an index for studying the influence of cardiovascular deconditioning. It must be used with caution, however, since it is well appreciated that the heart rate changes in response to a variety of stimuli, both psychic and physical.

The training program carried out during the 4-week ambulatory period in groups B, C, D, E, and F seemed to improve orthostatic tolerance. This proved true when each subject was used as his own control and also when subjects were compared to the control subjects of Group A. This suggests that the level of physical fitness and training preceding periods of inactivity such as encountered in bed rest may influence the degree of orthostatic tolerance and deconditioning subsequently noted, at least in subjects exposed to a 2-week period of inactivity of the bed rest type. The well-known principle that physical fitness improves orthostatic tolerance is demonstrated in such standard physical fitness tests as Schneider's Index. A remnant of Schneider's Index is the orthostatic tolerance test on the United States Air Force aviation examination. A sign of excellent physical condition is a slow heart rate with a minimal change in heart rate between lying and standing (orthostasis).

Again, it is important to emphasize that the cardiovascular reflexes associated with orthostatic tolerance are stretch receptors, not pressoreceptors. Physiological events which alter the blood volume within the vascular bed or the arterial flow induce complex reflex mechanisms. Exercise offers the opportunity to use or activate the various reflex mechanisms on the basis that the receptors are stretch receptors, not pressoreceptors.

By comparing the orthostatic tolerance as indicated by changes in heart rate after the first and second bed rest period, group A may be considered as the true controls. They demonstrated no significant change in orthostatic tolerance at the end of the two bed rest periods. This would be expected since nothing was really done to improve orthostatic tolerance. It is possible that even more subjects would have showed decreased orthostatic tolerance following the second bed rest period had their physical activity during the 4-week ambulatory period been more restricted. Group B subjects showed some improvement in orthostatic tolerance after the second bed rest period compared to the first bed rest period. The relative contribution of the physical exercise versus the tilt table training to this improvement cannot be determined from the present study. Other investigations, however, have shown that physical exercise improves orthostatic tolerance.[6] No increased benefit from the addition of in-bed exercise was apparent. The exercise program, containing mainly isometric exercises, probably did not tax the cardiovascular system to any significant degree. Isometric exercise ordinarily does not improve circulatory endurance.

The combination of preconditioning, intermittent venous occlusion, and the 10-degree head-up bed provided almost complete protection from the loss of postural tolerance during bed rest. Any advantage gained from intermittent venous occlusion must be the result of venous distension or some effect other than stimulation of the carotid sinus and similar receptors since no change in heart rate or intra-arterial pressure has been observed by us during inflation of the cuffs. The benefit of the tilted bed may be related to increased venous pressure in the legs or to increased activity of the vasomotor center. One deficiency of the present study was the absence of a procedure, such as the Flack maneuver, that fires vigorous carotid sinus reflexes. The effects of more frequent cuff inflation throughout the day and night and intermittent Flack maneuvers or similar procedures need evaluation.

The search for effective inflight procedures to maintain the circulatory system of the astronaut at a normal level could be approached more directly if more were known concerning the relative role played in the deterioration of cardiovascular antigravity responses during bed rest by inactivity and by the absence of the hydrostatic effects of the erect position. It has been demonstrated recently that inactivity in a space cabin simulator and inactivity during chair rest, both of which subject the individual to a normal g environment, are followed by significant orthostatic intolerance.[8, 9]

This finding seems paradoxical when compared to Whedon's report[13] that an oscillating bed largely prevented the loss of orthostatic tolerance in subjects immobilized in lower body casts. The head of the bed was tilted every 1¾ minutes for at least 8 hours each day. Perhaps various procedures may protect the integrity of cardiovascular antigravity mechanisms if the stimulus is sufficiently intensive. Reflex vasomotor activity and cardioacceleration occur both from exercise and from standing. Distension of peripheral veins by hydrostatic pressure may increase basal tone. Local stimulation of peripheral vessels from increased flow during exercise may be important in maintaining normal responses to orthostasis.

Thus the fact that intensive measures utilizing the effects of hydrostatic pressure prevent the loss of orthostatic tolerance during bed rest does not prove that the absence of the hydrostatic effects of ambulation during bed rest is a major factor in the development of orthostatic intolerance. The efficacy of vigorous activity during bed rest in preventing orthostatic intolerance needs evaluation.

This study demonstrates the effectiveness of the antigravity suit in preventing postural intolerance after bed rest. The antigravity suit provides an important stopgap measure for use in space flight until the extent of the problem of prolonged weightlessness is known and until effective inflight procedures are discovered for preventing the deterioration of cardiovascular antigravity mechanisms.

SUMMARY

Prolonged bed rest was studied in 72 subjects, utilizing two different intervals of 2 weeks' bed rest. Each subject thereby served as his own control. An additional group was identified as pure controls and carried throughout the experiment in order to protect the experimental design. A 15-fold increase in syncopal reactions occurred after 2 weeks of bed rest. Since syncopal episodes were almost nonexistent during the first 12 minutes of orthostasis, this provided an opportunity for study of the changes in orthostatic heart rate. There was a significant increase in orthostatic heart rate after a 2-week bed rest period, and an increase in the resting baseline heart rate.

Physical activity and tilt table training of 4 weeks' duration between the two bed rest periods decreased the resting heart rate comparably to that seen in other forms of physical training.

With each subject serving as his own control, an improvement in orthostatic tolerance was noted with the various prophylactic procedures utilized in this study. Improvement in orthostatic tolerance was also noted as an aftereffect of the physical conditioning program combined with tilt table training during the 4-week ambulatory period. A program consisting of exercise and tilt table training before bed rest and intermittent venous occlusion in the extremities during bed rest in a 10-degree head-up bed resulted in almost complete preservation of normal orthostatic tolerance.

Hematological changes are described which seem most reasonably explained on the basis of changes in plasma volume. The use of various in-bed prophylactic

procedures tended to prevent the hematological picture encountered with simple bed rest.

The use of the antigravity suit during tilt table testing after bed rest markedly reduced the incidence of syncopal reactions and the degree of orthostatic tachycardia observed during testing without the suit after bed rest.

These studies suggest avenues for further investigation of measures adaptable to inflight use to maintain normal cardiovascular reflex regulatory mechanisms during prolonged space flight.

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