Cardiovascular Deconditioning From Space Cabin Simulator Confinement

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DIFFICULTIES ENCOUNTERED in assessing the influence of weightlessness on the circulatory system have previously been discussed.[8] Problems other than weightlessness which profoundly influence the cardiovascular system must also be considered. One of these in confinement or inactivity resulting in cardiovascular deconditioning. Simulated hypogravic studies done to date all include inactivity as a major factor in the experiments.[1, 2, 3, 7, 8, 9] The supine position, whether it be in a body cast, water immersion, or bed rest, is perpendicular to the vertical g field (perpendicular to $+G_Z$ and$-G_Z$). Whether or not this has any particular physiological influence cannot be judged with certainty in the presence of a significant decrease in physical activity. The original studies of Dietrick[6] and Taylor[14, 15] were principally designed to study the influence of inactivity or bed rest. They were not intended to study the influences of weightlessness. Data obtained during manned orbital flight from the Mercury Project suggesting decreased orthostatic tolerance must also be regarded from the point of view of confinement, inactivity, or deconditioning, as opposed to the influences of weightlessness.[4, 5] Data obtained from future manned space flights cannot provide a significant answer relative to the problem of weightlessness unless adequate consideration of deconditioning due to inactivity is given. As long as the vehicle provides limited opportunity for activity the problems of deconditioning will complicate the picture.

Since previous reported studies of inactivity are complicated by the supine position or absence of vertical g, it has not been possible on these studies to separate the influence of inactivity versus absence of vertical g stimulation. To understand what might be seen in a space vehicle related to weightlessness one should first study the results of an environment exactly similar to the space capsule within the laboratory with normal g force application. The opportunity to do this occurred as the result of the pre- and post-examinations of subjects who were being studied for space cabin simulator flights. Since these individuals were either seated or moved about within a small confined area they presented the problem of confinement with inactivity during normal g force application. Such studies provide the beginnings of a method of controlled evaluation to which comparison of observations during space flight may be made. In a sense, studies designed in this manner represent the controls to evaluate observations made during manned space flight.

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METHODS AND MATERIALS

Thirty-six healthy, male subjects had pre- and post-confinement studies of particular interest to the cardiovascular area. Twenty-six of these subjects were then confined to a space cabin simulator environment for approximately two weeks. The remaining 10 subjects were confined for approximately 30 days. During space cabin simulator studies the individuals were active do-

TABLE I. AGE OF SUBJECTS, CONFINEMENT, AND ENVIRONMENT *

Subject	Age	Days	Environment
A1	23	14	258 mm. Hg pressure with 96% O_2
A2	24	14	
A3	27	14	
A4	26	14	
A5	25	14	
A6	31	14	
B1	24	14	7 days at 700 mm. Hg followed by 7 days at 200 mm. Hg with a mixed gaseous environment.
B2	25	14	
B3	33	14	
B4	28	14	
B5	27	16	8 days at 700 mm. Hg and 8 days at 200 mm. Hg.
B6	34	16	
B7	29	16	
B8	27	16	
C1	36	17	192 mm. Hg pressure with 96% O_2
C2	30	17	
C3	38	17	
C4	30	17	
C5	28	17	
C6	27	17	
C7	33	17	
C8	25	17	
D1	24	17	
D2	23	17	
D3	23	17	
D4	25	17	
E1	27	30	380 mm. Hg 42% O_2
E2	28	30	
F1	17	30	258 mm. Hg 100% O_2
F2	18	30	
F3	18	30	
F4	19	30	
G1	19	30	700 mm. Hg 33% O_2
G2	21	30	
G3	24	30	
G4	19	30	

* A detailed description of the protocol for chamber runs may be obtained from the following reports: Morgan, T. E., Jr., Ulvedal, F., Cutler, R. G., and Welch, B. E. *Aerospace Med.*, 34:589-592, July 1963; Morgan, T. E., Jr., Cutler, R. G., Shaw, E. G., Ulvedal, F., Hargreaves, J. J., Moyer, J. E., McKenzie, R. E., and Welch, B. E. *Aerospace Med.*, 34:720-726, August 1963; Cutler, R. G., Robertson, W. G., Herlocher, J. E., McKenzie, R. E., Ulvedal, F., Hargreaves, J. J., and Welch, B. E. *Aerospace Med.*, 1963 (In press).

ing instrument performance tests or carrying out other tasks. They were frequently seated for these duties. They had regular sleep periods which were planned for each study. Physical activity was limited by the small size of the cabin. The principal purpose of the experiments was to study the influences of different gaseous environments over a period of time on human subjects. The gaseous environmental factors for the composite group of 36 subjects were not uniform since it was desired to study different environments in different groups. The age of the subjects, the essential gaseous environmental factors, and the length of time of confinement for the different groups is given in Table I. The diet was carefully controlled to study experimental conditions and metabolic activities. These factors will be the subject of another report. The data from all of the subjects in this group were obtained from studies done by the Clinical Sciences Division of the USAF School of Aerospace Medicine pre- and post-flight. The pertinent features of these studies are included here. The inflight studies were done by the Environmental Systems Branch, USAF, School of Aerospace Medicine, and are not included in this report. Each subject received a comprehensive pre- and post-flight history and physical examination. The areas of greatest interest to cardiovascular deconditioning were principally accomplished by the cardiovascular group of the Internal Medicine Department. The same studies were not done in all subjects since this had not been a planned experiment but an after-the-fact observation. The majority of the subjects had pre- and post-flight body weight determination. Serum cholesterol studies pre- and post-flight were available in certain instances. Studies also included the determination of single pre- and post-confinement hemoglobin, hematocrit, red blood cells, blood volume, plasma volume and red blood cell mass. A double Master's exercise tolerance test was done pre- and post-run providing an opportunity to study exercise tolerance. Treadmill studies were also done and in certain instances the maximum oxygen consumption was available pre- and post-flight. The treadmill examination was carried out with a gradual change in the inclination of the treadmill, one per cent of arc per minute, gradually increasing the amount of work performed. Maximum oxygen consumption was measured by obtaining successive minute samples near the peak of physical exertion using this method.

Since principal concern was directed toward orthostatic tolerance, all 36 subjects chosen for this analysis had pre- and post-confinement tilt table studies. These were done by a method developed for aeromedical evaluations. A baseline heart rate recorded by electrocardiogram and a baseline blood pressure was obtained with the subject in the horizontal position. Once the baseline had been established the subject was tilted perpendicular 90 degrees. In most instances the patient was suspended with the parachute harness with no support to the lower extremities. The electrocardiogram and blood pressure were obtained at each minute through 12 minutes of orthostasis. At this point the subjects performed maximum breath holding usually of one minute's duration, followed by a three-minute recovery with the patient still in the orthostatic position. This was followed by hyperventilation, usually of 15 seconds' duration, followed by 45 seconds of breath holding. This stress was then followed by a three-minute recovery period with the subject still in the upright position. The procedure encompasses a little more than 20 minutes of orthostatsis, compounded with additional stresses of the type known to induce syncopal responses or stress the cardiovascular system's compensatory mechanism to prevent syncope.

Analysis of the change in the subject's ability to withstand orthostatic tolerance as judged by tilt table procedures were done in several different manners. The incidence of syncope and its time of occurrence during the procedure was studied pre- and post-flight. A syncopal reaction was judged to occur whenever the patient actually passed out or the syncopal symptoms were sufficiently severe to require that the subject be returned to the horizontal position.

For data analysis, at specified time intervals within the procedure, changes in blood pressure, heart rate, and pulse pressure were noted. The time intervals selected were baseline, 12, 16, and 20 minutes of orthostasis. The baseline systolic pressure was always chosen as the lowest systolic value. The baseline pulse pressure was obtained by taking the lowest pulse pressure obtained in the reading with the lowest systolic pressure. The heart rate was read directly from the electrocardiogram.

RESULTS

Body Weight. Seven subjects had an increase in body weight during the period of confinement. Six subjects

TABLE II. BODY WEIGHT AND SERUM CHOLESTEROI CHANGES

Subject	Weight before (lbs.)	Weight change (lbs.)	Cholesterol before (mg.%)	Change in cholesterol (mg.%)
A1	160	-6	186	-21
A2	157	-1	233	-1
A3	145	0	122	0
A4	137	-3	105	0
A5			256	
A6			296	-30
B1	150	-9	215	-96
B2	155	-4	231	-38
B3	131	-3	263	-54
B4	186	-8	193	-31
B5	177	-7	254	
B6	174	0	284	-122
B7	173	-5	189	-71
B8	157	-5	225	
C1	158	0	186	
C2	144	0	232	
C3	153	-5	265	-42
C4	174	-6	197	-7
C5	165	-8	272	
C6			250	-84
C7	153	-4	231	
C8	147	-5	230	
D1	130	+3		
D2	166	0	204	-68
D3	160	-5	235	
D4	160	-6	216	
E1	194	-16	219	
E2	191	-9	284	
F1	144	+10	165	-8
F2	154		206	-6
F3	132	+3	188	+7
F4	144	+10	195	+5
G1	190	+9	165	+25
G2	135	+1	174	-32
G3	168	0	190	0
G4	180	+7	200	+49

had no change in body weight, and 19 subjects had a weight loss ot 1 to 9 lbs. during confinement. The body weight for these studies was obtained 2 weeks before confinement and the day confinement ended. The average weight loss for those individuals confined for approximately 2 weeks was 3.7 lbs. The average weight loss for the entire group was 2.3 lbs. The changes in body weight are given in Table II. The 7 subjects who gained weight as a group were younger than the rest of the subjects in the series. Five were 17 to 19 years of age. None of the 6 subjects that were 17-21 years of age lost weight during a 30-day period of confinement. These subjects in group F and G had an ad lib high quality diet as opposed to other groups that had dehydrated food or a liquid diet.

Serum Cholesterol. The serum cholesterol values are given in Table II. Values before and after confinement were available in 23 subjects. It was decreased in 16, unchanged in 3 and increased in 4 subjects. In all 4 subjects with an increase in cholesterol, the subject's were 19 years of age or less and demonstrated weight gain during their 30-day confinement period. In 10 subjects who had pre- and post-flight cholesterol determinations and also demonstrated a weight loss, 9 had a decrease in serum cholesterol value, 1 remained unchanged. For the 10 subjects the average decrease in cholesterol was 36.1 mg. per cent.

Circulating Blood Changes. Hemoglobin determinations before and after confinement were available in 26 subjects. In 22 instances the hemoglobin decreased. In two instances it was unchanged and in 2 subjects it was increased. In subject C7 the apparent 2-gram increase in hemoglobin should be suspected as inaccurate, since the hematocrit did not change and decreases in blood volume, plasma volume and red cell mass were noted in other studies. In the 26 subjects the mean decrease in hemoglobin after confinement was 1 gram.

Pre- and post-confinement hematocrit values were available in 32 subjects. The hematocrit was increased in one, unchanged in 3 and decreased in 28 subjects. There was a mean decrease in the hematocrit of 4.3 per cent. The red blood cell count was available pre- and post-confinement in 27 subjects. The value was increased in 1, unchanged in 3, and decreased in 23 subjects. The mean decrease for the entire group was 530,000. The three individuals classified as having no change exhibited a change of less than 100,000.

Blood volume determinations by the I-131 isotope dilution technique were available pre- and post-confinement in 17 subjects. There was a decrease in 15 and an increase in the values for 2 subjects. There was a mean decrease of 522 cc. for the group.

The red blood cell mass was unchanged in 1, increased in 2, and decreased in 14 subjects. The mean decrease in red blood cell mass was 285 cc.

The plasma volume was decreased in 12 and increased in 5 subjects. There was a mean decrease in plasma volume of 280 cc. for the group.

Exercise Response. All 36 subjects had a standard double Master's exercise tolerance test. Following a period of confinement, the usual change was a significant increase in heart rate after exercise, as compared to the pre-confinement test. The mean increase during the baseline was 7.9 beats per minute. Immediately after exercise the mean increase was 12.8 beats per minute. At 2 minutes after exercise the mean increase was 15.8 beats per minute, and at 5 minutes after exercise it was 10.4 beats per minute. A tabulation

TABLE III. CHANGES IN CIRCULATING BLOOD

Subject	Hemoglobin (gms.)		Hematocrit (%)		RBC (cc.)		Blood volume (cc.)		RBC mass (cc.)		Plasma vol. (cc.)	
	Before	Change	Before	Change	Before	Change	Before	Change	Before	Change	Before	Change
A1			47	-10			4780	-140	1970	-310	2840	+170
A2			44	-7			6220	-180	2740	-500	3480	+310
A3	14.8	-.8	49	-5	4.9	-.3	5860	-940	2380	-180	3480	-780
A4	16.0	-2.7	48	-5	4.9	-.9	5210	-700	1990	0	3700	-1100
A5	14.8		47		5.0							
A6	14.4	0			4.35	0						
B1	15.2	-1.6	48	-5	5.2	-1.6						
B2	14.0	-1.5	47	0	5.1	-.7						
B3	14.8	-1.5	47	-7	5.0	-1.0						
B4	14.4	-1.4	46	-3	4.9	-.4						
B5	16.0	-1.2	49	-4	4.83	-.15						
B6	17.2	-1.2	50	-3	4.97	-.17						
B7	15.2	-1.0	45	-3	4.53	0						
B8	13.6	-1.0	43	-5	4.68	-.6						
C1	15.6		50	-5	5.2		5040	-300	2280	-160	2760	-130
C2					4.8		5770	-1150	2470	-670	3790	-970
C3	15.2		45	-4	4.2		5460	-40	2460	-160	3000	+120
C4			46	-1	4.8	-.3	6360	-660	2980	-480	3380	-180
C5	15.2	-2.0	48	-4	5.74	-1.15	5275	-582	2319	-250	2956	-254
C6	15.0	-1.0	48	-5	5.3	-1.21						
C7	12.0	+2.0	43	0	4.12	+.31	5496	-793	2281	-578	3215	-205
C8	15.0		42	-5	5.1		5568	-746	2060	-130	3508	-615
D1	15.0	-2.0	49	-2	4.71	-.1	4734	+477	2154	+211	2580	+208
D2	14.8	-1.2	47	-9	5.3	-.4	5974	+57	2509	-402	3465	+455
D3	14.5	-0.1	47	+1	5.75	-.35	6830	-1010	2880	-370	4050	-740
D4	15.0	-1.4	46	0	6.4	-2.1	6380	-1580	2500	-670	3880	-910
E1	15.0		47		5.35		6030	-180	2950	+60	3080	-240
E2			48	-2	5.12		6190	-410	2800	-50	3390	-360
F1	14.8	-0.6	46	-4	5.04	-.65						
F2	14.4	+0.4	45	-3	4.39	0						
F3	16.0	-1.2	48	-4	4.91	-.45						
F4	15.6	-1.4	48	-5	4.8	-.35						
G1	15.2	-1.0	48	-5	5.11	-.33						
G2	16.0	-1.2	45	-5	4.68	-.17						
G3	17.0	-1.6	51	-6	5.53	-.72						
G4	14.8	0	47	-4	5.06	-.36						

TABLE IV. CHANGES IN HEART RATE AFTER DOUBLE MASTER'S EXERCISE TEST

Subject	Pulses resting		Immediately		2 minutes		5 minutes	
	Before	Change	Before	Change	Before	Change	Before	Change
A1	65	+18	65	+6	62	+21	71	+19
A2	65	-10	60	+10	57	+11	60	0
A3	65	+3	83	-18	65	0	71	0
A4	75	-13	88	-9	79	-4	75	0
A5	68	+11	75	+50	65	+42	68	+26
A6	88	-13	115	-21	107	-24	100	-21
B1	60	-5	55	+13	60	-6	60	-3
B2	75	-7	75	+4	83	0	79	-8
B3	75	0	125	-31	88	0	83	+2
B4	88	0	65	+35	83	+11	90	+4
B5	88	+12	107	+8	107	0	100	0
B6	71	+4	79	+21	60	+28	75	+13
B7	88	+2	88	+19	100	0	100	-6
B8	65	+3	88	-13	79	-14	68	-3
C1	55	+21	65	0	60	+2	60	+11
C2	71	-16	79	+4	65	0	60	+5
C3	62	0	83	-23	65	+3	65	+3
C4	55	+2	71	+4	60	+15	54	+14
C5	44	+6	68	+20	65	+3	54	+11
C6	65	+15	88	+19	79	+35	60	+40
C7	45	+30	60	+23	55	+20	50	+33
C8	65	-8	60	-6	60	-6	60	0
D1	55	+13	55	+25	60	+15	57	+18
D2	60	+19	75	+5	60	+40	60	+15
D3	50	0	60	+5	55	-5	68	-18
D4	68	-18	88	+12	50	+33	68	+7
E1	60	+11	65	+50	62	+38	65	+23
E2	50	+12	60	0	60	+11	65	+6
F1	55	+28	57	+43	57	+47	68	+32
F2	60	+28	55	+45	50	+50	55	+28
F3	55	+24	83	+11	68	+32	60	+28
F4	50	+44	65	+35	50	+50	52	+29
G1	54	+14	50	+29	55	+20	50	+25
G2	55	+43	52	+48	75	+25	88	+12
G3	75	+13	94	+19	80	+35	94	+21
G4	60	0	60	+20	60	+20	60	+11
Mean change		+7.9		+12.8		+15.8		+10.4

TABLE V. CHANGES IN TREADMILL STUDIES

Subject	Time before	Change (min.)	Maximum O_2 consumption before(cc.)	Maximum O_2 consumption after (cc.)	Change (cc.)
A1	11	+3			
A2	17	-2			
A3	18	0			
A4	15	+1			
A5					
A6					
B1	17	+1	2500	2500	0
B2	16	-1	2400	2900	+500
B3	12	0	2000	2000	0
B4	11	0	2700	2400	-300
B5	11	-2	2050	2050	0
B6	14	-6	2100	1800	-300
B7	15	-4	2700	2100	-600
B8	18	-4	3000	2300	-700
C1	16	-4			
C2	14	+1			
C3	14	+1			
C4	13	+2			
C5	14	-2			
C6	13	-4			
C7	15	-2			
C8	16	-2			
D1	17	-2			
D2	17	-1			
D3	16	+1			
D4	10	0			
E1					
E2					
F1	16	-4	3000	2100	-900
F2	18	-3	3200	2600	-600
F3	17	-7	2600	2000	-600
F4	18	-7	2600	2500	-100
G1	21	-6	3600	3100	-500
G2	16	-7	2300	1700	-600
G3	13	-4	2500	2100	-400
G4	19	-9	3300	2300	-1000
Mean change		-2.3			-381.0

of heart rates and response to exercise pre- and post-confinement are given in Table IV.

The time required to reach a heart rate of 180 to 200 beats per minute during treadmill exercise decreased in 21, remained unchanged in 4 and increased in 7 subjects after confinement. In those subjects with an increase in exercise time it was minimal, whereas in subjects with a decrease in time it was often 6 or 7 minutes. The greatest change was noted in subjects confined for 30 days. For the entire group the mean decrease in time of exercise was 2.3 minutes. The maximum oxygen consumption measured at the end of the exercise test showed a mean decrease of 381 cc. The maximum oxygen consumption was increased in only 1 subject, was unchanged in 3 and decreased in 12 subjects. The value obtained from treadmill studies are given in Table V.

Tilt Table Studies. The results from the tilt table

TABLE VI. HEART RATE CHANGES DURING ORTHOSTASIS AFTER DECONDITIONING

Subject	Baseline		12 minutes		16 minutes		20 minutes	
	Before	After	Before	After	Before	After	Before	After
A1	79	-17	115	-27	115		18	
A2	79	-14	107	0	100	+25	115	-27
A3	71	+12	88	0	88			
A4	83	-4	100	+30	83	+32	94	+31
A5	65	+29	83	+24	88	+12	94	-68
A6	75	0	136	-42	88	+6	83	+11
B1	75	-10	115	-15	110	-16	83	+53
B2	79	+4	83	+32	94	+14	94	+21
B3	75	0	100	0	115	-8	100	+15
B4	115	-21	125	0	100	+25		
B5	107	-7	115		125		136	
B6	83	0	88	+12	94	+6	88	+6
B7	75	+25	75	+61	94	+26	83	+42
B8	62	+2	79		79		83	
C1	56	+12	65	+35	65	+35	65	+35
C2	79	-23	71	+8	75	0	75	-7
C3	65	+6	71	+8	75	0	75	+3
C4								
C5	54	0	71	+12	65	+42	71	+17
C6	83	0	83	+24	90	+10	88	+12
C7	68		83		79		71	
C8								
D1	62	+6	79	+15	65	+29		
D2	71	-13	107	0	79	+16	136	-36
D3	65	0	65	+29	60	+40	100	-6
D4	65	0	83	0	83	-12	83	0
E1	60	+15	100	+15				
E2	71	-13	83	+11	83	0	88	0
F1	79	+15	100	+25	100	+36	88	+37
F2	94	0	79	+21	88	+12	83	+17
F3	83	+14	107	Sync	115		107	
F4	100	-25	100	-17	107	-39	100	-21
G1	83	+5	120	+5	100	+25	88	0
G2	100	0	107	+29	115	+21	115	-8
G3	115	-8	115	+10	115	+10	100	+15
G4	83	+5	150	-14	150	0	136	+14

TABLE VII. HEART RATE CHANGES DURING ORTHOSTASIS AFTER CONFINEMENT

	Baseline	12 minutes	16 minutes	20 minutes
Mean change	-0.3/min.	+10.0/min.	+12.8/min.	+6.2/min.
Number of subjects with decreased heart rate	12	5	3	7
Number of subjects with unchanged heart rate	8	7	4	3
Number of subjects with increased heart rate	12	19	20	15

studies showed for the group a general decrease in orthostatic tolerance. The changes in heart rate are given in Tables VI and VII. Because of the wide variability in heart rate, tabulation shows many changes. As a group, the changes in baseline heart rate before tilting were not appreciably changed after confinement. An equal number of subjects showed an increase or decrease in heart rate. After 12 minutes of orthostasis there were 19 subjects with an increase in heart rate and only 5 with a decrease in heart rate. By the end of 20 minutes' orthostasis several subjects had been eliminated from the study due to syncopal episodes. This influences the figures showing an apparent better tolerance for 20 minutes as opposed to 12 or 16 minutes of orthostasis. The pulse pressure showed a relatively random change during the baseline for the study before tilting. For the group there was a mean decrease in 1.2 mm. Hg. The pulse pressure was decreased in 15 subjects and increased in 18 subjects. Because of syncopal episodes not all of the subjects could truly be tested through 20 minutes of orthostasis. The results indicate that with progressive orthostasis there was an increase in the number of subjects who had a decreased pulse pressure. At 16 minutes of orthostasis, 18 subjects had a decreased pulse pressure and only 9 showed an increased pulse pressure. The values obtained for pulse pressures during tilt table studies are given in Tables VIII and IX. The changes in systolic blood pressure are given in Tables X and XI. In general, during orthostasis, there was a decrease in systolic pressure. This is of even greater significance because the examples of circulatory collapse or syncope have already been eliminated at different stages of the tilt table procedure from the tabulation given in Table XI.

TABLE VIII. PULSE PRESSURE CHANGES DURING ORTHOSTASIS AFTER DECONDITIONING IN mm. Hg

Subject	Baseline		12 minutes		16 minutes		20 minutes	
	Before	Change	Before	Change	Before	Change	Before	Change
A1	44	+4	96	+16	142		16	
A2	60	-16	44	-16	44	-32	28	+4
A3	52	-36			83		30	
A4	54	-8	42	-22	46	-24	32	
A5	38	+10	30	-4	22	+2	12	+10
A6	48	-2	32	+2	34	-2	32	0
B1	44	-14	16	+14			22	0
B2	48	-6	46	-36	40	-22	26	-20
B3	36	+12	48	-10	44	-28	28	-22
B4	42	+10	26	+18	56	-20	38	-14
B5	60	-22	36		34		46	
B6	54	+6	38	+6	42	-6	34	+8
B7	42	+20	60	-42	52	-36	56	-36
B8	40	-14	36		52		54	
C1	30	+6	24	-4	30	+4	20	+12
C2	46	+2	26	+12	28	+2	40	-12
C3	50	-10	36	-12	36	-14	22	-2
C4	46	+12	36	-24	42		32	
C5	46	+2	38	0	38	-14	46	-14
C6	66	-14	54	-42	44	-14	56	-28
C7	74	+2	54	-30	72	-52	32	
C8	62	+6	48	+4	46		44	
D1	58	-20	48	-20	38	+6	50	+2
D2	38	0	52	-10	24	+6	20	+10
D3	50	+10	30	+32	12	+58		
D4	46	0	60	-30	30	+6	34	-6
E1	48	+6	72	-40				
E2	42	+6	10	+30	38	-6	34	-10
F1	40		44		52		40	
F2	60	-8	48	-18	32	+2	48	-20
F3	52	-2	24		36		22	
F4	50	+32	46	+34	40	+16	50	+10
G1	50	-2	30	-12	38	-8	38	+6
G2	42	+6	20	+41	30	0	30	+30
G3	38	+10	30	+14	28	-2	20	+18
G4	78	-32	50	-30	54		48	

TABLE IX. PULSE PRESSURE CHANGES DURING ORTHOSTASIS IN mm. Hg AFTER CONFINEMENT

	Baseline	12 minutes	16 minutes	20 minutes
Mean change	-1.2 mm.Hg	-2.5 mm.Hg	-7.1 mm.Hg	-3.5 mm.Hg
Number of subjects with decreased pulse pressure	15	19	18	11
Number of subjects with unchanged pulse pressure	2	1	1	2
Number of subjects with increased pulse pressure	18	12	9	10

TAXLE X. CHANGES IN SYSTOLIC PRESSURE IN mm. Hg

Subject	Baseline		12 minutes		16 minutes		20 minutes	
	Before	Change	Before	Change	Before	Change	Before	Change
A1	116	+2	106	+6	98		100	
A2	120	-18	108	-16	126	-46	106	-6
A3	128	+26	130		142		80	
A4	126	-8	118	-12	122	-10	118	
A5	108	+20	110	0	108	-2	104	-4
A6	126	-6	120	+10	120	0	120	+8
B1	108	+4	90	-20	82		102	+10
B2	120	+2	138	-46	134	-26	116	-20
B3	120	0	120	-4	122	-16	102	-6
B4	148	-22	142	+18	154	-30	150	-24
B5	146	-26	138		144		152	
B6	146	-10	140	-8	132	-2	128	+8
B7	120	+10	142	-32	132	-12	136	-26
B8	124	+10	132		134		144	
C1	90	+6	100	+2	102	+8	100	+14
C2	116	+4	128	0	128	-8	134	-12
C3	130	-14	124	-22	130	-16	120	-10
C4	118	-14	114	-32	120		118	
C5	110	+8	116	-12	130	-22	130	-16
C6	134	-12	132	-40	124	-14	124	-22
C7	116	0	122	-22	152	-66	120	
C8	120	+12	126	0	126		124	
D1	120	-8	122	-14	120	+6	130	-8
D2	102	+12	118	-2	110	+14	100	+10
D3	118	+20	112	+30	82	+64		
D4	116	0	122	-2	118	+8	118	+10
E1	118	+4	166	-54				
E2	120	0	110	+10	130	-12	122	-6
F1	120		124		130		120	
F2	132	-8	140	-18	130	-10	154	-22
F3	120	+26	116	Sync.	122		120	
F4	122	+20	116	+28	114	+14	120	+30
G1	156	-16	116	+22	132	+8	132	+8
G2	124	+16	130	+12	126	+14	134	-14
G3	140	+12	136	+6	122	+12	130	+16
G4	160	-30	150	-20	162		152	

TABLE XI. FREQUENCY OF SYSTOLIC PRESSURE CHANGES DURING ORTHOSTASIS AFTER CONFINEMENT

	Resting	12 minutes	16 minutes	20 minutes
Number of subjects with decreased systolic pressure	13	18	15	14
Number of subjects with no change in systolic pressure	4	3	1	0
Number of subjects with an increased systolic pressure	18	10	9	8

Syncopal episodes occurring before and after chamber runs are given in Table XII. Prior to confinement

TABLE XII. SYNCOPAL EPISODES BEFORE AND AFTER DECONDITIONING

	12 minutes	Breath holding	16 minutes	Hyperventilation and breath holding	20 minutes
Preflight syncope		D3 E1			A3 B4
Postflight syncope	A3 B5 B8 F4	C4	A1 C8	A5 C7	

none of the 36 subjects demonstrated syncope during the initial 12 minutes of orthostasis. After confinement, 4 (11 per cent) subjects had syncopal episodes in less than 12 minutes of simple orthostasis. Throughout the entire procedure, there were only 4 subjects that demonstrated syncopal episodes during pre-confinement testing as compared to 9 (25 per cent) subjects after confinement. Only one subject demonstrated syncope both before and after the confinement period. This was subject A3. It is noteworthy that the syncopal episode occurring prior to confinement did not occur until the end of 20 minutes of orthostasis, combined with two periods of additional stress testing (breath holding and hyperventilation followed by breath holding). This same subject had syncope after 7 minutes of orthostasis after confinement. None of the other 3 subjects evidencing syncopal episodes during pre-confinement testing demonstrated any such event after confinement.

DISCUSSION

The study of subjects pre- and post-confinement in space cabin simulator environment presented the general picture of cardiovascular deconditioning. The comparison of these studies with similar examinations done in bed rest studies, water immersion studies and other immobilization experiments, points up some basic similarities. The one thing that all of these studies have had in common is inactivity. In the supine position used for bed rest and water immersion studies, the earth's g force is perpendicular to the long axis of the body, or transverse. Although the subjects have been upright there have been variations in gaseous environment and barometric pressure during the chamber studies, not present in the bedrest studies. Both of these studies yield strikingly similar results.

A decrease in body weight during inactivity has previously been noted. In Dietrick's[6] study change in muscle mass was noted. Loss of weight does not necessarily occur and did not occur in the study of Birkhead.[3] Of particular interest in the cabin subject group was the difference in weight loss associated with different age groups. The subjects who showed a weight gain were very young subjects compared to the rest of the group and this may be due to difference in diet. The direct relationship of weight loss to decreased cholesterol value was quite apparent. This is entirely consistent with studies that have shown that during weight loss there is a decrease in the serum cholesterol value. It is not likely that these are due to laboratory variations since such a high preponderance of the determinations showed a decrease after confinement. Compared to studies of changes in blood cholesterol during increased physical activity, the two opposite ends of the spectrum both demonstrate a decrease in plasma cholesterol, correlated with change in body weight, as opposed to physical activity.

Another clear-cut manifestation of cardiovascular deconditioning was seen in the response to the double Master's exercise tolerance test. It is well known that deconditioning decreases the circulatory system's ability to cope with exercise.[11, 12, 15] The increased heart rates noted in this group after exercise following the period of confinement is a general indication of the deconditioning influence. The ability to carry out prolonged exertion on the treadmill was similarly decreased. This and a decreased maximum oxygen consumption are further indications of cardiovascular deconditioning. Similar results have been noted in exercise studies done on bed rest subjects.[3, 15] This implies that their occurrence during bed rest is not necessarily equated to the direction of application of g force but more appropriately to the problem of confinement and inactivity.

Subject C2 had typical findings of neurocirculatory asthenia two weeks after the experiment, manifested by faintness and palpitation. These symptoms are frequently found in the deconditioned individual.

The general decrease noted in hemoglobin, hematocrit, blood volume and red blood cell mass are all features that have previously been noted during bed rest studies.[3, 14] Dietrick[6] noted a slight decline in blood volume which is not quite as great as that noted in this study. Decrease in hematocrit and hemoglobin, when measured, have been observed in almost every experiment dealing with bed rest or immobilization. The changes in plasma volume were less constant, although as a group they showed a decrease. The changes in the circulating blood are particularly noteworthy in view of the interest of the influence of oxygen and gaseous environment upon the hematological picture. The use of control subjects is of some benefit in solving this problem, but the bed rest studies compared to the cabin subject studies make it relatively clear that a major component which may contribute to the hematological picture in space cabin environments is the influence of inactivity. Even in the presence of minimal venipuncture and blood sampling, the general hematological picture noted in the cabin subjects have also been noted in immobilization subjects. The multiple different determinations and the high percentage showing a decreased value tends to eliminate the possibility that these changes are due to simple laboratory variation. In the latter instance, they should vary on either side of the spectrum which was noted in this study.

The tilt table studies demonstrated unequivocally an increased incidence of syncopal reactions following chamber confinement. This is even more impressive when the general clinical events associated with tilt table work are considered. Usually if there is an anxiety factor associated with fainting during tilt table procedures it will be noted during the subject's first experience with the tilt table. Studying subjects with the tilt table is somewhat like recording the clinical blood pressure. Multiple tilt table procedures tend to develop a baseline value less influenced by anxiety. Multiple baseline tilt studies were not done in this group since an experimental design for this study was not envisioned. The lack of a pre-planned experiment, however, has certain advantages, since any possibility for bias associated with the subsequent results is essentially eliminated. Of the 4 subjects that had syncopal reactions prior to the chamber flight, 3 of these subjects had no syncope after confinement. This strongly suggests that their initial syncopal episode was related to anxiety. The fact that all but one of the 9 individuals (25 per cent) that had syncopal episodes after confinement had normal tilt table responses before deconditioning tends to remove any significant bias associated with anxiety.

Further evidence of orthostatic intolerance is demonstrated by the general increase in heart rate and decrease in pulse pressure. Heart rate times stroke volume represents the cardiac output. The pulse pressure is an indicator of the stroke volume. In order to prevent a syncopal episode in the face of significant pooling of the circulating blood volume in the dependent areas of the body, the cardiac output must be significantly increased.

The pre- and post-confinement study of space cabin simulator subjects provided a means of studying confinement while the subjects were exposed to a usual normal g force environment. The subjects were seated upright during a large portion of each day and there was nothing in the cabin environment which in any way could be construed as similar to the absence of gravitational force stimulation. These studies provide a meaningful control to look at the significance of studies obtained from bed rest experiments, and the observations noted during manned orbital space flight. The bed rest experiments with normal atmospheric environment provide a group of subjects with restricted activity that can be compared to the chamber subjects with altered atmospheric environment. Comparing these various groups from the different studies, a picture emerges of the influence of marked limitation of physical activity independent of the associated factors of recumbency or atmospheric changes. The importance of cardiovascular deconditioning has long been stressed by Rabb.[11, 12] His emphasis has been directed more toward the heart muscle and the storage of catecholamine products within the heart muscle. Another factor of deconditioning is a frequent tendency toward decreased body weight, probably associated with decreased muscle mass. In the presence of decreased body weight there is at least a transitory decrease in blood cholesterol. Whether or not this persists would require more prolonged periods of study and evaluation. There is a general decrease in circulating blood volume. This is commonly associated with a decreased hemoglobin, hematocrit, red blood cell count, and red blood cell mass. Cardiovascular deconditioning is associated with a decreased tolerance to physical exertion. This is manifested by the increase in heart rate after a double Master's exercise test, the decrease in the ability of the individual to perform endurance exercise such as treadmill exertion, and the common decrease in maximum oxygen consumption. The latter suggests a decreased ability of the heart to achieve the same level of cardiac output noted during a normal physical condition.[13] Associated with the general picture of deconditioning was strong evidence of decreased orthostatic tolerance. This is indicated by increased heart rate, a common decrease in systolic pressure and often a decrease in pulse pressure. In the extreme degree it was manifested by a fairly high incidence of syncopal episodes. The syncopal episodes could not be specifically attributed to any one derangement associated with deconditioning. Similar changes in the circulating blood were noted in individuals who did not faint as compared to those who did. The general deconditioning of the heart, the vascular system, the skeletal muscle system, as well as changes in circulating blood volume, are all contributory factors which can lead to a syncopal reaction.

The severity of the clinical picture of cardiovascular deconditioning likely bears a direct relationship to the degree and duration of immobilization. When a body cast and strict immobilization is used, the changes noted may be more marked. If the period of confinement and restricted activity is extended over a sufficiently long period of time, the evidence of deconditioning will be more apparent. Lesser degree of restricted activity show similar but less marked manifestations. Deconditioning really represents the opposite spectrum of the well trained athlete. In the latter individual the heart is large with a large stroke volume, the heart rate is usually slow and the response to minimal exertion such as the double Master's exercise tolerance test frequently shows minimal increases in heart rate after exertion.

The fortuitous circumstance of studying individuals in a space cabin environment emphasizes the need for clarification of the interpretation of immobilization experiments. Simple bed rest studies cannot be equated to the weightless environment. Because of the presence of relative inactivity and immobilization, changes noted during space cabin simulator experiments cannot be solely attributed to the internal gaseous environment and barometric pressure. The physical limitations of space for manned space vehicles at the present time necessitates marked limitation of activity. Until sufficient physical activity can be maintained within the space vehicle, the influence of weightlessness encountered during manned space flight cannot be appropriately assessed. Some concept of this influence might better be appreciated by comparison to adequately controlled runs of a similar nature in the earth's gravity environment. Many of the other factors during space flight which predispose to orthostatic intolerance are not likely to be simulated, such as the emotional aspects of the actual flight and the normal post-flight reaction.

The appropriate evaluation of an environmental change requires that only one environmental factor be changed at a time. At present there is limited data available on the influence of simple confinement with subjects normally seated and their daily activity markedly restricted. The influence of the level of activity used by a subject is a useful baseline before an attempt is made to study the influence of changes in gaseous environment, barometric pressure, or changes in g force. Without such baseline controls the experimental design is exceedingly more difficult.

At this writing it has not been proved that weightlessness will present a major or significant problem to circulatory dynamics. The multiple factors involved have been discussed in a previous article.[10] The numerous immobilization experiments cannot be equated to the weightless state. The evidence of orthostatic intolerance reported in the Schirra and Cooper flights cannot be definitely attributed to weightlessness.[4, 5] Influences directly related to deconditioning and other factors known to contribute to orthostatic intolerance were present. It cannot be stated that weightlessness will not produce certain influences upon the circulatory system. If such influences do occur whether or not they are significant cannot be judged until the problem of physical inactivity resulting in deconditioning can be properly evaluated. Supporting the body weight requires energy. Weightlessness may augment physical inactivity by the absence of body weight. Body mass will still be present and body movements will require a force to stop as well as start a physical movement.

It would appear to be much simpler to solve the problem of physical inactivity leading to cardiovascular deconditiong than it would be to solve the problem of absent g force. The importance of clarification and separation of the problem of cardiovascular deconditioning as opposed to other influences of weightlessness can hardly be overemphasized. The success of manned space flight can well depend in part upon a clear understanding of the difference between these two problems. The comparison of these multiple studies suggest that cardiovascular deconditioning associated with physical inactivity is a major factor. Physical training and peak performance capability leading to peak cardiovascular conditioning would seem a logical part of training for manned space flight. Methods of maintaining appropriate physical conditioning or adequate physical activity to prevent cardiovascular deconditioning would logically appear to be an important component of manned space flight. The evidence that physical inactivity produces cardiovascular deconditioning suggests the necessity for careful review of all studies directed toward the influence of changes in gaseous environments, barometric pressure, and decreased g force. Such consideration could then lead to more accurate experimental designs resulting in more valid conclusions.

The deleterious influence of physical inactivity whether or not the subject is at bed rest is suggested by this study. Two weeks of significantly limited physical activity even with the subjects frequently in a seated position can produce evident cardiovascular deconditioning. These observations on space cabin simulator subjects suggest that more attention should be given the requirement for physical activity even during illness. The differentiation may not be so much the difference between bed rest and chair rest as it is between presence or absence of adequate physical activity. No doubt there is more physical activity required simply by being in a seated position as opposed to recumbent position, but even limited activity with intermittent standing, sitting position and lying, as included in the space cabin simulator profile, may not be adequate to maintain proper cardiovascular conditioning. The multiple changes associated with inactivity appear to have widespread physiological influences.

SUMMARY

1. A group of 36 subjects undergoing space cabin simulator studies were examined in detail pre- and post-confinement. This group demonstrated cardiovascular deconditioning similar to studies noted in bed rest and other immobilization experiences.

2. Cardiovascular deconditioning effects occur in the presence of normal g force application in subjects undergoing a normal 24-hour day cycle with frequent periods of sitting upright and intermittent work-sleep periods. This demonstrated that the prone body position or weightlessness was not necessary to produce these manifestations of deconditioning.

3. Cardiovascular deconditioning as noted in this study complicated by given chamber environments included the following: decreased blood volume, decreased hemoglobin, decreased hematocrit, decreased exercise tolerance manifested by increased pulse rate after Master's exercise tolerance test, decreased exercise endurance on the treadmill, decreased maximum oxygen consumption, and decreased orthostatic tolerance.

4. Decreased orthostatic tolerance was manifested by an increased incidence of syncope. Twenty-five per cent of the subjects had syncopal episodes on a simple tilt table test after deconditioning. The remainder of the subjects as a group manifested during orthostasis, increased heart rate, decreased pulse pressure, and decreased systolic pressure as compared to pre-confinement studies.

5. Cardiovascular deconditioning in the presence of normal g force application can be sufficiently marked that influences of g force diminution or absence of vertical g forces cannot be determined without adequate consideration of the influence of physical inactivity. Current and previous immobilization studies may reflect simple cardiovascular deconditioning as opposed to simulated weightlessness or absent vertical g.

6. Chamber work, or activities in simulated space vehicles, or actual recent manned space flights impose the problem of physical inactivity and deconditioning which make it more difficult to learn the real effects of weightlessness, changes in gaseous environment, changes in barometric pressure or other environmental factors. Studies in these areas should include evaluation of the influence of physical deconditioning.

7. At the time of this writing there are no uncomplicated studies reported that clearly demonstrate that weightlessness creates an adverse effect upon the circulatory system. This includes the observations of manned space flights for the Mercury Project.

8. The importance of cardiovascular deconditioning of a significant degree occurring while subjects are in the upright position, as well as in subjects at bed rest,

has an important medical application. It suggests that whether patients are at bed rest or in a chair the important question is the amount of physical activity they are getting. Further attention needs to be given to improving physical activity above the level of simply being seated upright, when medically possible. An assessment of the problem of physical inactivity is an important requirement in medical management.

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