NASA Technical Memorandum 103987

Exercise Countermeasures for Bed-Rest Deconditioning (1986): Final Report

Edited by John Greenleaf

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Foreword

This somewhat different reporting format of including published papers, those in press, or those in preparation for publication, should provide greater credibility when the reader interprets our results and conclusions because most of these papers have been reviewed by expert referees. Not all investigators have prepared their data for publication, and a few have not been able to prepare their data for this report. Major data that have not been prepared for publication or inclusion in a chapter have been placed in the appendices to be available for future analysis.

An overview of the scope and major findings of this study can be found in section 1, Summary. More complete documentation can be found in the chapters in section 6, Results, where manuscripts extant, in press, and in preparation are located. A complete list of publications from this study is presented as appendix H.

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Acronyms and Abbreviations

BR	bed rest
BV	blood volume
C	control
cm	centimeter
d	day
EMG	electromyogram
EVA	extravehicular activity
EX LD	exercise load
gm	gram
Hct	hematocrit
Hb	hemoglobin
Hg	mercury
HRF	Human Research Facility
hr	hour
ht	height
IKE	isokinetic exercise
ITE	isotonic exercise
kg	kilogram
l	liter
m	meter
min	minute
ml	milliliter
mo	month
N	number
N-m	Newton meter
NASA	National Aeronautics and Space Administration
NOE	no exercise
NS	non significant
PEG	posture, equilibrium, and gait
PT	proprioception training
PV	plasma volume
RCV	red cell volume
rpm	rotations per minute
s	second
SA	surface area
SD	standard deviation
SE	standard error
wk	week
wt	weight
yr	year

CONTENTS

1. Summary

The purpose for this 30-day bed-rest study was to investigate the effects of short-term, high-intensity isotonic and isokinetic exercise training on maintenance of aerobic work capacity (peak oxygen uptake); muscular strength and endurance; and orthostatic tolerance, equilibrium, and gait. Other data were collected on muscle atrophy, bone mineralization and density, endocrine analyses of vasoactivity and fluid-electrolyte balance, muscle intermediary metabolism, and performance and mood of the subjects.

Nineteen men (32–42 yr) were allocated into three groups: no-exercise control (peak oxygen uptake and isokinetic tests once/wk, N = 5), isotonic exercise training (electronic Quinton ergometer, supine, N = 7), and isokinetic exercise training (electronic Lido ergometer, supine, N = 7). The exercise training regimens were conducted near peak levels for 30 min in the morning and 30 min in the afternoon 5 d/wk. The protocol consisted of a 7-d ambulatory control period during which the subjects equilibrated on the standardized diet, 30 d of 6° head-down bed rest, and a final 4.5 d of ambulatory recovery. Their diet consisted of commonly available fresh and frozen foods; mean caloric consumption of 2,678 ± SE 75 kcal/d (control), 2,833 ± SE 82 kcal/day (isotonic), and 2,890 ± SE 75 kcal/d (isokinetic) resulted in mean weight losses during bed rest of 1.01 kg, 0.85 kg, and 0.0 kg, respectively.

The results indicated that: (1) The subjects maintained a relatively stable mood, high morale, and high esprit de corps throughout the study. Scores improved in nearly all performance and mood tests in almost all the subjects. Isotonic training, as opposed to isokinetic exercise training, was associated with decreasing levels of psychological tension, concentration, and motivation, and with improvement in the quality of sleep. (2) Peak oxygen uptake was maintained during bed rest with isotonic exercise training; it was not maintained as well with isokinetic (–9.0%) or no-exercise (–18.2%) training. If a 9% reduction in aerobic power is acceptable, isokinetic exercise training could be used for maintenance of strength, endurance, and the reduced aerobic capacity in astronauts during flight. (3) In general, there were few decreases in strength or endurance of arm or leg muscles during bed rest, in spite of reduction in size (atrophy) of some leg muscles. (4) There was no effect of isotonic or isokinetic exercise training on orthostasis, because tilt-table tolerances were reduced similarly from 42–53 min to 30–34 min in the three groups following bed rest. (5) Bed rest resulted in significant decreases of postural stability and self-selected step length, stride length, and walking velocity, which were not influenced by either exercise training regimen. Pre-bed-rest responses were restored by the fourth day of recovery.

2. Introduction

In September 1985 NASA Life Science managers from Ames Research Center and Johnson Space Center agreed to conduct a collaborative 30-d bed rest study to devise and test exercise-training protocols for astronauts to perform during flight that would maintain their physical strength, endurance, and aerobic capacities (peak oxygen uptake) at pre-flight levels. The primary purpose was to compare the effectiveness of intensive lower extremity, isotonic, ergometer exercise training; isotonic treadmill exercise training; and isokinetic exercise training to maintain peak oxygen uptake and muscular strength and endurance. The secondary purpose was to determine effects of these training regimens and no exercise training on post-bed rest orthostasis (ability to stand without fainting) and posture (equilibrium and gait). Additional data of a more fundamental nature on various physiological systems were collected to help understand how these deconditioning responses occur.

The study was to be completed by October 1, 1986, so the findings could be applied to the selection of exercise devices for Space Station Freedom. Because of the Challenger accident on January 28, 1986, this study completion deadline was waived, but we decided to complete it by the original October 1986 deadline.

The original protocol involved three 30-d bed rest periods using 32 middle-aged men as astronaut surrogates. There were to be three exercise-training groups of eight men each plus a no-exercise-training group of eight men. Because construction of the vertical treadmill was delayed, the study preceded without the treadmill training group. The final day of subject testing was September 29, 1986.

Hopefully these findings will assist in prescribing exercise training regimens for use by astronauts to maintain their working capacity, performance, and well-being on Space Station Freedom and longer-duration spaceflights.

Acknowledgments

The authors express their warm gratitude and appreciation to the 125 people who had a significant role in this study; especially to the test subjects, Dee O'Hara, manager of the Human Research Facility, Edith Crofoot, the nursing staff and aides, the exercise testing group from the University of California, Davis; Andrew Ertl, Todd Trowbridge, Dave McKenzie, and Gene Myers; the dietitians Robin Williams and Victoria Major and the food preparation staff; the medical monitor Ralph Pelligra; the Bionetics Corporation personnel managers Gail Bennet-Hiley and Ranita Dalton; the coinvestigators and their staffs, especially Bonnie Rosenberg and Kristen Lindseth-Gomez for performance and mood testing assistance; the Laboratory for Human Gravitational Physiology support and technical staff: Jeff Ball, Victor d'Aloia, Sally Greenawalt, Teresa Hutchison, Linda Kirby, Sandra Lewis, Joann Meredith, Andrea Ertl, and Joan Silver; and Bridget Eller, Angela Hardesty, and Shannon Watenpaugh for manuscript preparation. A special thanks to the members of the AIBS review panel who shared their thoughts, comments, and recommendations with us: Reggie Edgerton, Philip Gollnick, William Haskell, Michael Pollock, William Stauber, and Charles Tipton (Chair).

This work was supported by NASA Tasks 199-21-12, 199-22-12, 199-22-22, 199-22-32, 199-220-44, NAG2-410, and Army Task MRDC-3A161101A-91C.

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3. Background

The normal eugravitational forces on the body during spaceflight are reduced by several orders of magnitude and hydrostatic pressure within the body is negated, resulting in a "disuse" adaptive deconditioning syndrome (ref. 9), where the decrease in muscle size (atrophy) may be accounted for by loss of muscular tissue and fluid (ref. 14). Without utilization of exercise countermeasures, the ability to maintain aerobic work capacity and to generate muscular force decreases, not only during spaceflight, but also during limb immobilization and prolonged bed rest deconditioning in eugravity (refs. 5, 6, 11, and 12). Exercise is the primary method utilized by both astronauts and cosmonauts for maintaining or preventing muscular deconditioning during flight. While exercise training can restore or maintain muscular strength and endurance during deconditioning, continuing negative mineral and nitrogen balances indicate that muscular deterioration has not been totally arrested (ref. 9). Factors associated with or causing decreased strength and endurance could be increased oxidative enzyme levels, increased protein catabolism, and decreased muscle substrate reserves (refs. 1, 5, 9, and 12).

The ability to generate appropriate muscular force is a requirement during intravehicular activity, especially during extravehicular activity (EVA), and also during egress from the Shuttle after landing. Leg muscles are used mainly during EVA; usually for body stabilization during upper body isometric and dynamic work to overcome resistance of the pressurized spacesuit, to move large masses such as satellites, and to handle other structures during construction of Space Station Freedom. Conversely, use of the upper extremities to stabilize the body during lower extremity exercise may provide sufficient stimuli (load) to maintain upper body strength and endurance (ref. 3). Since lower extremity muscles receive reduced stimuli during flight, leg exercise training must be emphasized.

When the activity to be performed is of short duration, high intensity, with a progressively increasing level of stress, successful adaptation requires increases in strength, endurance, and substrate reserves, as well as hypertrophy of muscle cells (ref. 12). The differing types of muscular contractions—concentric (fiber shortening) or eccentric (fiber lengthening)—used during exercise training usually result in different levels of adaptation. High intensity, concentric (isotonic) exercise training results in elevated oxidative enzyme levels similar to that during endurance training, while use of only concentric isokinetic contractions during training results in increases in strength without significant muscular hypertrophy (ref. 4). Thus, muscle size may not be a reliable indicator of muscle strength or function. Maintenance of lower extremity muscle mass during flight may afford some protection against post-flight orthostatic intolerance because tissue compliance in the lower leg appears to be increased, in conjunction with the decrease in muscle size following prolonged bed rest (refs. 2 and 3).

Exercise-training protocols will continue to be evaluated as countermeasures for spaceflight deconditioning, especially for the musculoskeletal and cardiovascular systems (ref. 13). The type, intensity, and duration of these protocols ultimately will be tailored to the varying problems encountered during flight, and also to the various job requirements of the astronauts. Pilots may train differently than those engaged in EVA (ref. 8).

An optimal exercise countermeasure program should not only meet the physiological requirements of the astronauts, but should also be efficient in time and energy utilization (refs. 7 and 8). Maintenance of aerobic work capacity, strength, and endurance during prolonged spaceflight may be acquired best by exercises requiring development of intermittent, maximal, muscular tension rather than longer duration submaximal exercise training (ref. 10). Therefore, the present study was designed to evaluate the effects of high intensity and relatively short duration exercise training regimens to ameliorate some effects of bed-rest deconditioning.

4. General Procedure

Subject Selection

Candidates had to meet the following specifications: (1) male, 32–42 yr old, (2) non-smoker for at least 10 yr and no history of non-medical drug use, (3) pass an Air Force III or equivalent physical examination that included a treadmill test, (4) moderate to good physical fitness as defined by a maximal aerobic capacity of at least 35 ml O_2/min/kg body weight, (5) psychological fitness as determined by the screening process described below. An initial pool of over 2000 applicants responded by telephone to a newspaper advertisement that requested volunteers for a NASA-sponsored study. The advertisement emphasized the exercise aspect of the study and indicated the desirability of teachers as subject candidates. The study was described to each candidate during the telephone interview, and candidates were then screened on the basis of the specifications listed above, their interest in the study, and their willingness to make a commitment to participate. Between five and six hundred of these candidates were selected for a 25-min personal interview with two personnel specialists experienced in screening candidates for bed-rest studies. The interview was designed to identify and select candidates with favorable characteristics, including healthy and physically fit appearance, friendliness, good social skills, self-reliance, good sense of humor, and high degree of motivation to participate in the space program. Candidates were rejected if they appeared physically unfit, overweight, excitable, fidgety, overbearing, or if they revealed a vague or indecisive commitment to the study. A candidate's interest in the payment for study participation was considered an unfavorable indicator only if it was the sole motivation for participation. Candidates were selected or rejected immediately after the interview, with the exception of questionable individuals who were evaluated at the end of the day. Candidates were selected individually on the basis of the interview criteria; no attempt was made to meet selection quotas. Most rejections resulted from candidates' decisions not to participate. As a result of the interviews 120 candidates were selected and asked to attend a briefing. Of these, 70 attended and were asked to take a physical examination. After the examination 27 candidates were selected to participate in the orientation (training) phase of the study prior to admission to the Human Research Facility (HRF). During orientation the behavior of the candidates in response to the experimental test protocol in the HRF was observed by investigators, the HRF manager, and the medical monitor. Following orientation the candidates were rejected if their behavior, based upon experience in bed-rest studies, was likely to preclude successful completion of the study. Adverse behavioral characteristics included uncooperativeness, overbearing or obsessive personality, and lack of compatibility with other subjects. At the end of the orientation period 23 subjects were selected to participate in the study. The final group included 12 subjects in the first phase (group I) that began 30 June 1986, and seven subjects in the second phase (group II) that began 18 August 1986.

Candidates for this study were not subjected to personality testing procedures. Experience with prior bed-rest studies conducted in the HRF indicated that interview and personal observation were more reliable indicators of adaptability to this bed-rest study environment than standard personality tests such as the Minnesota Multiphasic Personality Inventory.

Nursing Staff Selection and Duties

The nursing staff consisted of a head nurse and two nursing aides on each 8-hr work shift. Candidates responded to a newspaper advertisement that requested nursing assistance for a NASA-sponsored study. Staff personnel were selected after a personal interview with the head nurse; half had worked on previous bed-rest studies conducted in the HRF. Remaining staff members were selected from one third of the interviewed candidates. Favorable selection criteria included motivation to work on a NASA-sponsored study, relatively high degree of previous bedside experience, positive attitude toward the study, and inclination for cooperative teamwork.

The nursing staff was responsible for transporting subjects to experimental test sites (photo 1), and to the shower (photo 2) and telephone; maintaining hygiene; providing food, massage, and medical care; and supporting the subjects' needs within the constraints of the protocol. The nursing staff was, therefore, the primary source of social contact between the subjects and other personnel.

Habitability Characteristics of the Human Research Facility

This study was conducted in the HRF at Ames Research Center, Moffett Field, California. The HRF consists of two rooms with four beds each, two rooms with two beds each, a dining area, a recreation area, and a central nursing station (fig. 1). Room illumination utilized fluorescent lights (lights on at 0700 hr, off at 2300 hr, 20–50 foot-candles at the head of each bed), and incandescent lights above the beds controlled by the subjects. Within the HRF each subject was provided with reading material (books, magazines, and newspapers),

Photo 1. Limousine transportation to other testing sites.

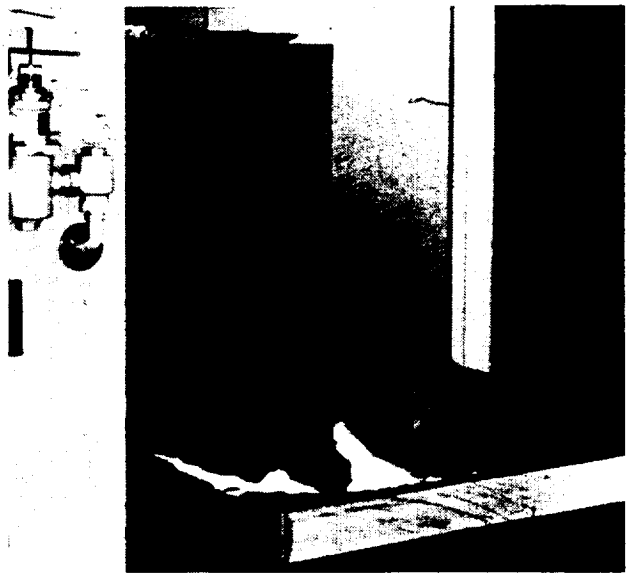

Photo 2. Horizontal shower in the Human Research Facility.

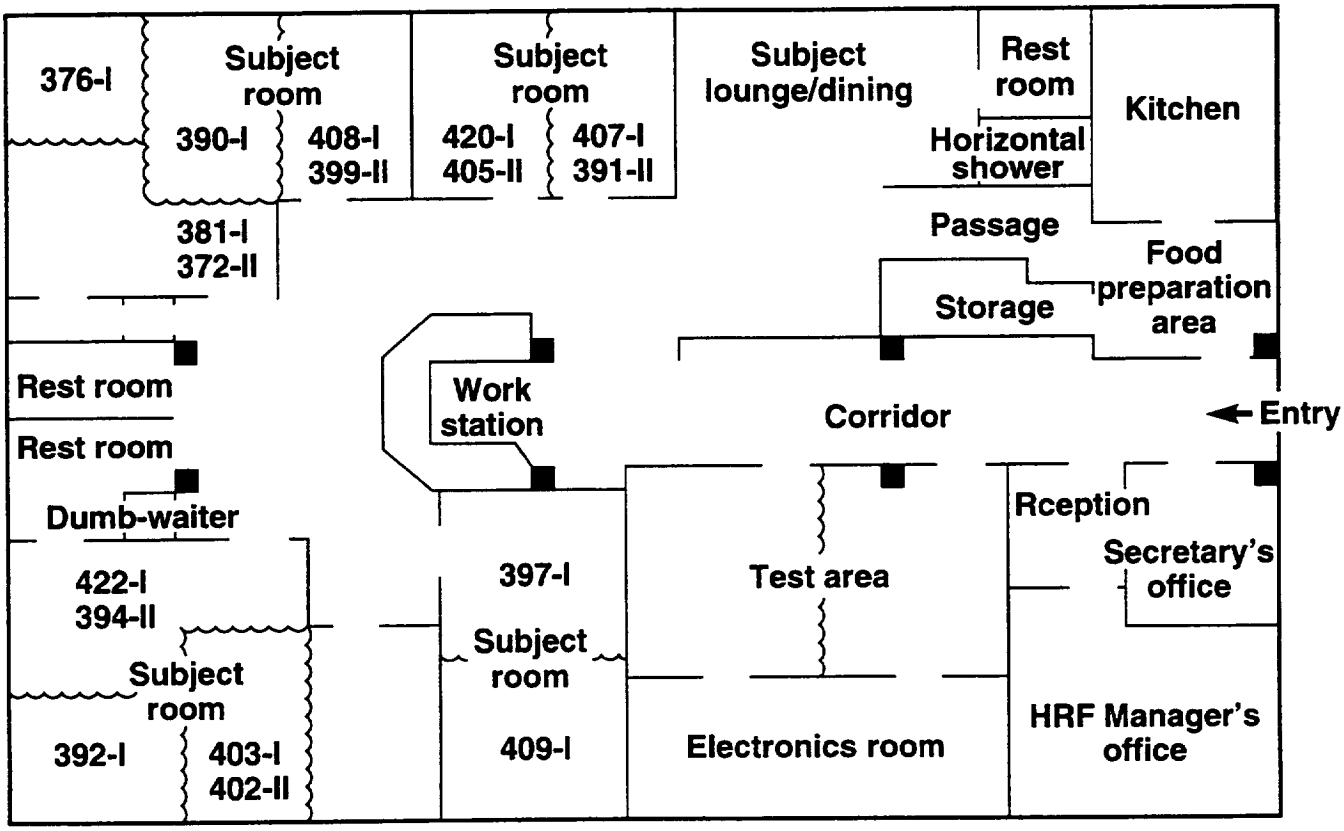

Figure 1. Human research facility plan. Test subject numbers and Group (I or II) assignments are listed. Wavy lines indicate moveable room partitions.

games, AM/FM radio, and color television mounted on the ceiling (photo 3). Headphones permitted individual selection of radio and television stations. Videocassette movies were transmitted to the individual television sets from a videocassette recorder.

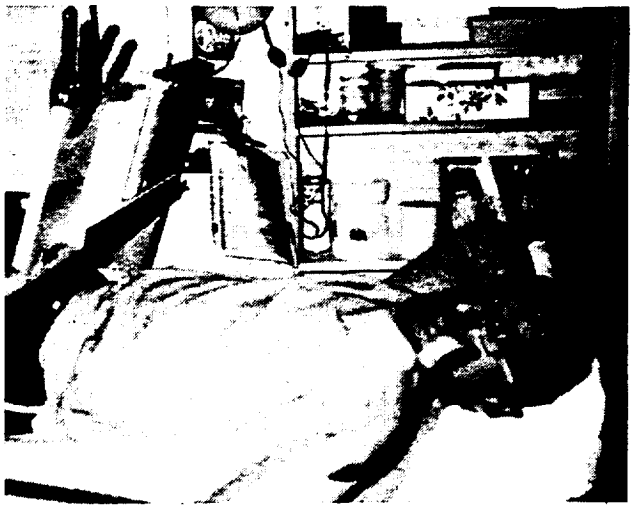

Photo 3. Test subject room in the Human Research Facility.

Subject Group Allocation

Nineteen men, aged 36 ± SD 4 yr, ht 178 ± SD 7 cm, wt 76.5 ± SD 7.6 kg, body surface area 1.94 ± SD 0.12 m^2, percent fat 15.5 ± SD 6.5%, peak leg strength 683 ± SD 110 Nm, and 5,529 ml blood volume were allocated into three experimental groups: no-exercise training (NOE, N = 5) control, isotonic exercise training (ITE, N = 7), and isokinetic exercise training (IKE, N = 7) (table 1).

The two separate bed-rest study groups were designated Group I (photo 4) and Group II. The subjects were assigned selectively to test regimen groups on the basis of age, height, weight, peak oxygen uptake, and isokinetic leg strength, in that order of priority. Selected characteristics of subjects assigned to each exercise group are listed in table 1. However, the subjects were allowed to choose bed locations in the HRF in the order of their admission (i.e., half of the subjects on the first day and half on the second day), their order of daily test scheduling within each group, and their participation in the first or second part of the study to allow those with work commitments in the fall to participate in the summer phase.

Diet, Body Weight, and Vital Signs

The diet consisted of commonly available fresh and frozen foods, and 17 different daily menus were rotated during each 42-d session. These menus were controlled to provide approximately 20% protein, 62% carbohydrate, and 18% fat (table 2). Mean (±SD, N = 19) daily consumption of some basic minerals (mg/d) and protein (g/d) during the 7-d ambulatory and 30-d BR periods were: Ca^{+2} (1,288 + 53 and 1,298 ± 75), P^{+3} (1,847 ± 53 and 1,856 ± 104), Na^{+} (5,626 ± 172 and 5,442 ± 495), and protein (114 ± 4 and 113 ± 8), respectively. The mean daily intakes of these dietary components were not different although daily intake varied: calcium (1,000–1,900 mg), phosphorus (1,450–2,700 mg), and near the end of bed rest there was a reduction in sodium intake to slightly less than 5 g for two d. The planned caloric intake was 2,800 kcal/d for the NOE control group, and 3,100 kcal/d for the ITE and IKE groups. There were no caloric adjustments for subjects with different body weights since the average weight for the three groups was approximately the same. The measured mean caloric consumption was 2,678 kcal/d (NOE), 2,833 kcal/d (ITE), and 2,890 kcal/d (IKE), which resulted in mean weight (±SD) changes during bed rest of –1.01 ± 1.81 kg, –0.85 + 1.56 kg, and 0.00 ± 1.36 kg, respectively (fig. 2). The subjects were supervised 24 hr/d and all testing, showering and excretory functions were conducted in the horizontal or 6° head-down positions. Basal vital signs (blood pressure, pulse rate, respiratory rate, and oral temperature) were normal and virtually unchanged during the study (fig. 3).

Table 1. Subject anthropometric and physiologic baseline data

Subj.-No.	Age (yr)	Ht. (cm)	Wt. (kg)	S.A. (M^2)	Fat (%)	Peak VO_2 (L/min)	Peak VO_2 $(\frac{ml}{min \cdot kg})$	Exercise load, max. $(\frac{kg \cdot m}{min})$	Exercise duration maximum (min)	Leg* strength (Nm)	Blood volume (ml)	Blood volume (ml/kg)
No exercise (N = 5)												
ALF-407	40	183	86.4	2.09	14.9	3.45	40	1800	12.15	774	6457	75
BEL-409	32	170	85.4	1.97	24.8	2.84	33	----	----	628	5252	61
MUM-397	32	177	58.2	1.72	10.4	2.60	45	1400	11.15	537	4880	84
SCH-376	37	175	68.2	1.83	13.3	4.07	60	2000	10.25	624	4958	73
STE-391	37	180	75.0	1.94	14.2	2.99	40	1600	10.30	661	5616	75
$\bar{X}$	36	177	74.6	1.91	15.5	3.19	44	1700	10.96	645	5433	74
SD	4	5	11.9	0.14	5.5	0.58	10	258	0.77	86	642	8
SE	2	2	5.3	0.06	2.4	0.26	5	129	0.29	38	287	4
Isotonic exercise (N = 7)												
MIN-392	34	188	85.0	2.11	15.4	2.97	35	1400	11.00	765	6032	71
MON-422	34	188	84.5	2.11	21.1	4.27	51	2000	10.26	832	5953	70
RAN-301	39	175	80.9	1.97	25.4	3.24	40	1400	10.05	744	5089	63
SCO-408	42	170	79.1	1.91	29.4	2.85	36	1400	12.00	501	4931	62
AYA-399	32	172	75.0	1.88	13.2	2.99	40	1600	11.45	628	4245	57
GRE-372	37	185	81.8	2.04	16.2	4.58	56	2200	13.00	786	6752	83
RAW-402	35	168	75.0	1.85	18.9	3.31	44	1600	10.15	740	4230	56
$\bar{X}$	36	178	80.2	1.98	19.9	3.46	43	1657	11.13	714	5319	66
SD	3	9	4.1	0.11	5.8	0.68	8	321	1.45	113	958	9
SE	1	3	1.5	0.04	2.2	0.26	3	121	0.55	43	362	4
Isokinetic exercise (N = 7)												
DOR-403	32	168	68.2	1.77	10.3	3.67	54	1800	12.50	677	5791	85
KAM-390	32	174	70.4	1.81	7.7	3.54	50	1600	11.25	618	5891	84
NEL-412	42	171	69.1	1.81	7.7	3.22	47	1600	12.50	662	5172	75
NOR-420	42	188	82.3	2.09	21.3	2.77	34	1400	8.30	918	5413	66
GOL-405	37	183	83.6	2.06	8.0	3.57	43	2000	12.15	736	6174	74
MCL-394	33	180	73.6	1.93	7.8	3.10	42	1400	12.30	631	5528	75
STO-385	37	178	72.6	1.90	14.4	3.77	52	1800	12.30	506	6696	92
$\bar{X}$	36	177	74.3	1.91	11.0	3.38	46	1657	11.61	678	5809	79
SD	4	7	6.2	0.13	5.2	0.36	7	223	1.41	127	511	9
SE	2	3	2.4	0.05	2.0	0.14	3	84	0.53	48	193	3
All subjects (N = 19)												
$\bar{X}$	36	178	76.5	1.94	15.5	3.36	44	1667	11.28	683	5529	73
SD	4	7	7.6	0.12	6.5	0.54	8	257	1.21	110	731	10
SE	1	2	1.8	0.03	1.5	0.12	2	60	0.29	25	168	2

* $\bar{X}$ Peak torque (extension + flexion, 5 repetitions)

Photo 4. Test subjects of Group I.

Table 2. Mean daily dietary composition

	Energy (kcal)	CHO (g)	PRO (g)	FAT (g)	H_2O (ml)	Na (g)	K (g)	Ca (g)	P (g)
	No exercise (N = 5)								
$\bar{X}$	2678	339	113	97	2080	5.4	4.9	1.3	1.8
±SE	75	11	2	3	104	0.2	0.0	0.0	0.0
		62%	21%	18%					
	Isotonic exercise (N = 7)								
$\bar{X}$	2833	365	114	102	2512	5.5	4.8	1.3	1.9
±SE	82	12	3	3	109	0.2	0.1	0.0	0.0
		63%	20%	18%					
	Isokinetic exercise (N = 7)								
$\bar{X}$	2890	375	112	104	2389	5.6	4.8	1.3	1.9
±SE	75	11	3	3	100	0.2	0.1	0.0	0.0
		63%	19%	18%					
	All subjects (N = 19)								
$\bar{X}$	2813	362	113	101	2353	5.5	4.8	1.3	1.9
±SE	47	7	2	2	70	0.1	0.1	0.0	0.0
		63%	20%	18%					

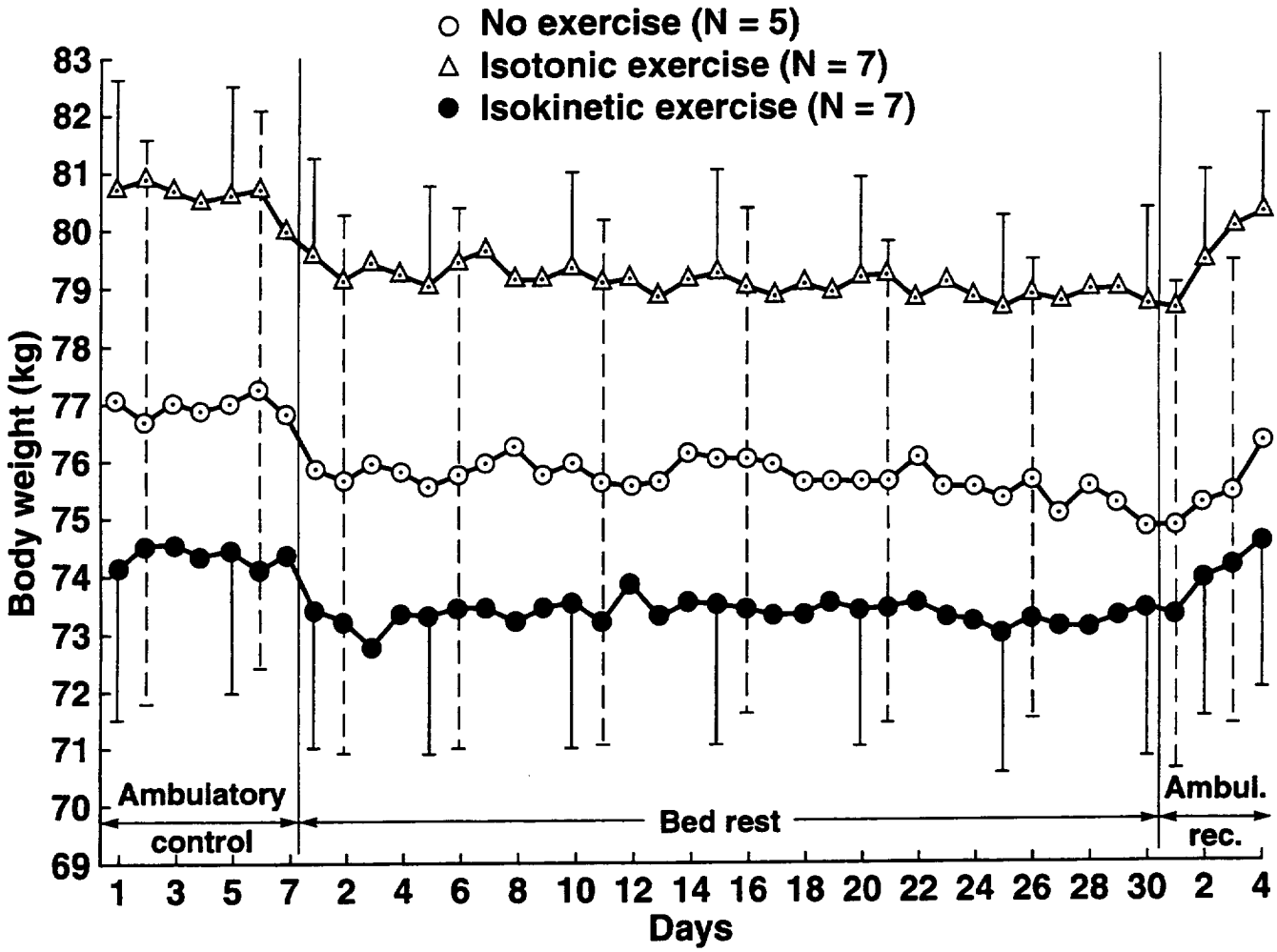

Figure 2. Mean (±SE) daily body weights for the three test groups.

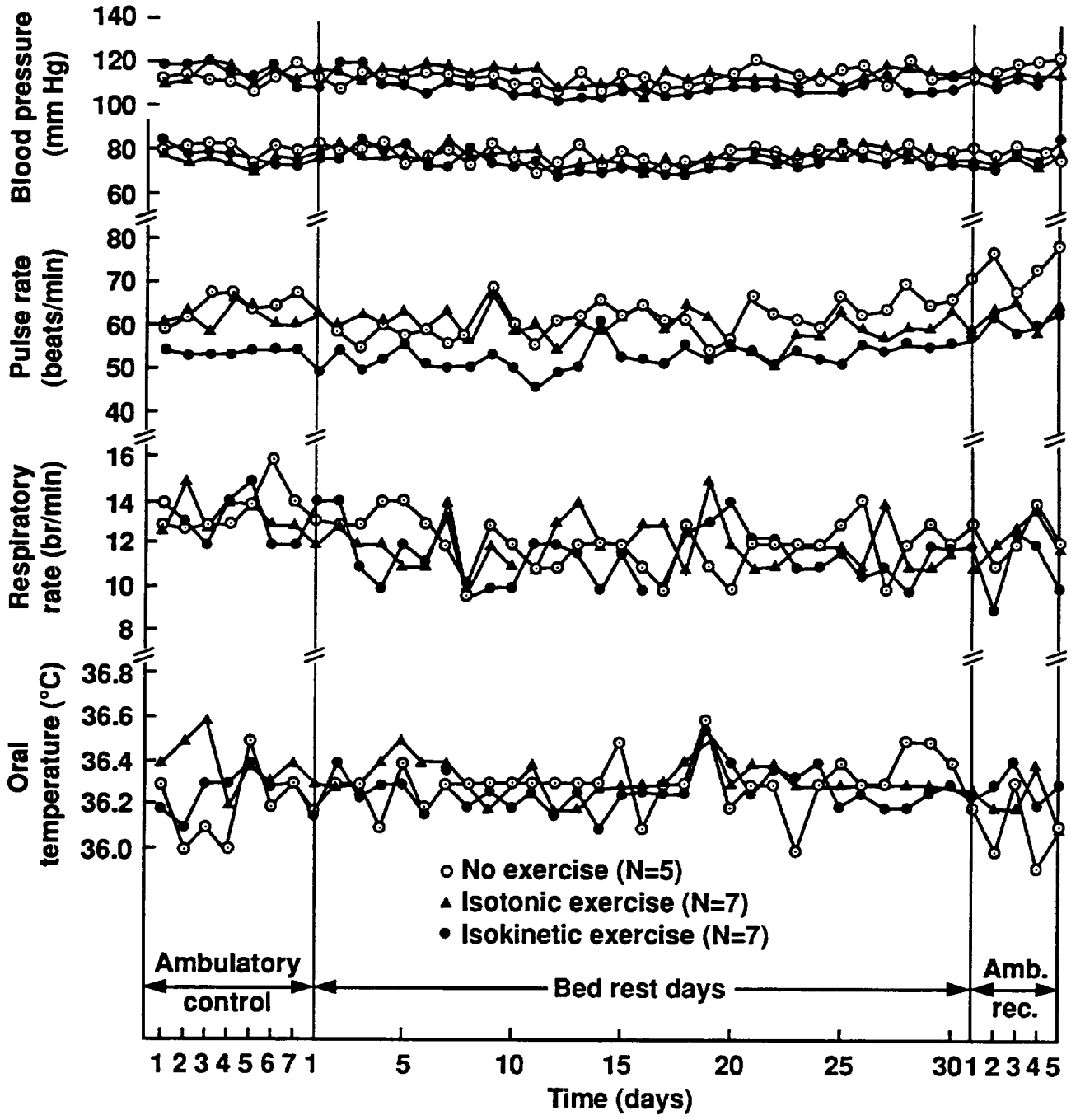

Figure 3. Mean daily basal blood pressure, pulse rate, respiratory rate, and oral temperature for the three test groups.

5. Experimental Protocol

Overview

The subjects participated in a wide range of activities during the study (fig. 4). During the bed-rest phase the subjects in the exercise groups participated in twice-daily 30-min exercise regimens, except on the maximal isotonic exercise test-days in which there was one daily exercise regimen. The control group participated in maximal isotonic and isokinetic exercise testing once per wk. All subjects had weekly blood sampling, cardiac output measurements, and ultrasound (photo 5) measurements. During the pre- and post- bed-rest phases all subjects had measurements of equilibrium (photo 6), gait (photo 7), orthostatic tolerance (photo 8), body density via water immersion (photo 9), arm and leg P-31 magnetic resonance spectroscopy (photo 10) measured at the University of California–San Francisco Medical School, leg magnetic resonance imaging (photo 11) measured at the University of California–San Francisco Radiology Imaging Laboratory, and radius (photo 12) and lumbar spine (photo 13) densities. All subjects received 15-min performance and mood tests (photo 14) at least once/d throughout the 41.5-d study.

The subjects were confined to the HRF during the bed-rest phases of the study, except for the last day when they were transferred to an adjacent building for tilt-table testing. During the pre- and post-bed-rest phases of the study the subjects were also confined to the HRF except for tilt table and body density measurements in the adjacent building, and magnetic imaging and bone densitometry measurements for which they were transported to San Francisco by limousine.

During bed-rest the subjects were restricted to head-down (–6°) recumbency. However, they were allowed one pillow, freedom of movement horizontally within this constraint, and to rise on one elbow during meals. The subjects were allowed to interact freely with staff, investigators, and to visit other subjects in their rooms via gurneys. Personal activities (e.g., hobbies, personal stereo system, musical instruments) were permitted within the constraints of the experimental design with care taken to avoid disturbing others.

Peak Oxygen Uptake Procedure

Peak oxygen uptake was measured six times, before the ambulatory control test on control day – 6, with an abbreviated protocol to minimize training effects (fig. 5). A seven-min warm-up period was used; the next load was 400 kg-m/min below the peak load for two min, then 200 kg-m/min for the next two min, and finally the peak load for at least 2.5 min. This was followed by an appropriate cooling-down period. Two measurements were taken in the sitting position, and all subsequent tests (control and during bed rest) were performed with the subjects in the horizontal-supine position on an Imaging/Ergometer Table (model 846 T, Quinton Instruments Co., Seattle, WA 98121) (photo 15). Mean data from the four supine control period tests were used to establish baseline peak data for group allocation. One subject (BEL) from the NOE group, who exhibited irregular electrocardiogram tracings, was precluded from participating in later tests of peak oxygen uptake. Peak testing was performed weekly (days 7, 14, 21, and 29) during bed rest in all three groups (fig. 4, max cycle). Aerobic power was measured using a low-resistance, low dead-space Rudolph valve (model 2700, Hans Rudolph, Inc., Kansas City, MO 64108), a Tissot tank calibrated electronic spirometer (model S-301 Pneumoscan, K.L. Engineering Co., Slymar, CA 91342), and a three-liter mixing chamber from which the gas was sampled at 0.5 l/min and then sent through anhydrous calcium sulfate (N.A. Hammond Drierite Co., Xenia, OH 45385) to O_2 and CO_2 analyzers (Applied Electrochemistry, models S3-A and CD-3A, respectively; Ametek, Thermox Instruments Division, Pittsburg, PA 15238). The analyzers were calibrated with gases standardized with the Lloyd-Haldane apparatus. Analog data were processed with an analog-to-digital converter (VISTA System IBM model 17002, Vacumed, Ventura, CA 93003) and fed to an IBM (model AT) computer; output data were printed each 15 s. Peak oxygen uptake data were the mean of the final four 15-s values.

Isotonic Exercise Training Protocol and Testing Schedule

Subjects in the ITE group exercised in the supine position (photo 15) during the 30-min morning and afternoon exercise periods. The daily isotonic cycle ergometer exercise training (Quinton model 846T) consisted of a seven-min warm-up period at a relative load of 40% of peak $\dot{V}O_2$ followed by two min of exercise at 60%, 70%, 80%, 90% and 80% loads, with each separated by the 40% load (fig. 6(a)). The weekly testing schedule is given in figure 6(b).

Ambulatory control								–6° Head-down bed rest																										Ambulatory recovery				
–8	–7	–6	–5	–4	–3	–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	1	2	3	4	5
ADMIT SUBJECTS		MAX CYCLE	BC/U-S/ARM LIDO/24-hr URINE	BS/CAT-ENDO-CA W/CYCLE	LIDO/MI	P-G/REST. CO W/CYCLE	BD-SF	BS W/BR	U-S		24-hr URINE/CO W/CYCLE		CAT-ENDO-CA W/CYCLE	LIDO	MAX CYCLE	BB/PV	U-S	ARM LIDO	CO W/CYCLE		LIDO	BB/MAX CYCLE		U-S			LIDO	BB/MAX CYCLE		U-S		REST. CO W/CYCLE	24-hr URINE/ARM LIDO	CAT-ENDO-CA W/CYCLE	LIDO	MAX CYCLE/U-S	PV/TILT/CAT-ENDO	P-G	BD-SF/BC/REST. CO W/CYCLE	MI	BB/P-G/U-S	

BB = Basal blood samples
P-G = Posture-gait
PV = Plasma volume
BS = Blood sample
BC = Body composition
CO = Cardiac output

LIDO = Isokinetic exercise
CYCLE = Isotonic exercise
MI-US = Magnetic imaging-ultrasound
CAT-ENDO-CA Catecholamine-endocrine-calcium blood samples
BD-SF = Bone densitometry- San Francisco
24-hr URINE = 24-hr urine/calcium

Figure 4. Schedule of tests.

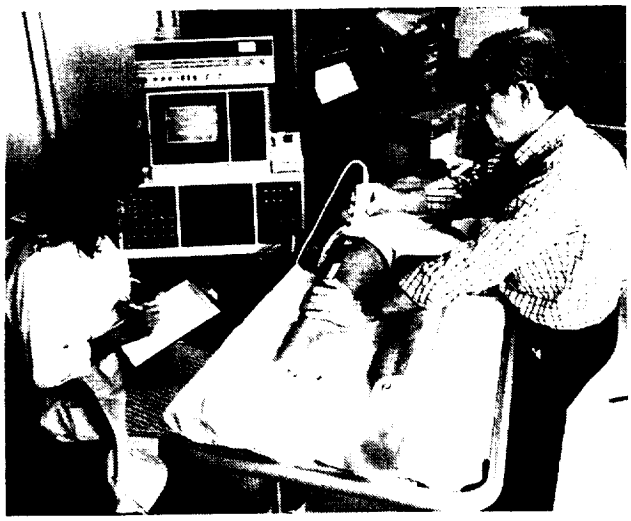

Photo 5. Ultrasound test procedure.

Photo 6. Body equilibrium testing.

Photo 7. Body gait testing.

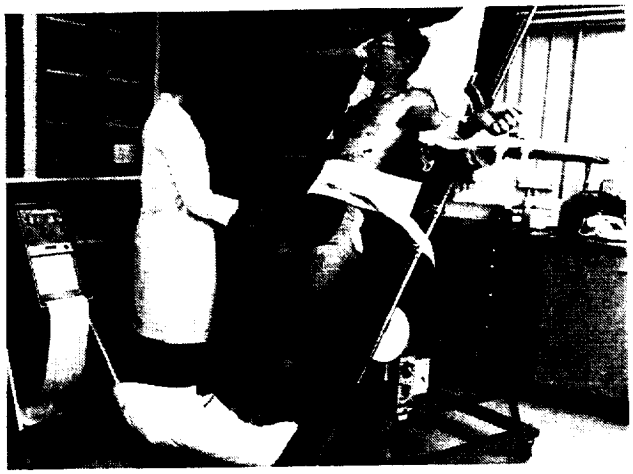

Photo 8. Orthostatic tolerance testing on the tilt table.

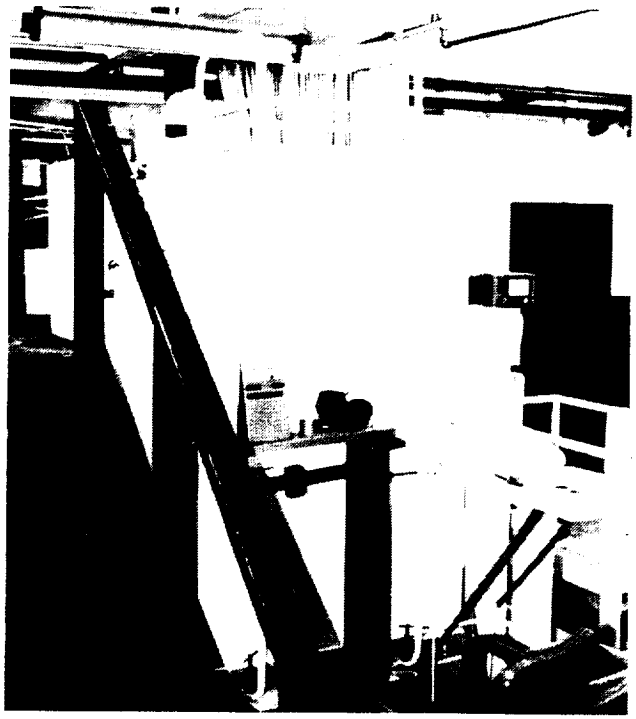

Photo 9. Body density testing in water tank.

Photo 10. Arm and leg P-31 magnetic resonance spectroscopic testing.

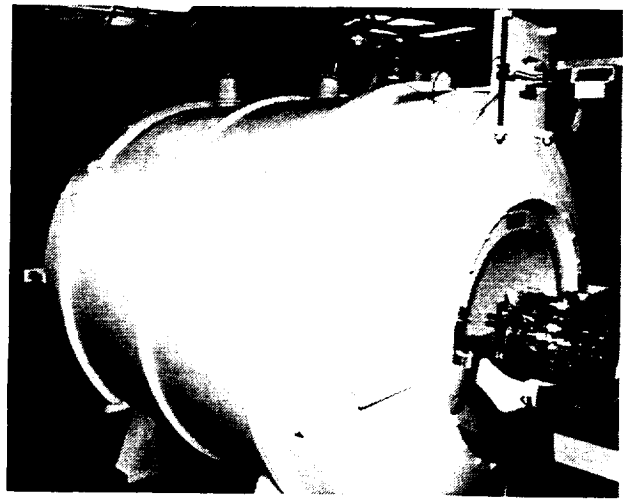

Photo 11. Leg magnetic resonance imaging testing.

Photo 12. Radius bone density measurement.

Photo 13. Lumbar spine bone density measurement.

Photo 14. Performance and mood testing.

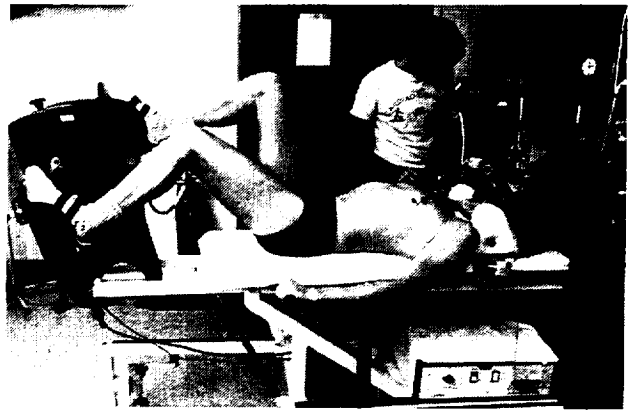

Photo 15. Daily isotonic (dynamic) leg exercise training and peak oxygen uptake testing on cycle ergometer.

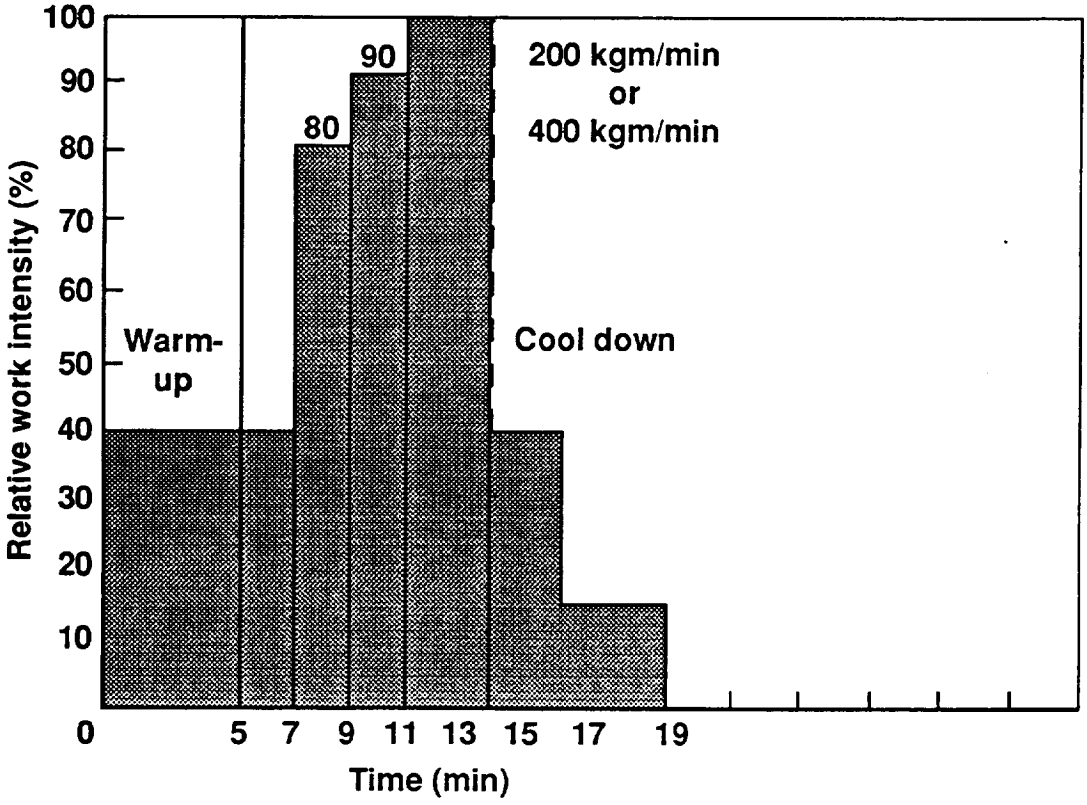

Figure 5. Peak oxygen uptake protocol.

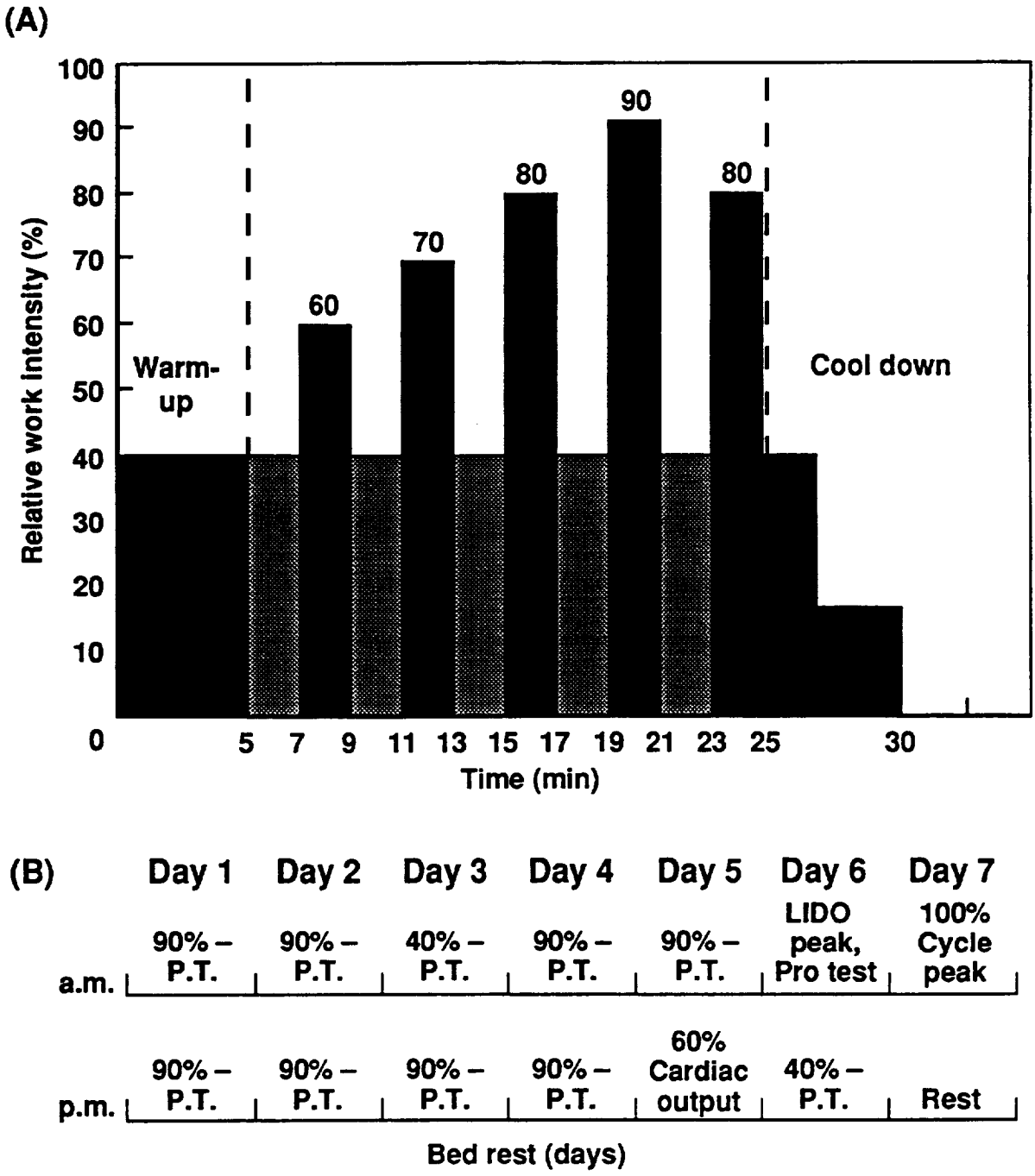

Figure 6. Isotonic exercise training protocol and testing schedule.

Isokinetic Exercise Training Protocol and Testing Schedule

The daily isokinetic exercise training was performed on the LIDO^{TM} Isokinetic Rehabilitation System ergometer (Loredan Biomedical, Inc., Davis, CA 95617) (photo 16). The daily exercise training protocol and weekly peak exercise test schedule are given in figures 7(a) and 7(b), respectively. Five maximal leg flexions and extensions through a 90° to 100° arc were performed in 10 s (velocity 100°/s); this exercise was repeated at the beginning of each minute for 15 min per leg. Each set of five repetitions in 10 s with one lower extremity was followed by a 50-s rest, for a total of 10 sets in 10 min (fig. 7(a)). Shoulder (arm) peak strength and endurance using abduction and adduction were measured weekly (photo 17). Peak isokinetic testing was performed weekly (days 6, 13, 20, and 28) during bed rest (fig. 4, LIDO) in all three groups. A schematic of the LIDO and its major functional components is presented in figure 8.

Calibration of the LIDO digital head on three separate days during the pre-ambulatory control practice period revealed similar variability on each day. Results from one calibration test are presented in figure 9. The procedure involved placing weights, indicated on the X-axis, on the calibration arm (attached to the digital head), allowing the weight to fall through 180° five times, and then recording the mean flexion torque. There was no difference in the errors (measured torque) for the flexion and extension calibrations.

Isokinetic Proprioception Protocol and Testing Procedure

The 2.5-min warm-up and cool-down periods shown on the isokinetic testing schedule (fig. 7(a)) were devoted to proprioception training (PT) of both extension and flexion of the right knees. Only the IKE group participated in this daily proprioception training. The other two groups performed this 2.5-min routine once each wk during the warm-up period of the weekly muscular strength test (day 6, Pro. Test). Special software was written to control the LIDO ergometer during collection of proprioceptive data.

During proprioception training and weekly testing the subject was requested to follow a dynamically expanding (representing knee extension) and contracting (representing knee flexion) bar-graph video display moved randomly by the computer; with a horizontal line on the display (photo 15); the movement of which was controlled by his flexion-extension lower extremity movements at a speed of 60°/s. A Fourier analysis was used to compute the error between the subject's limb-position curve with the computer-driven curve. A linear scale provided a score indicating how well the subject was able to follow the moving bar with the horizontal line; 100 was perfect. To reduce subsequent learning responses, the subjects were given 10–15 practice sessions on the proprioceptive test before bed rest commenced.

Photo 16. Daily isokinetic leg exercise training and peak strength and endurance testing on isokinetic ergometer.

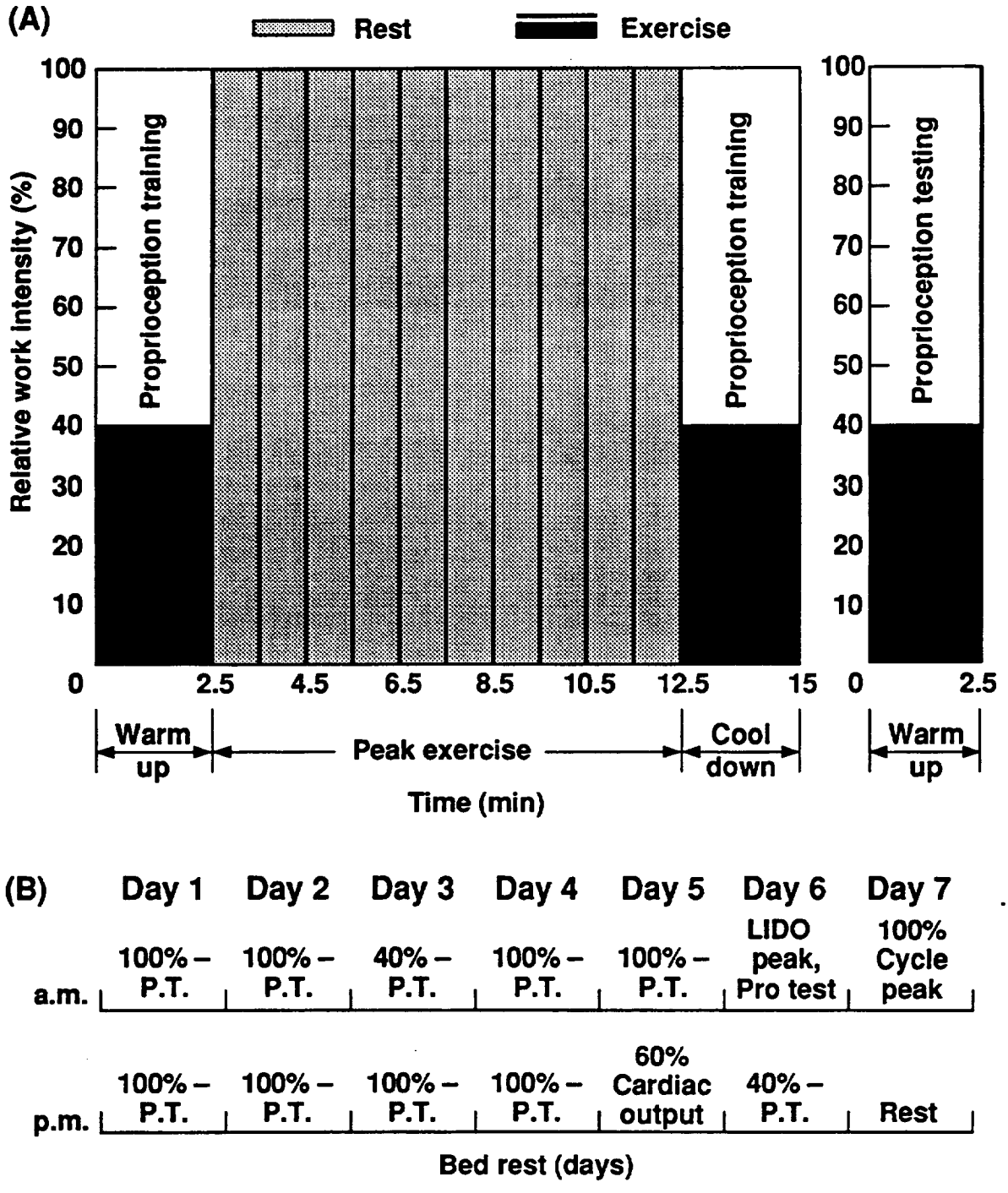

Figure 7. Isokinetic exercise training protocol and testing schedule.

Photo 17. Weekly shoulder peak strength and endurance testing on isokinetic ergometer.

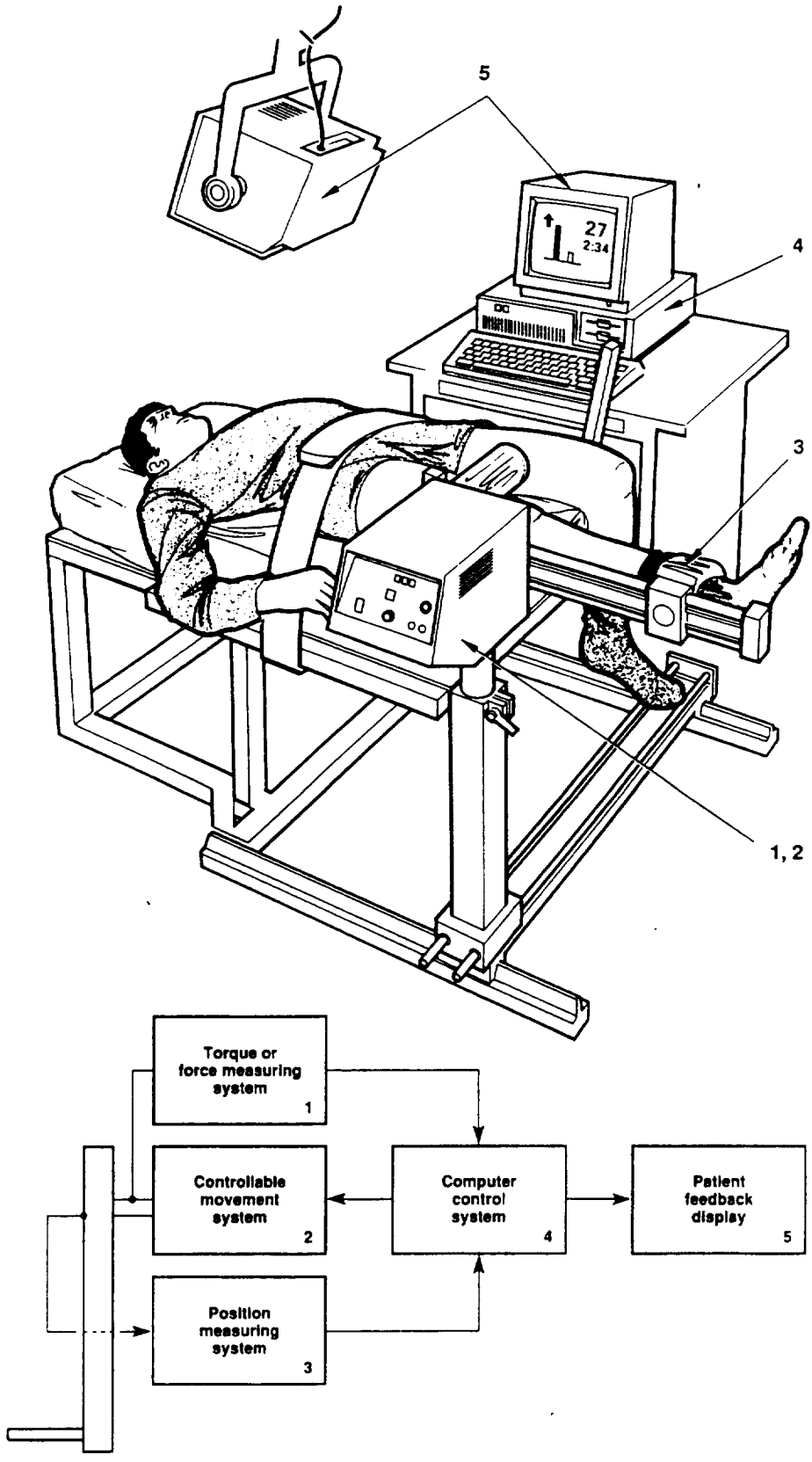

Figure 8. Isokinetic (LIDO) ergometer components.

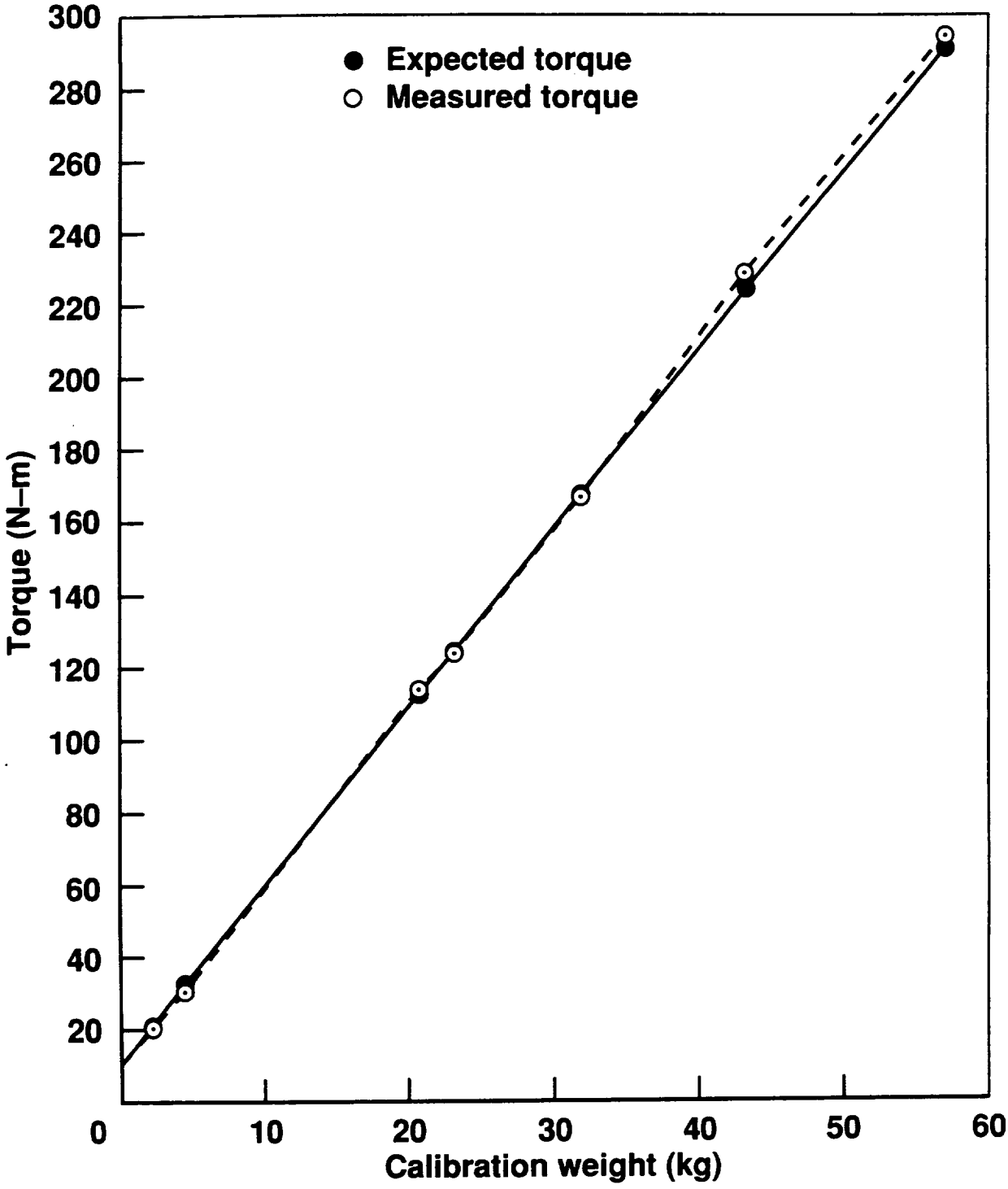

Figure 9. LIDO torque calibration.

Orthostatic (Tilt-Table) Tolerance Protocol

Orthostatic testing was performed on ambulatory control day-7 and bed rest d 30 (fig. 4) on a motorized Laberne Physical Therapy Treatment table (photo 7). This was the first occasion that the subjects were head-up after bed rest. The protocol consisted of 45 min control in the horizontal supine position for the pre-bed rest test, and in the 6° head-down supine position for the post-bed rest test. The subjects were tilted 60° head up within 10–15 s, remaining in that position for 60 min or until the onset of presyncopal signs and symptoms (e.g., nausea, dizziness, sweating, lightheadedness, or tunnel vision), and had at least a 10-min recovery period in the 6° head-down position. An antecubital vein was catheterized 45 min before tilt. Plasma volume was measured between –15 and –5 min of the control period with the standard Evans blue dye (T-1824) dilution technique. When tilted the subjects stood on a pillow placed on a 7-cm foam cushion on the foot-board. The subject was instructed to remain quiet and relaxed without overt muscular contractions. Heart rate and blood pressures were taken periodically during the control and tilting periods.

Further details for each study are contained in the individual reports in the following section (6. Results).

ISOTONIC EXERCISE

Work capacity during 30 days of bed rest with isotonic and isokinetic exercise training

J. E. GREENLEAF, E. M. BERNAUER, A. C. ERTL, T. S. TROWBRIDGE, AND C. E. WADE
Life Science Division, NASA Ames Research Center, Moffett Field 94035; Human Performance Laboratory, University of California, Davis 95616; and Letterman Army Institute of Research, Presidio of San Francisco, California 94129

GREENLEAF, J. E., E. M. BERNAUER, A. C. ERTL, T. S. TROWBRIDGE, AND C. E. WADE. *Work capacity during 30 days of bed rest with isotonic and isokinetic exercise training.* J. Appl. Physiol. 67(5): 1820–1826, 1989.—The purpose was to test the hypothesis that twice daily, short-term, variable intensity isotonic and intermittent high-intensity isokinetic leg exercise would maintain peak O_2 uptake ($\dot{V}O_2$) and muscular strength and endurance, respectively, at or near ambulatory control levels during 30 days of −6° head-down bed rest (BR) deconditioning. Nineteen men (aged 32–42 yr) were divided into no exercise control (peak $\dot{V}O_2$ once/wk, $n = 5$), isokinetic (Lido ergometer, $n = 7$), and isotonic (Quinton ergometer, $n = 7$) groups. Exercise training was conducted in the supine position for two 30-min periods/day for 5 days/wk. Isotonic training was at 60–90% of peak $\dot{V}O_2$, and isokinetic training (knee flexion-extension) was at 100°/s. Mean (±SE) changes (* $P < 0.05$) in peak $\dot{V}O_2$ ($ml \cdot m^{-1} \cdot kg^{-1}$) from ambulatory control to BR *day 28* were 44 ± 4 to 36* ± 3, −18.2%* (3.27–2.60* l/m) for no exercise, 39 ± 4 to 40 ± 3, +2.6% (3.13–3.14 l/min) for isotonic, and 44 ± 3 to 40* ± 2, −9.1%* (3.24–2.90* l/min) for isokinetic. There were no significant changes in any groups in leg peak torque (right knee flexion or extension), leg mean total work, arm total peak torque, or arm mean total work. Mean energy costs for the isotonic and isokinetic exercise training were 446 kcal/h (18.8 ± 1.6 $ml \cdot min^{-1} \cdot kg^{-1}$) and 214 kcal/h (8.9 ± 0.5 $ml \cdot m^{-1} \cdot kg^{-1}$), respectively. Thus near-peak, variable intensity, isotonic leg exercise maintains peak $\dot{V}O_2$ during 30 days of BR, while this peak, intermittent, isokinetic leg exercise protocol does not.

deconditioning; maximal exercise; peak oxygen uptake; strength; endurance

THE PHYSICAL WORKING CONDITIONS during construction of the Space Station will require astronauts to spend many weeks in microgravity with long hours of extravehicular activity (EVA) working within the confines of a space suit. Sustained EVA can impose fatiguing loads as the result, in part, of the extra effort necessary for overcoming suit resistance to movement from the stiffening effect of pressurization. Thus efficient and productive work during EVA requires astronauts to maintain high levels of aerobic work performance, strength, and muscular endurance (work capacities).

Major unanswered questions are what levels of working capacities are actually necessary and what types of exercise training protocols (prescriptions) astronauts should use on the ground, in the Space Station, and after flight, to acquire, maintain, and restore the appropriate levels of physical fitness for the work they must perform. Before optimal exercise prescriptions can be written, it is necessary to determine the type and intensity of exercise that would maintain these working capacities at or near their eugravity levels during exposure to microgravity. These optimal protocols apparently have not yet been formulated (7, 8, 10).

Therefore, the purpose of the present study was to determine whether short-term variable intensity isotonic and intermittent high-intensity isokinetic leg exercise of relatively short duration would be effective for maintaining peak O_2 uptake ($\dot{V}O_2$) and muscular strength and endurance, respectively, during head-down bed rest (BR) acclimatization.

METHODS

Subjects. From an initial group of ~2,000 candidates, informed written consent was obtained from 19 men (aged 32–42 yr) who had passed a comprehensive medical examination that included a complete medical history, physical examination, and standard laboratory tests. All subjects were nonsmokers and none took nonprescribed medications. They performed recreational exercise two to three times per week and, with one exception, considered themselves to be in fair to good physical condition; three indicated they were in excellent condition.

Procedure. The subjects were divided into three groups on the basis of age and peak $\dot{V}O_2$: no exercise training control ($n = 5$), isotonic exercise training ($n = 7$), and an isokinetic exercise training ($n = 7$) (Table 1). After an intensive familiarization period for 3 mo before BR, 12 subjects (*section 1*: 4 no exercise, 4 isotonic, and 4 isokinetic exercise) entered the Human Research Facility at Ames Research Center and were tested July and August 1986. The remaining seven subjects (*section 2*: 1 no exercise, 3 isotonic, and 3 isokinetic exercise) were tested in August and September 1986. The experiment entailed 7 days of ambulatory control when the subjects equilibrated to the standardized diet and performed the pre-BR base-line tests, 30 days of −6° head-down BR, and a 4.5-day ambulatory recovery period. The subjects performed sitting ergometer exercise for 0.5 h daily during the ambulatory control period to retard the semiconfinement deconditioning. They were supervised 24 h/day. Room lighting was turned on at 0700 h and off at

2300 h. The subjects were requested to remain in bed, and we have no evidence that any subject stood up. All testing, showering, and excretory functions were performed in the horizontal or head-down positions. The men were allowed to use one pillow and to rise on one elbow to eat. Average energy expenditure was measured continuously for each 30-min exercise period, which included the rest periods during isokinetic exercise.

Diet. The diet consisted of fresh and frozen foods. Seventeen different daily menus were rotated approximately in a sequential manner during the 42 days. The prescribed daily caloric intake was 2,800 kcal/day for the no exercise group and 3,100 kcal/day for the two exercise groups. No caloric adjustment was made for body weight. Body weight was measured daily.

Because of the difficulty in arranging meals around the exercise periods, some gastrointestinal disturbances, and dislike of some foods, not all of the prescribed food was consumed. Composition of uneaten food was measured, and the actual dietary intakes were calculated from Gebhardt et al. (5). Water and other fluids were consumed ad libitum, and the volume was recorded.

Design of exercise regimens. The major premise was that the level of pre-BR aerobic capacity and strength and endurance could be maintained best by employing exercise training regimens during BR that emphasized high intensity and shorter duration (10), rather than those utilizing moderate intensity for longer durations (1, 2, 7–12). Investigators that utilized the latter have found that ambulatory aerobic capacity could not be maintained during prolonged BR (7, 8). Our exercise training regimen criteria were *1*) maximal stimulation for the body's adaptive mechanism, *2*) 1 h of exercise per day, and *3*) minimal risk of undue fatigue and serious injury. The first design criterion required the use of alternating or intermittent intensities to provide maximal stimuli while preventing undue fatigue and injury. The second was to equate total $\dot{V}O_2$ for the two training protocols, but this required much more than the 1 h of exercise/day. Thus it was decided to use the two present protocols and measure their total work-rest energy levels because the major purpose for the study was to attempt to maintain strength, endurance, and aerobic capacities.

Peak and daily isotonic exercise. Peak $\dot{V}O_2$ was measured six times before the ambulatory test on control *day 2*. Two measurements were taken in the sitting position, and all subsequent tests (control and during BR) were performed while the subjects were in the horizontal-supine position on a Quinton (model 845) electronic ergometer. Mean data from the four supine control period tests were used to establish base-line peak $\dot{V}O_2$. One control (no exercise) subject exhibited irregular ECG tracings and was precluded from participation only in subsequent $\dot{V}O_2$ tests, hence $n = 4$.

The peak $\dot{V}O_2$ protocol (Fig. 1) used on control *day 2* and weekly during BR involved a 7-min warm-up at the 40% relative work intensity derived from the base-line peak $\dot{V}O_2$. The first load, performed for 2 min, was ~400 $kg \cdot m^{-1} \cdot min^{-1}$ below the peak load; the second increase in load was ~200 $kg \cdot m^{-1} \cdot min^{-1}$ below peak for 2 min, and then the "peak" load was undertaken. If the subject completed 2 min at this peak load, it was increased by 200 $kg \cdot m^{-1} \cdot min^{-1}$ until he was unable to maintain 50 rpm. This effort was followed by a controlled cool-down period (Fig. 1). Shoulder braces and handgrips were used for stabilization during supine exercise. This abbreviated test was used to help reduce any possible training effect.

Daily isotonic leg exercise training was conducted in seven subjects in the horizontal-supine position for 30-min periods in the morning and afternoon ~5 days/wk (Fig. 2). The subjects warmed up for 7 min at a relative intensity of 40%. The warm-up period was followed by 2 min of exercise at 60, 70, 80, 90, and 80%, with each bout separated by 2 min at 40%, and a final 5-min cool-down period. The total 30-min exercise was conducted at a relative intensity of 40% on *day 3* (A.M.) and *day 6* (P.M.) to allow for recovery and to reduce injury. Other exercise tests (submaximal cardiac output at 60% load, peak isokinetic exercise, and peak isotonic exercise) substituted for the normal training protocol on the 2 remaining days (Fig. 2, lower schedule). Once the absolute and peak exercise loads were established in the ambulatory control

TABLE 1. *Anthropometric and physiological base-line data for three groups*

	Age, yr	Ht, cm	Wt, kg	Surface Area, m^2	Fat, %	Peak $\dot{V}O_2$, supine		Leg Total Strength, N/m	Blood Volume*		Plasma Volume*		Erythrocyte Volume*	
						l/min	$ml^{-1} \cdot min^{-1} \cdot kg^{-1}$		ml	ml/kg	ml	ml/kg	ml	ml/kg
No exercise (n = 5)														
Mean	36	177	74.6	1.91	15.5	3.19	44	645	5,433	71	3,401	45	2,032	27
±SD	4	5	11.9	0.14	5.5	0.58	10	86	642	8	443	6	240	3
±SE	2	2	5.3	0.06	2.4	0.26	5	38	287	4	198	3	107	1
Isotonic exercise (n = 7)														
Mean	36	178	80.2	1.98	19.9	3.46	43	714	5,319	66	3,255	40	2,064	26
±SD	3	9	4.1	0.11	5.8	0.68	8	112	958	10	503	5	461	5
±SE	1	3	1.5	0.04	2.2	0.26	3	42	362	4	190	2	174	2
Isokinetic exercise (n = 7)														
Mean	36	177	74.3	1.91	11.0	3.38	46	704	5,809	79	3,665	49	2,144	29
±SD	4	7	6.2	0.13	5.2	0.36	7	102	511	9	441	6	208	4
±SE	2	3	2.4	0.05	2.0	0.14	3	38	193	3	167	2	78	2

* Ambulatory control *day 1*.

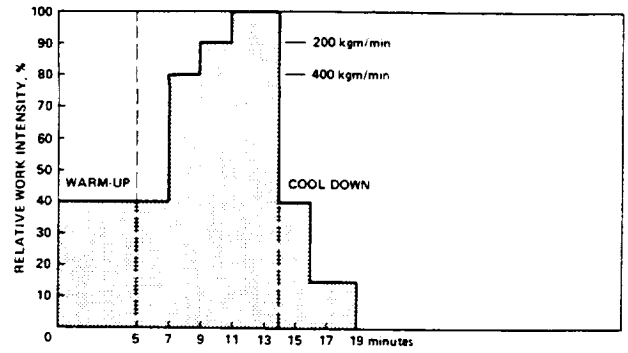

FIG. 1. Weekly peak isotonic exercise protocol for 3 groups.

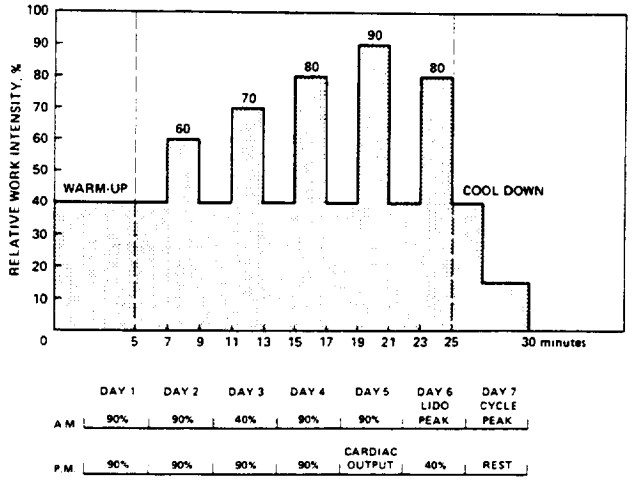

FIG. 2. Daily isotonic exercise training protocol and daily testing schedule for isotonic group.

period, they were used throughout the study in all three groups. Ergometer calibration was checked periodically.

The metabolic system utilized a low-resistance, low-dead-space Rudolph valve, a calibrated (Tissot tank) Pneumoscan (model S-3000) spirometer, and a 3-liter mixing chamber from which the gas was sampled at 0.5 l/min and then sent through anhydrous calcium carbonate to O_2 and CO_2 analyzers (Applied Electrochemistry, models S3-A and CD-3A, respectively). The analyzers were calibrated with gases standardized with the Lloyd-Haldane apparatus. Analog data were processed with an analog-to-digital converter (Vacumed, model Vista) and fed to an IBM (model XT) computer; output data were printed each 15 s. Peak $\dot{V}O_2$ data were the mean of the final four 15-s values.

Peak and daily isokinetic exercise. Peak isokinetic strength was measured six times before the control period, on control *day 5*, and at weekly intervals on *day 6* during BR with the subjects in the horizontal-supine position. The test consisted of one set of five peak right and left knee flexion and extension repetitions from 90° to 100° range of motion at 100°/s on a Lido isokinetic ergometer (Loredan Biomedical). Also, right and left shoulder total work and peak torque were measured weekly using one set of five abduction and adduction repetitions at 100°/s with range of motion from 90° to 100°. Arm training was not performed.

Daily isokinetic leg exercise training was conducted in seven subjects in the horizontal-supine position for 30-min periods (15 min for each leg) in the morning and afternoon ~5 days/wk (Fig. 3). After a 2.5-min warm-up period for each leg, the subjects performed 10 sets of five peak flexion-extensions at 100°/s with one leg. Each set took ~10 s and was followed by a 50-s rest period. A 2.5-min cooling-down period followed the 10th set. The subjects then performed this procedure with the other leg. The Lido ergometer was calibrated periodically.

Peak torque (N/m) is the maximal torque produced for flexion and for extension during one of the five repetitions at the specified velocity of 100°/s; it is maximum muscular force (strength) under this particular set of conditions. Total work (N/m) equals the sum of the work per five repetitions. The work/repetition is the average time integral of torque × velocity for the five flexion and extension movements; it indicates the ability of the muscle group to produce force throughout the range of motion.

Blood volume. After 30-min rest in the supine position, plasma volume (PV) was measured with the standard Evans blue dye dilution technique from one 10-min post-injection blood sample; blood volume (BV) was calculated from the PV and microhematocrit (Hct) corrected for trapped plasma (0.96) and whole body Hct (0.91) (6). Erythrocyte volume was BV − PV.

Statistical analyses. These data were analyzed with dependent and independent *t* tests and analysis of variance using the UCLA BMDP program P2V. The Newman-Keuls, Tukey, and Dunnett tests were used to identify specific, significant, time-related differences. The conservative Greenhouse-Geisser and Huynh-Feldt tests were used to compensate for the presence of type I errors (false positives). The null hypotheses was rejected when $^*P < 0.05$. Nonsignificant differences are denoted by NS. Variability is expressed ±SE unless indicated otherwise.

RESULTS

Daily vital signs and caloric intake. Early morning resting (sitting for 30 min in the control and recovery periods) mean systolic and diastolic blood pressures, pulse and respiratory rates, and oral temperatures were

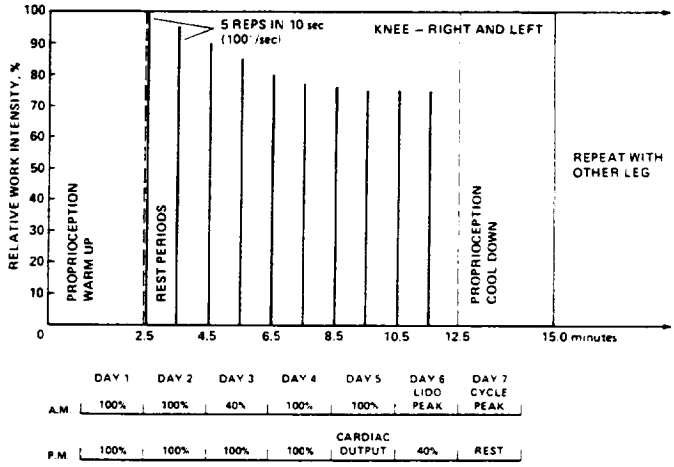

FIG. 3. Daily isokinetic exercise training protocol and daily testing schedule for isokinetic group.

essentially unchanged during the ambulatory control, BR, and ambulatory recovery periods; and there were no consistent, significant differences in these responses between groups (Fig. 4). Mean systolic and diastolic pressures varied between 115–120 mmHg and 70–80 mmHg, respectively; pulse rates averaged about 60 beats/min, and respiratory rates ~10–12/min. The average ±SE mean oral temperatures during BR for the no exercise, isotonic, and isokinetic exercise groups were 36.31 ± 0.02°C, 36.33 ± 0.01°C (NS), and 36.30 ± 0.02°C (NS), respectively. Mean ±SE daily caloric intake for the no exercise (2,678 ± 75 kcal), isotonic (2,833 ± 82 kcal), and isokinetic (2,890 ± 75 kcal) groups resulted in body weight losses during BR of 1.01 ± 0.81 kg (NS), 0.85 ± 0.59 kg (NS), and 0.0 ± 0.52 kg (NS), respectively.

Peak $\dot{V}O_2$. Mean (±SE) aerobic power (peak $\dot{V}O_2$) was maintained at ambulatory control levels in the isotonic exercise training group but not in the other two groups (Fig. 5). Because body weights were maintained relatively constant, the O_2 data expressed as l/min exhibited the same trends and statistical significance levels as those expressed in $ml \cdot min^{-1} \cdot kg^{-1}$ of body weight. The peak $\dot{V}O_2$ in the isotonic group went from 39 ± 4 $ml \cdot min^{-1} \cdot kg^{-1}$ (3.13 ± 0.29 l/min) on control *day 2* to 40 ± 3 $ml \cdot min^{-1} \cdot kg^{-1}$ (3.14 ± 0.23 l/min) (Δ = +2.6%, NS) on BR *day 28*. Comparable data were 44 ± 3 $ml \cdot min^{-1} \cdot kg^{-1}$ (3.24 ± 0.17 l/min) to 40 ± 2 $ml \cdot min^{-1} \cdot kg^{-1}$ (2.90 ± 0.16 l/min) (Δ = −9.1%, $P < 0.05$) in the isokinetic group and 44 ± 4 $ml \cdot min^{-1} \cdot kg^{-1}$ (3.27 ± 0.31 l/min) to 36 ± 3 $ml \cdot min^{-1} \cdot kg^{-1}$ (2.60 ± 0.26 l/min) (Δ = −18.2%, $P < 0.05$) in the no exercise control group. Peak $\dot{V}O_2$ in the isokinetic group showed a decreasing trend by 5.2% (NS) on BR *day 7*, and it decreased (* $P < 0.05$) by 6.7%*, 9.9%*, and 8.8%* throughout the BR period. Conversely, while the $\dot{V}O_2$ of the no exercise group showed a decreasing trend by 9.5% and 10.6% (NS) on BR *days 7* and *14*, respectively, it continued to decrease (* $P < 0.05$) to −13.8%* and −18.0%* during BR (Fig. 5). When compared with control *day 2* data, there were no statistically significant changes in peak exercise load, ventilation, or respiratory exchange ratio (RER) during BR in any group. The RER and ventilation tended to follow the peak $\dot{V}O_2$ levels. Changes in peak heart before to after BR were 184 ± 2 to 181 ± 7 beats/min (NS) for no exercise, 170 ± 5 to 185 ± 5 beats/min ($P < 0.05$) for isotonic, and 167 ± 5 to 175 ± 4 beats/min (NS) for isokinetic.

Peak strength and endurance. There were no statistically significant changes in peak torque for right knee extension and flexion in any group (Fig. 6). There was a trend for both peak torques to increase with isokinetic training, and for peak torques to remain constant or decrease in the no exercise and isotonic groups. In general, knee flexion and extension peak torques for both knees remained within ±10% of ambulatory control levels.

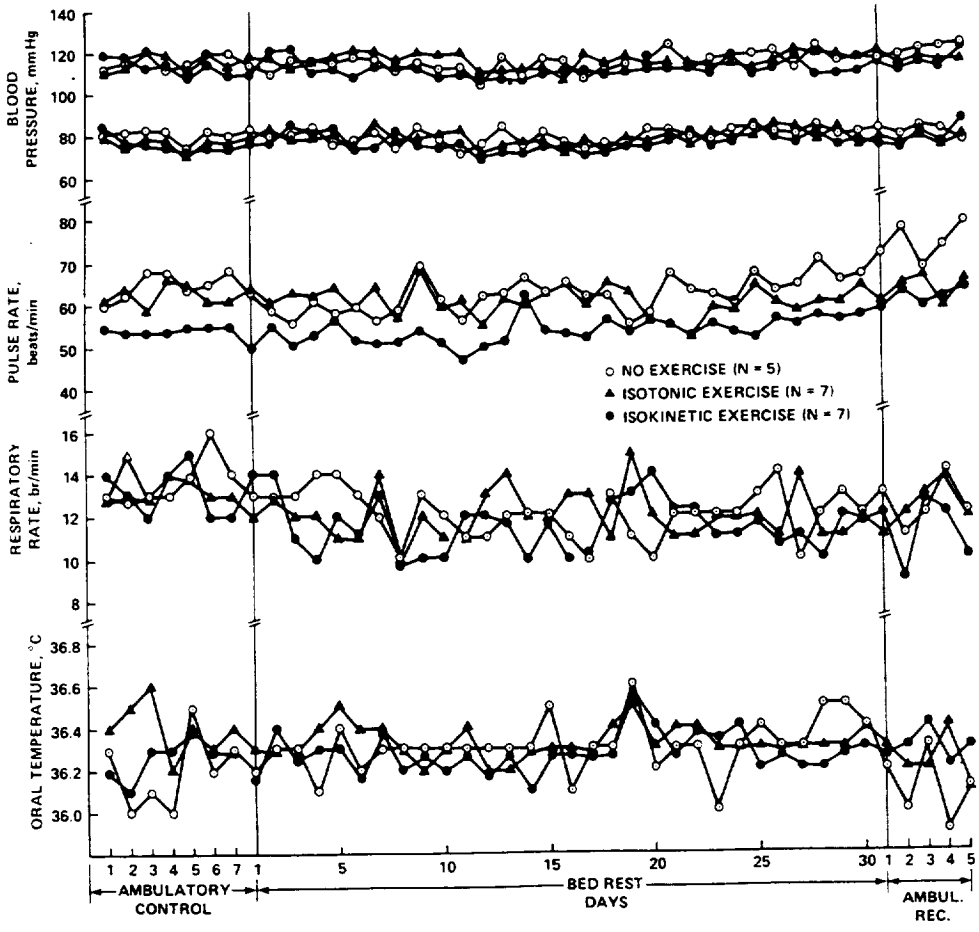

FIG. 4. Mean daily vital signs for 3 groups in ambulatory control, bed rest, and ambulatory recovery periods.

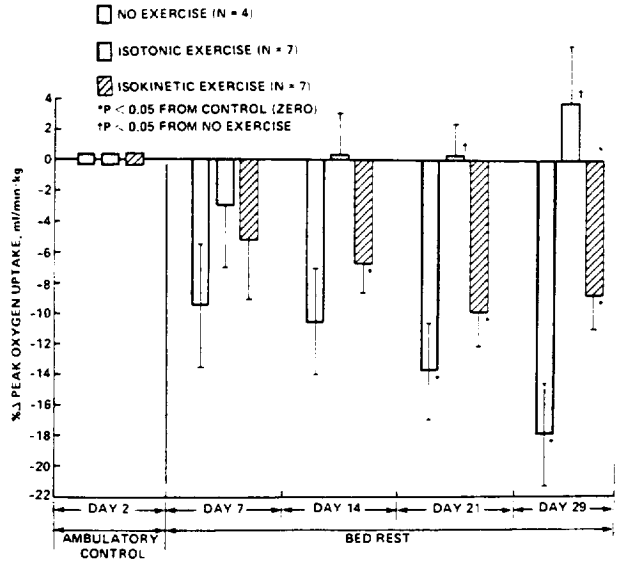

FIG. 5. Mean ± SE weekly peak O_2 uptakes ($ml \cdot min^{-1} \cdot kg^{-1}$) in 3 groups during ambulatory control and bed rest periods.

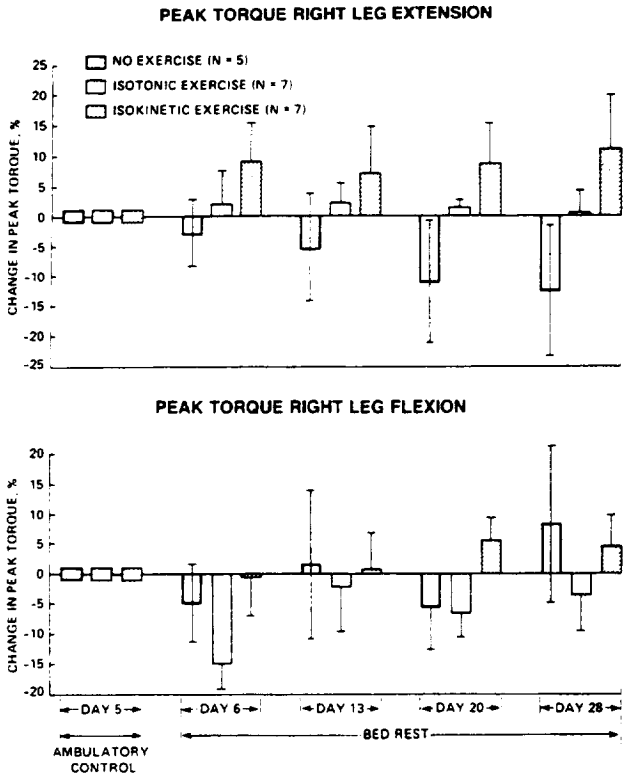

FIG. 6. Mean ± SE changes in peak torques for right knee extension and flexion during bed rest in 3 groups.

Leg mean total work (right leg flexion and extension + left leg flexion and extension) values were not changed significantly during BR in any group (Fig. 7). Isotonic and no exercise group total work tended to decrease (NS), whereas isokinetic group work tended to increase from 600 to 700 N/m (NS).

Arm mean (±SE) total work and total peak torques (right arm abduction and adduction + left arm abduction and adduction) were also unchanged during BR in the three groups. The range for total work was 350–400 N/m and 41–65 N/m for peak torque (Fig. 8).

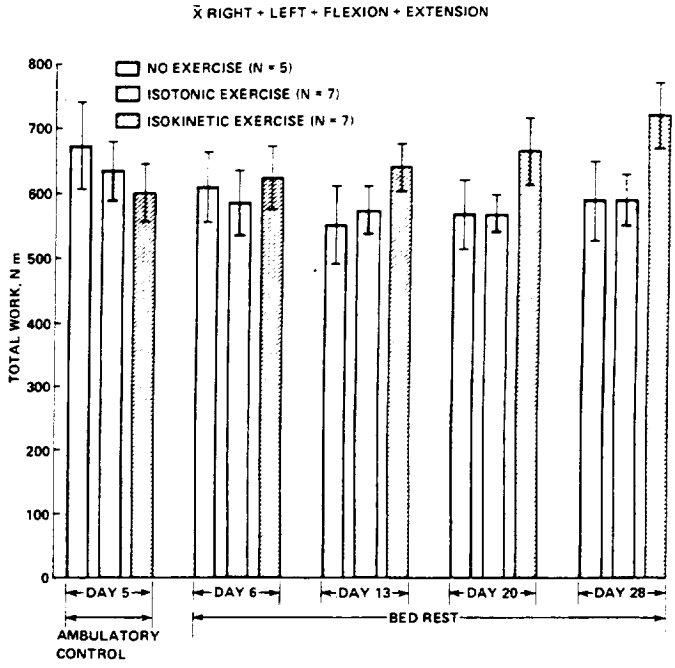

FIG. 7. Mean ± SE total work for both legs with flexion and extension during ambulatory control and bed rest for 3 groups.

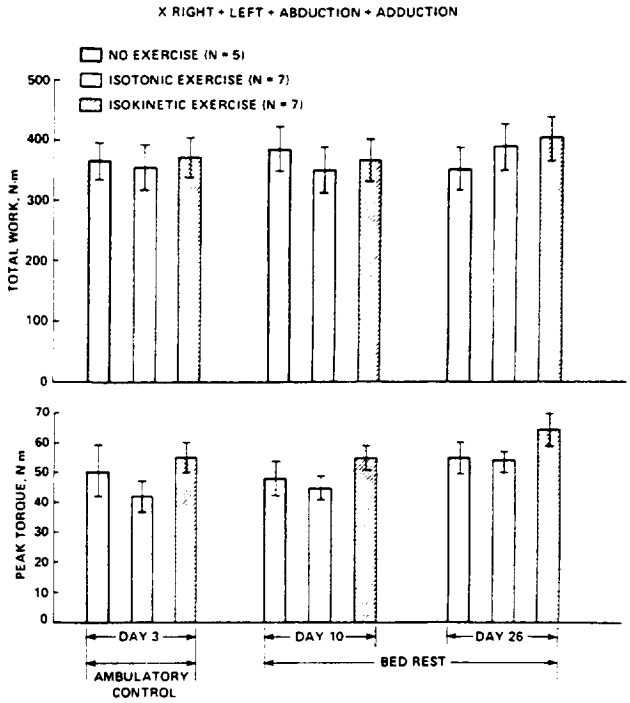

FIG. 8. Mean ± SE total work and peak torque for both arms with abduction and adduction during ambulatory control and bed rest for 3 groups.

DISCUSSION

The purpose for this study was to design and test two-leg exercise-training protocols that would maintain peak $\dot{V}O_2$ and muscular strength and endurance during 30 days of −6° head-down BR deconditioning. These training protocols prevented the losses expected during BR. Although not increased significantly (compared with ambulatory control levels), peak $\dot{V}O_2$ (isotonic group) and

peak torque (strength), as well as total work (endurance) in the isokinetic group exhibited increasing trends by the end of BR. The basic guideline for the design of both exercise training protocols was to maximize intensity and minimize duration and risk of overtraining and injury. The 50-s rest periods allowed for recovery during isokinetic training, and the 2-min loads at 40% of peak $\dot{V}O_2$ interspersed between the higher isotonic loads was reported to be less stressful than exercise without them. In the event peak $\dot{V}O_2$ declined during BR, the 90% load was selected as the highest, so the subjects would not work too far above 100% of their ambulatory peak load. Findings from the performance-mood tests suggested some subjective fatigue in the isotonic group (C. DeRoshia, personal communication), but only three subjects had symptoms that required alterations in the prescribed protocol. *Subject GRE* (isotonic) substituted 40% bouts for 90% bouts on three consecutive occasions because of calf muscle strain; *Subject MCC* (isokinetic) cancelled left leg training on two consecutive occasions because of muscle pain; and *Subject STO* (isokinetic) cancelled training one morning and performed at a reduced level in the afternoon because of gastrointestinal distress.

Åstrand and colleagues (11) were among the first to study physiological effects of high-intensity (2,160 kpm/min) equal intermittent work and rest periods between 0.5 and 3.0 min. The shorter periods of 0.5 and 1.0 min duration were well tolerated by the single male subject for 1 h of single sitting cycle ergometer exercise, whereas the 2- and 3-min periods were much more difficult. After 1 h of exercise at the 0.5-, 1.0-, and 2.0-min periods, rectal temperature increased by ~1.35°C to 38°C; after the 3-min experiment rectal temperature increased by ~2.00°C to 38.9°C. So 3-min work/rest periods were excessive. Hickson et al. (9) utilized six 5-min intervals of cycling at peak $\dot{V}O_2$ separated by 2-min intervals at 50–60% peak $\dot{V}O_2$ for 40 min/day, 3 days/wk for 10 wk. On the alternate 3 days/wk the subjects ran for distance 40 min/day. After 10 wk, peak $\dot{V}O_2$ increased linearly by 44% and averaged 17 $ml \cdot min^{-1} \cdot kg^{-1}$ (0.82–1.65 l/min). Wenger and Bell (12) have concluded that exercise training intensity of 90–100% peak $\dot{V}O_2$ produces the greatest improvements in aerobic power when bouts are undertaken four times (days)/wk and each bout should be >35 min. Thus our isotonic exercise training protocol of 2.0-min periods of progressively increasing intensity from 40 to 90% peak $\dot{V}O_2$ alternating with 40% levels for two 30-min bouts/day for about 5 days/wk seemed to fit these optimal requirements. The isokinetic exercise training protocol was designed to fit with the isotonic protocol, i.e., peak exertion for 10 s followed by 50 s rest also for two 30-min bouts/day for about 5 days/wk.

Maintenance of peak $\dot{V}O_2$ during BR may be equated to a positive training response of 18–20%, the decrease in peak $\dot{V}O_2$ of the no exercise control group. Also, the isokinetic regimen reduced peak $\dot{V}O_2$ by 8–10%, about half the loss of the no exercise group. Compared with isotonic exercise results, it is possible that the greater reduction of peak $\dot{V}O_2$ in the isokinetic group during BR was the result of the lower intermittent exercise energy expenditure. Comparable metabolic data are available from a 14-day horizontal BR study where continuous isotonic cycle ergometer leg exercise was performed for two 30-min periods/day at a relative $\dot{V}O_2$ of 68% of peak $\dot{V}O_2$ or 32 $ml \cdot min^{-1} \cdot kg^{-1}$ (11). Peak $\dot{V}O_2$ was reduced by 9.2% ($P < 0.05$). In the present study, 30 min of isotonic exercise was performed at a relative $\dot{V}O_2$ of 50%, or 18.8 $ml \cdot min^{-1} \cdot kg^{-1}$, and the change in peak $\dot{V}O_2$ at 14 days of BR was +1.1% (NS). Thus greater continuous exercise training energy expenditure was associated with greater decreases in aerobic capacity, so it appears that the higher exercise intensity rather than energy utilized is more important for maintaining aerobic capacity during BR. But firm conclusions should await results from the studies where energy cost for isotonic and isokinetic regimens are equal, or where peak $\dot{V}O_2$ during BR is reduced similarly.

The lack of significant decreases in strength and endurance in the no exercise training group during BR was unexpected, although there was a decreasing trend in peak torque (right leg extension) and leg total work. The subjects had many other tests to perform during BR, so they were moderately active. We did not want them unduly confined because astronauts in microgravity are not unduly confined. It is possible that the weekly peak isokinetic exercise test was sufficient stimulation to attenuate the normal decrease in strength and endurance during BR. The use of only one isokinetic velocity (100°/s) was to determine whether this type of exercise training would maintain strength analogous with the intensive isotonic training regimen for peak $\dot{V}O_2$ and to reduce the chances for injury. Before firm conclusions can be made, a more complete spectrum of velocities should be tested in deconditioned subjects.

Subjects' peak $\dot{V}O_2$ during BR has not been maintained at ambulatory control levels in virtually all well-controlled BR studies where submaximal isotonic leg exercise was used as the training stimulus (3, 11). The usual decreases in peak $\dot{V}O_2$ during short-term BR (<30 days) averaged 7–10% without and 4–5% with exercise training during BR. During a 14-day horizontal BR study, near-peak, intermittent, isometric leg extension exercise training for 1 h/day resulted in reductions of peak $\dot{V}O_2$ of 4.8% compared with 9.2% after cycle ergometer leg exercise training at 68% of peak $\dot{V}O_2$ for 1 h/day and 12.3% in the no exercise control group (11). The greatest individual decrease in peak $\dot{V}O_2$ reported was 31.4% (in the present study). Conversely, Chase et al. (2) reported increases in peak $\dot{V}O_2$ (after 15 days of horizontal BR) of 8.5% (cycling 30 min/day at 40% peak $\dot{V}O_2$) and of 16.4% (horizontal trampolining 30 min/day at 32% peak $\dot{V}O_2$). It is not clear how such low training intensities could increase peak $\dot{V}O_2$ but, in the same study, the performance of 70–75% peak $\dot{V}O_2$ for 45 min/day over 30 days of BR resulted in a mean decrease of only 4.6% in peak $\dot{V}O_2$. Kakurin et al. (10) reported that 17 min/day of variable intensity isotonic leg ergometer exercise and 30 min/day of rowing, impact loading, and breathing exercise maintained peak $\dot{V}O_2$ and muscular force and endurance at ambulatory control levels in six men during 49 days at −4° head-down BR.

The rate of loss of $\dot{V}O_2$ capacity up to 30 days of BR in nonexercised control subjects is ~0.8%/day (3), i.e., $\dot{V}O_2 = -0.82$ (BR days) + 0.10. This regression curve could not decline in a linear fashion continuously because, if this rate of loss continued, peak $\dot{V}O_2$ would reach 100% loss (i.e., death) after 122 days. The levels of peak $\dot{V}O_2$ in nonexercised subjects beyond 30 days of BR are not well-documented under controlled conditions.

In spite of the suggestion that one bout of peak isotonic leg exercise just before reambulation (after 10 days of −6° head-down BR) may be sufficient to restore pre-BR work capacity (4), results from the present study indicated this may not be the case. When compared with the magnitude of the decreases in peak $\dot{V}O_2$ from the literature mentioned above, the weekly peak $\dot{V}O_2$ tests in the present study did not appear to retard significantly the progressive decrease in peak $\dot{V}O_2$ in the no exercise group (Fig. 5). It would seem that factors associated with readaptation to the upright posture, rather than to only the maximal exercise test performed after 3 h of ambulatory recovery, also contributed to the restoration of work capacity in Convertino's subjects (4). However, this finding is of considerable interest and emphasizes the importance of intensity rather than duration when designing training protocols for BR deconditioning.

It is likely that focused, short bouts of near-peak exercise can reduce the long hours of submaximal exercise training currently used. Because this type of protocol appears to function well for maintaining aerobic power in ambulatory (12) and in bed-rested (10, present study) subjects, there is no reason to assume it should not work equally well for astronauts in microgravity. Optimal protocols for maintenance of strength and endurance need further study.

The authors express their warm gratitude and appreciation to the 125 people who had a significant role in this study: especially to Dee O'Hara, manager of the Human Research Facility, and to Edith Crofoot and nursing and aides staff; to the exercise testing group from University of California Davis—Dave McKenzie and Gene Myers; to the dietitians Robin Williams and Victoria Major and the food preparation staff; to the medical monitor Ralph Pelligra; to the Bionetics Corp. personnel managers Gail Bennet-Hiley and Ranita Dalton; to Atticus Tysen for the statistical analyses; to the co-investigators and their staffs; and to the Laboratory for Human Environmental Physiology support and technical staff (Jeff Ball, Victor D'Aloia, Sally Greenawalt, Teresa Hutchinson, Linda Kirby, Sandra Lewis, Joann Meredith, Andrea Ertl, and Joan Silver). A special thanks to the members of the AIBS review panel who shared their thoughts, comments, and recommendations with us—Reggie Edgerton, Philip Gollnick, William Haskell, Michael Pollock, William Stauber, and Charles Tipton.

This work was supported by NASA Tasks 199-21-12, 199-22-12, 199-22-22, 199-22-32, 199-22-44, NAG2-410, and Army Task MRDC-3A161101A-91C.

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Received 20 September 1988; accepted in final form 12 July 1989.

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LETTERS TO THE EDITOR

Dear Sir:

In recent years there has been great interest in the use of physical exercise training to counteract the deconditioning (adaptation) experienced by astronauts during exposure to the microgravity environment of spaceflight. As alcoholic-based elixers and tonics were hawked by drummers to settlers of the Western territories and states in the late 19th century, so exercise training is being sold as the preventive and remedial procedure (countermeasure) for many of the maladies suffered by astronauts during microgravity deconditioning save perhaps orthostatic intolerance and immune dysfunction. It has been suggested that isotonic, isometric, and isokinetic exercise training will be useful in preventing muscle wasting, atrophy, and associated deterioration in strength and endurance, calcium loss and bone demineralization, reduction in working capacity, decrements in mood and cognitive performance, and the reductions in plasma volume and probably total body water (2–7).

There has been little concern for management of exercise-training procedures inflight because essentially all protocols have been developed by the astronauts themselves from personal exercise preferences. Most crewmembers exercise for 1 to 2 h/d inflight, and some Russian cosmonauts have exercised up to 4 h/d on flights up to 1 year in duration. The general management philosophy has been to provide various exercise machines and devices and to encourage the astronauts to use them. However, on Skylab flights 2, 3, and 4, the mandatory daily exercise time was increased from 0.5 h to 1.0 h to 1.5 h, respectively. Soviet physician-cosmonauts have supervised crews and encouraged crew compliance in completing daily exercise-training protocols inflight (O. Atkov, personal communication).

With current planning for Space Station Freedom, a moon-base, and flights to Mars, an ever-increasing number of crewmembers will be spending longer periods of time in microgravity and in other hostile environments. The complexity of these projects will continue to strain the financial resources available for them, so exercise training protocols must be devised to consider not only the physiological remedial benefits, but also the financial cost.

To maintain the health and well-being of astronauts weighing 75 kg during flight when about 1 h of additional exercise-training is performed, nutritional requirements for each astronaut will be about 3,100 kcal/d and 2.2 L of drinking fluids/day (1); i.e., about 1,131,500 kcal/year and 803 L/year. Assuming that 3,100 kcal weighs 1.0 kg, and that 2.2 L of drinking fluids equals 2.2 kg, then the daily food and liquid ration would weigh 3.2 kg. If the cost for lifting 1.0 kg into orbit or carrying it to the space station is $20,000, then the total cost of lifting a 1-year supply of food and water rations is 3.2 kg/d × 365 d/year × $20,000/kg = $23,360,000/person/year; hence the emphasis on recycling.

TABLE I. MEAN EXERCISE ENERGY UTILIZATION PER 75-kg SUBJECT WORKING FOR 1 h/d AT THREE EXERCISE-TRAINING PROTOCOLS DURING PROLONGED BED REST.

Exercise protocol	Yearly energy cost, kcal/person/year	Δ Working capacity, %
A. Continuous isotonic leg exercise at 68% of maximal working capacity (32 $mlO_2 \cdot min^{-1} \cdot kg^{-1}$ = 720 kcal/h)	262,800	−9.2*
B. Alternating isotonic leg exercise at 50% of maximal working capacity (19 $mlO_2 \cdot min^{-1} \cdot kg^{-1}$ = 428 kcal/h)	156,220	+0.3†
C. Intermittent isokinetic leg exercise at 100% of maximal working capacity (9 $mlO_2 \cdot min^{-1} \cdot kg^{-1}$ = 202 kcal/h)	73,730	−10.5†

* 14 Days of bed rest (7).
† 30 Days of bed rest (2).

TABLE II. ESTIMATED YEARLY MONETARY COST PER ASTRONAUT OF ORBITING ADDITIONAL FOOD AND WATER NEEDED TO PERFORM THE THREE REPRESENTATIVE EXERCISE-TRAINING PROTOCOLS FROM TABLE I.

Assuming	3,100 kcal/d	=	1.0 kg	=	$20,000/d
	2.2 L/d	=	2.2 kg	=	$44,000/d
A.	262,800 kcal/year	=	85 kg	=	$1,700,000/year
	161* L/year	=	161 kg	=	3,220,000/year
			Σ	=	4,920,000/year
B.	156,220 kcal/year	=	50 kg	=	$1,000,000/year
	118* L/year	=	118 kg	=	2,360,000/year
			Σ	=	3,360,000/year
C.	73,730 kcal/year	=	24 kg	=	$480,000/year
	18* L/year	=	18 kg	=	360,000/year
			Σ	=	$900,000/year

* Sweat rate estimated as 440 g/h during continuous isotonic exercise at bed rest (4).

Hourly and yearly caloric utilization for three representative exercise training protocols during prolonged bed rest are presented in Table I. Also included are the mean changes in working capacity (maximal oxygen uptake) after bed rest. Note that the two protocols with the largest (A) and smallest (C) average energy utilizations had similar reductions in maximal working capacities, while that with intermediate (B) energy utilization had no change in maximal capacity. Thus, there are options regarding caloric cost and physiological remedial parameters; e.g., the maximal working capacity that can be manipulated when exercise-training protocols are designed and prescribed.

Estimated yearly monetary cost for food and water for the three exercise-training protocols from Table I are listed in Table II. It is clear that compared with protocol A, use of protocol C will save about $4,020,000 per astronaut per year—a considerable sum by itself, and especially when multiplied for a crew of eight.

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Isokinetic Strength and Endurance during 30-Day 6° Head-Down Bed Rest with Isotonic and Isokinetic Exercise Training

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Abstract

Greenleaf JE, Bernauer EM, Ertl AC, Bulbulian R., Bond M. Isokinetic strength and endurance during 30-day 6° head-down bed rest with isotonic and isokinetic exercise training. Aviat. Space Environ. Med. 1993; 64:0000-0000.

The purpose was to determine if an intensive, intermittent, isokinetic, lower extremity exercise training program would attenuate or eliminate the decrease of muscular strength and endurance induced by prolonged bed rest (BR). Nineteen men (36 ± 1 yr, 178 ± 2 cm, 76.5 ± 1.7 kg) were allocated into a no exercise (NOE) training group (N = 5), an isotonic (lower extremity cycle ergometer) exercise (ITE) training group (N = 7), and an isokinetic (knee isokinetic flexion-extension) exercise (IKE) training group (N = 7). Both ITE and IKE training entailed two 30-min periods daily for 5 d/wk. Peak knee and shoulder (abduction-adduction) functions were measured weekly in all groups with one 5-repetition set. After BR, knee total work average extension *decreased* significantly by 16% with NOE, *increased* significantly by 27% with IKE, and was unchanged with ITE. Average flexion total work and peak torque (strength) responses were unchanged in all groups. Force production *increased* significantly by 20% with IKE and was unchanged with NOE and ITE. Shoulder total work was unchanged in all groups, while gross average peak torque *increased* significantly by 27% with ITE, *increased* significantly by 22% with IKE, and was unchanged with NOE. Thus, while ITE training can maintain some isokinetic functions during BR, maximal intermittent IKE training can significantly increase other functions above pre-BR control levels.

Introduction

Physical exercise training has been utilized extensively (refs. 5 and 19) and will continue to be performed by astronauts in microgravity, especially during extended (>3 mo) flights. Major adaptive physiological changes occur in humans during exposure to microgravity; in the cardiovascular-respiratory, fluid, neurovestibular, and muscular systems earlier in flight (refs. 4, 14, 16, and 17) and in musculoskeletal systems later on extended flights (refs. 4, 5, and 18). Exercise training maintains and strengthens those physiological systems in normal ambulatory subjects (ref. 11), in subjects undergoing bed-rest-deconditioning (refs. 11 and 15), and in astronauts during exposure to microgravity (refs. 11 and 19).

Muscular strength and endurance responses during BR, immersion, and microgravity have been evaluated; data from 13 BR studies, carried out from seven to 120 d without remedial exercise training, indicated that virtually all major muscle groups exhibited significant decreases in maximal isometric strength (ref. 11). The strength loss in smaller muscle groups (–13%) was about half the loss of that in the larger muscle groups (–23%). Data from four of these 13 studies, where remedal exercise was performed during BR (15 to 72 d), indicated that mean decrease in strength of the smaller and larger muscle groups combined was only 4% (ref. 11).

The major question is what types (for example isometric, isotonic-dynamic, isokinetic), intensities, and durations of exercise are required to maintain astronaut performance and well-being before and during flight, upon landing, and during the post-flight period on the Earth, Moon, and Mars. It is probable that different exercise training protocols will be required for various phases of these missions. A large, active muscle mass (via lower extremity isotonic-dynamic exercise) is necessary to change maximal oxygen uptake ($\dot{V}O_2$) appreciably. We and others have employed lower extremity isotonic and isometric exercise training during BR (ref. 11), but apparently isokinetic exercise training has not been used extensively to maintain strength and endurance during BR deconditioning.

There is no unanimity of opinion concerning optimal exercise-training prescriptions probably because there has been insufficient thought and discussion directed toward the major purposes for the exercise protocols, and the ancillary but critical question of how much exercise is enough? On longer flights beginning with Skylab in the 1970s, the procedure was to increase exercise time (0.5 to 1.0 to 1.5 hr/d) and variety of regimens on successive flights (refs. 11 and 19). Some Russian cosmonauts have exercised 2 to 3 hr/d during flight (ref. 5). This mass action philosophy for prescribing exercise seems

appropriate for shorter (<30 d) flights when food and fluid are adequately supplied, but the cost of these nutrients increases dramatically on extended flights to meet the increased exercise energy requirements (ref. 9). Thus, the major goal now should be to formulate and test exercise protocols for long flights (3–24 mo) that will not only maintain astronauts health and performance, but will also do so with the lowest possible energy utilization.

The purpose of the present overall BR study was to devise and test exercise training protocols that would maintain peak aerobic capacity (isotonic exercise) and muscular strength and endurance (isokinetic exercise) in men during 30 d of absolute BR. The purpose of this paper was to determine if this isokinetic exercise training regimen would attenuate or eliminate the decrease of muscular strength and endurance during prolonged BR. Shoulder strength testing was included to assess the effect of lower extremity training on a non-trained muscle group; i.e., a general systemic training effect. Results of the isotonic exercise training (refs. 8 and 10), some preliminary isokinetic exercise training data (refs. 8 and 10), and other aspects of the study (refs. 1, 6, 7, 11–13) have been published. The complete isokinetic data are reported here.

Methods

Nineteen men (X = 36 years, range 32-42 yr) gave informed consent and passed a thorough medical examination, including a treadmill test, and had normal comprehensive blood and urinary analyses. All were nonsmokers and none reported intake of nonprescribed medications.

Full details of the overall procedure and methods are presented elsewhere (refs. 10, 12, and 13). The study was conducted in the Human Bed-Rest Research Facility at Ames Research Center from July to October, 1986. The men were allocated into three groups: no exercise (NOE) training (N = 5), isotonic exercise (ITE) training (N = 7), and isokinetic exercise (IKE) training (N = 7). The experimental protocol required living for 41.5 d in the facility and eating the controlled, nutritionally normal diet consisting of 20% protein, 62% carbohydrate, and 18% fat (ref. 12). There were 7 d of ambulatory control (C – 8 to C – 1) with the subjects exercising for 30 min/d on a cycle ergometer; 30 d of absolute (no standing or trunk raising) 6° head-down bed rest (BR 1 to BR 30); and 4.5 d of ambulatory recovery (R1 to R4). The men were allowed to have one pillow and to rise on one elbow to eat. Mean (±SE) caloric intake was 2,678 ± 75 kcal/d (NOE), 2,833 ± 82 kcal/d (ITE), and 2,890 ± 75 kcal/d (IKE); group non-significant body wt changes during BR (BR 30 minus C – 1) were: –1.01 ± 0.81 kg (NOE), –0.85 ± 0.59 kg (ITE), and 0.00 ± 0.52 kg (IKE).

Isotonic lower extremity exercise training (30 min a.m. and 30 min p.m.) was performed by the ITE group throughout BR (fig. 1(b)). The subjects warmed up for seven min at a relative intensity of 40% of peak $\dot{V}O_2$. This was followed by 2 min of exercise at 60, 70, 80, 90, and 80% of peak $\dot{V}O_2$, with each 2-min bout separated by 2 min at 40%, and then a final 5-min cool-down period at 40% and 15% (fig. 1(a)). Peak $\dot{V}O_2$ testing was performed weekly during BR (d7-cycle peak) in all three groups. Both isotonic exercise training and testing (ref. 10) were done with the subjects in the horizontal, supine position on an electronic cycle ergometer (Quinton Imaging/Ergometer Table, model 846T, Seattle, WA 98121).

The IKE training protocol, five repetitions of maximal knee flexion and extension (velocity of 100°/s) through a 90° to 100° arc, was performed on a LIDO computer controlled ergometer (Loredan Biomedical, Inc., Davis, CA 95617) with a test subject video feedback display of his leg position (ref. 1). Each set of five repetitions in 10 s with one lower extremity was followed by 50 s rest for a total of 10 sets in 10 min. Hand gripping was used for leverage and stabilization. After cool-down the other extremity was exercised similarly for an additional 15 min. Peak isokinetic strength was measured six times in the pre-control period, on control day-3 (C – 3), and once each wk on day 6 during BR (d6, 13, 20, and 28). The test was one set of five peak right and left knee flexion and extension repetitions (90°–100° range of motion) at 100°/s. A speed of 60°/s is perceived as a heavier load, 180°/s as a lighter load, and 100°/s as an intermediate load.

Lower extremity proprioceptive training (fig. 1(b), PT) was performed in the 2.5 min warm-up and cool-down periods and proprioceptive testing was done in the respective 2.5-min warm-up periods; these results have been presented separately (ref. 1).

Shoulder peak abduction and adduction strength and endurance were measured weekly after peak knee testing with the subjects in the horizontal, supine position on the LIDO ergometer to evaluate non-trained muscle groups. Each testing protocol consisted of five maximal abduction-adductions (100°/s) through a 90° to 100° arc in 10 s with 50 s rest. There were four 5-repetition sets with each shoulder. The wrist and elbow were locked during the test so forearm and arm muscles were contracted essentially maximally during shoulder movement. The non-exercising arm was placed across the abdomen and not used for leverage. Data from right and left shoulders were combined to compensate for increased

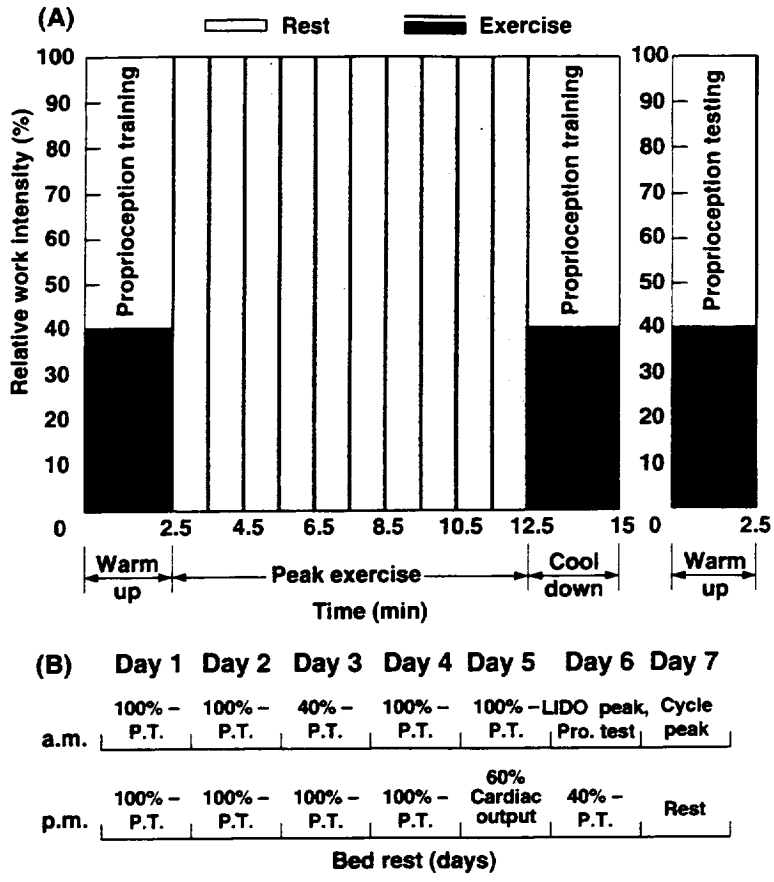

Figure 1. Daily isokinetic exercise training protocol and weekly testing schedule (b) for the isokinetic and isotonic training groups. PT is proprioceptive training; pro test is proprioceptive testing (day 6).

variability due to dominant handedness; three subjects were left-handed.

Peak torque (N-m) is maximum torque (i.e., strength) produced for extension and flexion during exercise at the specified speed. *Work per repetition* (N-m) is the average time integral of torque X velocity for all flexion and extension movements, indicating the ability of the muscle group to produce torque (force) throughout its range of motion. *Total work* (N-m) is the sum of work per repetitions. *Fatigue-endurance index* (%) is (work per last repetition)/(work per first repetition) × 100. It indicates the endurance or fatigability of a muscle group.

Evaluation of maximal variability (LIDO plus subject) was obtained from isokinetic tests during the pre-control period. Eighteen subjects performed four consecutive maximal right and left knee flexions and extensions and force tended to decrease with successive contractions. Mean (±SD) force and ranges, obtained from eight extensions (right plus left) and eight flexions (right plus left), were (820 ± 130 and 624 to 1055 N-m, respectively) for extension and (564 ± 95 and 370 to 778 N-m, respectively) for flexion.

The data were analyzed with appropriate independent and dependent t-tests, two-factor group (NOE, ITE, IKE) X time (C – 3, BR 6, BR 13, BR 20, BR 28) repeated measures analysis of variance (Statview II, Abacus Concepts, Berkeley, CA 94704-1038). Results of statistical tests are presented as exact probabilities associated with making a Type I error given the null hypothesis. Non-significant differences were NS.

Results

Average total work data from the IKE group for each of the 10 daily exercise training bouts on day C – 3, BR 5, and BR 28 are presented in figure 2, upper panel. Each point is the mean of five repetitions each for the right and left knees summed for the seven subjects for extension and for flexion. On day C – 3 extension total work was unchanged while flexion total work decreased significantly ($t_{10\text{-}1} = 3.88$, $0.01 < P < 0.001$) over the 10 bouts.

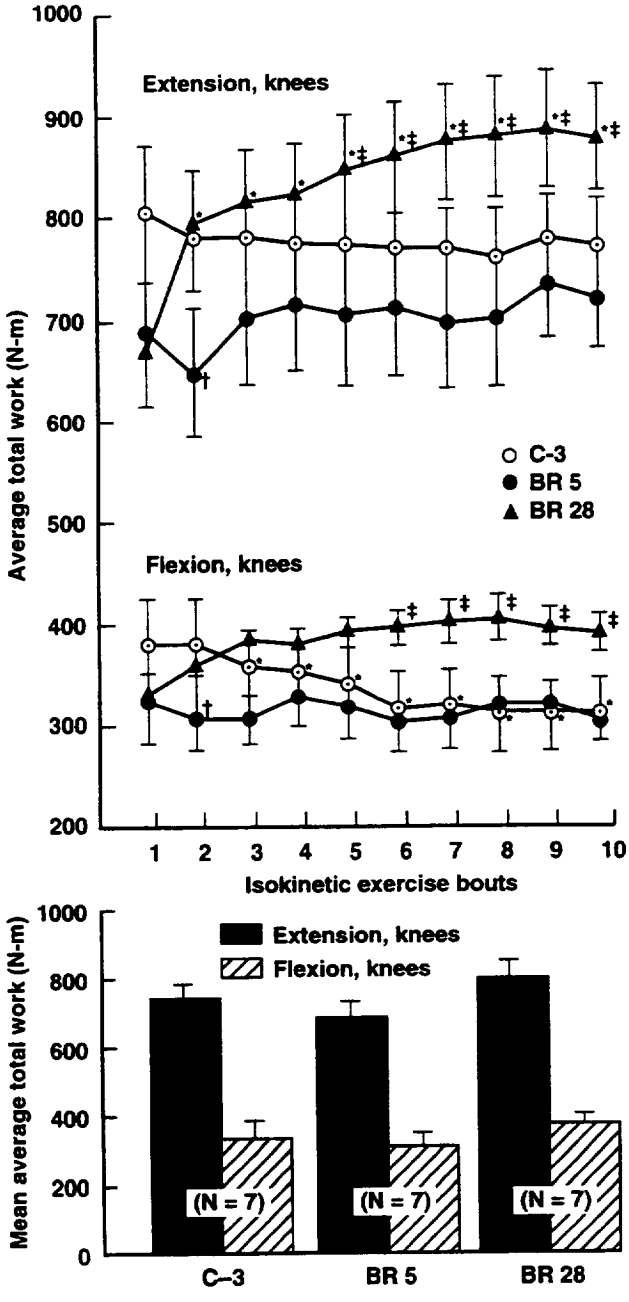

*Figure 2. Average total work for extension and flexion ($\bar{X}$ right and left legs) data for the 10 daily bouts in the isokinetic group on experiment days C – 3, BR 5, and BR 28. *P < 0.05 vs. bout 1, P < 0.05 vs. C – 3, P < 0.05 vs. BR 5 (upper panel). Mean (±SE) of the average total work data for the 10 daily bouts for leg extension and flexion in the isokinetic group on experiment days C – 3, BR 5, and BR 28. P < 0.05 vs. BR 5 (lower panel).*

On BR 5 both extension and flexion responses began somewhat lower (NS) than their respective C – 3 levels and were unchanged over their 10 bouts. However, BR 28 total work for the first bouts of extension and flexion were the same as their respective levels on BR 5, but both were increased significantly over BR 5 levels (extension $t_{10\text{-}1} = 4.32$, $0.01 < P < 0.001$; flexion $t_{10\text{-}1} = 2.79$, $0.05 < P < 0.02$) from bout 6 to bout 10 (fig. 2, upper panel). Thus, there was little change in extension and flexion average total work over the 10 bouts during the first wk of BR, but both extension and flexion work increased significantly during exercise by the end of BR.

Mean average total work data for the 10 daily bouts on day C – 3, BR 5, and BR 28 from figure 2 (upper panel) are presented in figure 2 (lower panel). Compared with C-3, there was no change in extension total work, and a small but significant increase ($t = 3.00$, $0.005 > P < 0.02$) in mean average total work for flexion responses between BR 28 and BR 5. Thus, there were no changes in extension and flexion mean average total work during the first wk (BR 5 vs C – 3), and progressively greater flexion work performed during consecutive bouts and higher final levels were evident by BR 28.

Thigh strength– There was a statistically significant increase in IKE knee extension average (X right and left legs) total work during BR (fig. 3, upper panel), while total work for the NOE and ITE groups decreased by BR 6 and remained at those levels throughout BR (the group x time interaction term was significant: $F(8, 64) = 7.676$, $P = 0.0001$). Compared with their respective ambulatory control levels: on BR 28 the NOE group average total work *decreased* significantly from 929 ± 80 to 776 ± 81 N-m (= –16%) and the IKE group average total work *increased* significantly from 789 ± 55 to 1000 ± 72 N-m (= +27%) (fig. 3, upper panel). Thus, the IKE training regimen not only terminated the decreasing trend NOE and ITE in total work during BR, but it also resulted in a significant increase in knee extension total work. The unchanged response of average total work in the ITE group (837 ± 53 to 797 ± 51 N-m) indicated this training regimen also attenuated the decrease in but did not increase total work exhibited by the NOE group. The levels of average total work for flexion were about half as great as those for extension. There were no significant changes in flexion average total work (fig. 3, lower panel) in any of the experimental groups. The group x time interaction term was not significant: $F(8, 64) = 0.5332$, $P = 0.8547$.

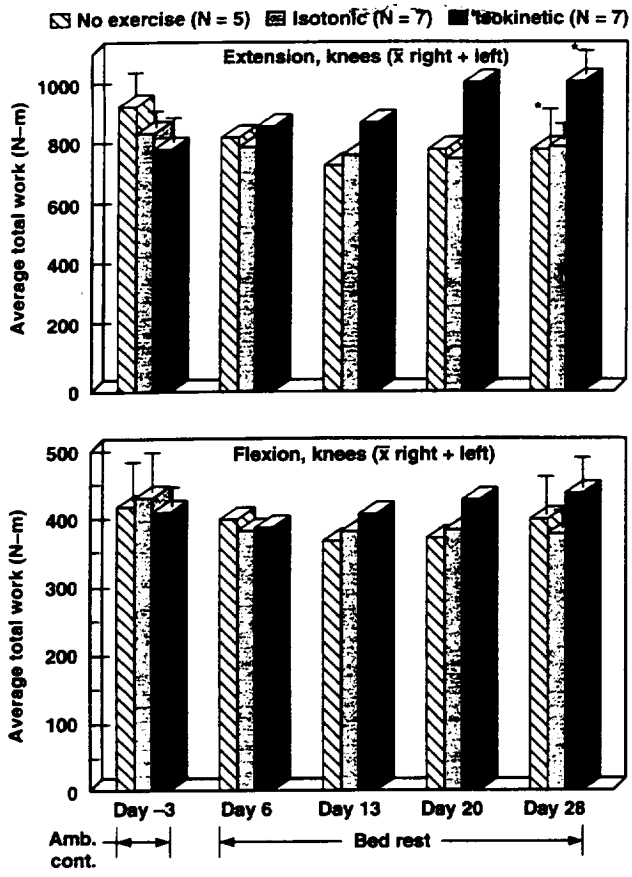

*Figure 3. Mean (±SE) average total work for leg extension (upper panel) and leg flexion (lower panel) on ambulatory control day –3 and weekly during bed rest for the three groups. *P < 0.05 vs. C – 3.*

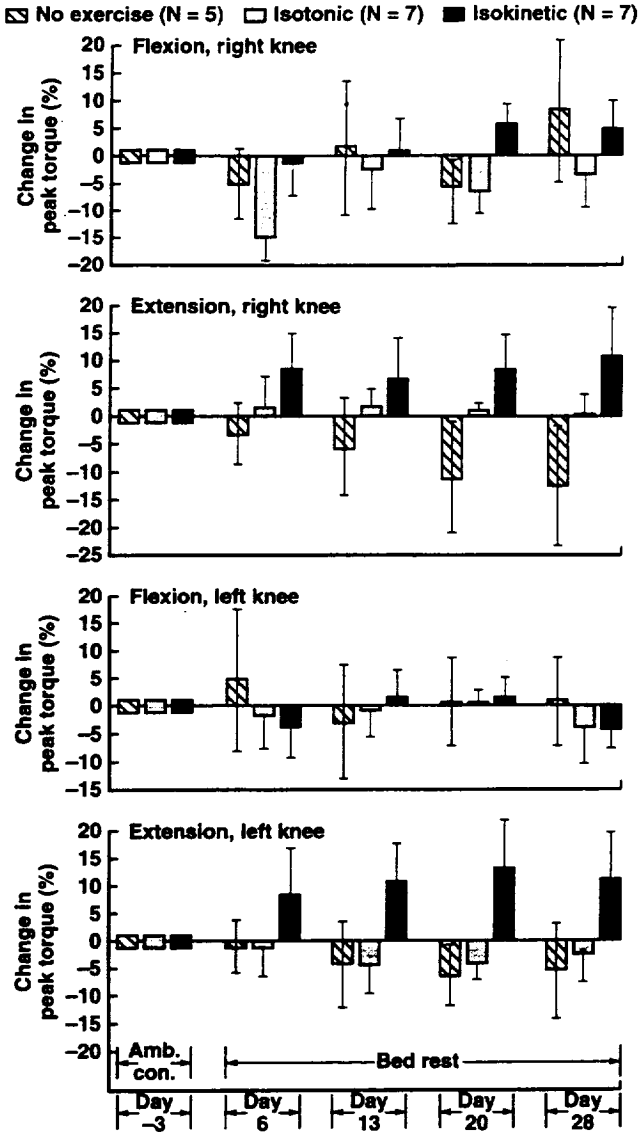

*Figure 4. Mean (±SE) percent changes in peak torque for right and left leg flexion and extension on ambulatory control day –3 and weekly during bed rest for the three groups. *P < 0.05 vs. C – 3.*

There were no statistically significant changes in average peak torque for extension or flexion during BR (data not shown). But the pattern of extension responses (fig. 4) was similar to those of average total work: all NOE mean values were below zero, all IKE values were above zero, and ITE values varied around zero. Gross average (X right + left + flexion + extension) work/repetition of the thighs also followed the response pattern of total work and peak torque during BR: a statistically significant *increase* with IKE from a control level of 120 ± 8 to 144 ± 10 N-m (= +20%) on BR 28, and no change with NOE or ITE training. Muscular endurance was unchanged during BR with all three regimens.

Shoulder strength– Gross average total work was unchanged in all three groups during BR (fig. 5, upper panel); the range was 346 ± 29 N-m (NOE) to 400 ± 34 N-m (IKE). Total peak torque was unchanged during BR with NOE (fig. 5, lower panel), but on BR 26 it increased significantly from a control level of 44 ± 4 to 56 ± 4 N-m (= +27%) with ITE and from 58 ± 5 to 70 ± 5 N-m (= +22%) in the IKE group. Shoulder force production and fatique-endurance index were unchanged in all groups during BR.

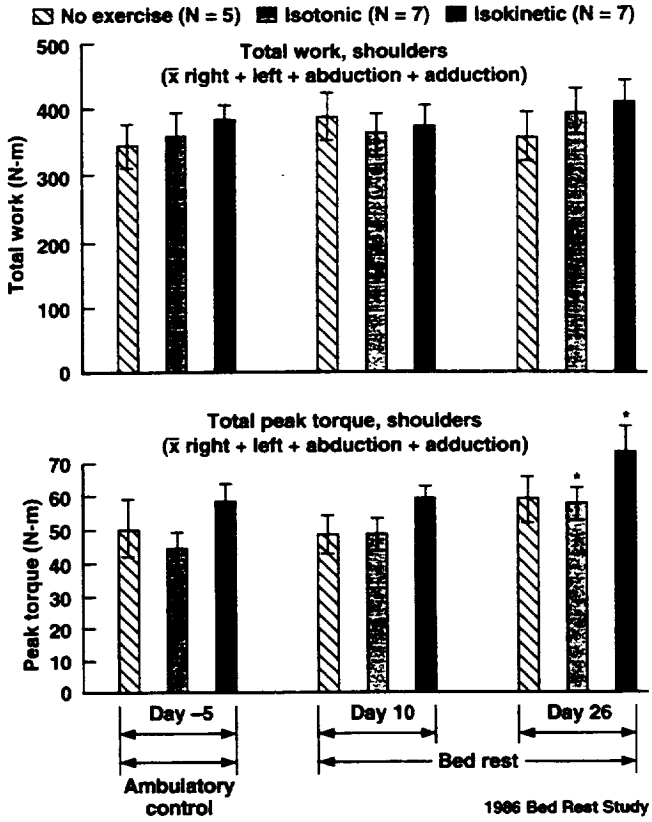

*Figure 5. Mean (±SE) gross average ($\bar{X}$ right + left + flexion + extension) arm total work (upper panel) and peak torque (lower panel) on experiment days C – 5, BR 5, BR 26 for the three groups. *P < 0.05 vs. C – 5.*

Discussion

The general significant findings were that during BR lower extremity isotonic exercise training maintained thigh (knee flexion and extension) total work, strength, and force production, and increased shoulder strength; while isokinetic lower extremity training not only maintained these functions but also significantly increased knee extension total work and force production, and shoulder strength.

Thigh (knee) responses– Some thigh responses decreased (total work average extension by 16%) in the NOE group. It is unclear why flexion total work and peak torque were unchanged in all groups. If muscles involved in flexion are used to a lesser extent than those involved in extension movements during normal activity, the flexion muscle groups could be less trained and therefore less sensitive to detraining during BR. Perhaps body movements during BR required more knee flexion than extension force because it was not necessary to maintain an upright posture; so knee flexion responses could have been maintained while those for extension decreased.

Apparently maximal IKE flexor training was not effective, while extensor training was very effective as indicated by the significant 27% increase in extension total work. Since flexion total work and strength were unchanged, extension IKE training not only restored the 16% decrease in total work of the NOE group, but it also increased total work by 27%; the combined increase was 43%. That extension total work decreased with NOE, increased with IKE, but was unchanged with ITE training indicates that the latter also exerted a significant training effect, but not as great as with IKE training.

Contributory factors that could have influenced the differing ITE and IKE work and strength responses between the three regimens were time of exercise training, peak and average exercise training intensities, and exercise energy utilization. Total daily exercise training time for IKE (both lower extremities) was 30 min/d for warm-up, cool-down, rest, and exercise including 6.7 min/d of maximal work; daily exercise time for ITE was 60 min/d including 40 min of loads at or below 40% of peak $\dot{V}O_2$, and 20 min/d of loads from 60% to 90% of peak $\dot{V}O_2$ (10). Peak training intensities during exercise were 80% to 90% of peak $\dot{V}O_2$ for 12 min/d (ITE), and 100% (maximal) peak torque (~135 N-m) for 6.7 min (IKE); average intensities were 50% of peak $\dot{V}O_2$ (ITE) and 100% of peak torque (IKE). Energy utilization in the NOE group was 3.6 ± 0.2 ml $O_2 \cdot min^{-1} \cdot kg^{-1}$ (83 kcal/hr); resting energy plus energy utilized during IKE training was 8.9 ± 0.5 ml $O_2 \cdot min^{-1} \cdot kg^{-1}$ (214 kcal/hr), and 18.8 ± 1.6 ml$O_2 \cdot min^{-1} \cdot kg^{-1}$ (446 kcal/hr) for the 60 min/d ITE regimen (10). Maximal peak torque exerted by the ITE group during cycle exercise training, calculated from maximal isotonic exercise power, was about 112 N-m (table 1); so a substantial isokinetic-isometric force component was acting during cycle exercise training. This force component probably contributed to the maintenance of extension peak torque during BR.

Novice cyclists exert most power on the downward or push phase of the pedal rotation, i.e., a knee extension force; so perhaps the thigh, leg, and hand-grip muscular action during ITE and especially during IKE testing provided some remedial training effect for extension total work, but not for flexion total work. Neither exercise regimen had an effect on thigh average flexion total work, peak torque, or the fatigue-endurance index. Since peak torque was not being utilized continuously during ITE, peak torque flexion and extension responses may not have been stimulated sufficiently to have been increased above pre-BR levels in that group. In spite of the much shorter total exercise time in the IKE group (6.7 min versus 60 min for ITE), and the somewhat shorter exercise times at near maximal levels (6.7 min versus 12 min for ITE), the IKE group generally exhibited greater increases in

thigh total work and force production responses compared with ITE responses. But ITE training maintained thigh average extension total work and peak torque.

Another possible factor contributing to impaired muscular performance is the hypohydration which occurs in BR subjects (refs. 12 and 13). Total body hypohydration induced acutely (ref. 2) or chronically (ref. 3) reduces some isometric muscular strength and endurance parameters in normal, ambulatory subjects, and it could well contribute to reduced strength during BR. The ITE regimen maintained plasma volume during bed rest (= $-1.5 \pm 2.3\%$, NS), while it decreased significantly in the other groups by $14.7 \pm 2.8\%$ (NOE) and by $16.8 \pm 2.9\%$ (IKE); red cell volume followed plasma volume (ref. 12). Since the weekly IKE test was only five maximal repetitions in 10 s, it seems unlikely that such a short effort would be affected by a cardiovascular-respiratory mechanism compromised by hypovolemia; e.g., cardiac output or muscular blood flow. Red cell volume (blood O_2) was maintained with ITE but it decreased significantly with NOE and IKE. Perhaps the unchanged plasma and red-cell volumes in the ITE group were responsible for or at least contributed to maintenance of the work and peak torque parameters.

Shoulder responses– Shoulder total work, force production, and fatigue-endurance responses were unchanged during BR in all groups. Support for body movement and stabilization, as well as significantly different vascular volume changes during BR cannot account for these results; nor can the specific effects of these two forms of exercise training. However, peak torque (strength) was increased significantly in the two exercise groups perhaps because the upper extremities were used to stabilize the torso during both daily exercise and weekly testing. Also, it is possible that the strength-inducing effect of the weekly isokinetic test, coupled with the more general isokinetic-isometric exercise training component of the ITE training regimen, was sufficient to contribute to the increased shoulder strength in the ITE group.

In conclusion, it appears that lower extremity cycle isotonic exercise training during BR can maintain and, in one instance, increase isokinetic total work and strength parameters. But specific lower extremity isokinetic exercise training can maintain or increase these parameters to a greater degree than the isotonic exercise training. These considerations, coupled with a work-rest total energy utilization about half that of the isotonic exercise training regimen, makes isokinetic training protocols attractive for use by astronauts on extended spaceflights.

Acknowledgments

The authors express their warm gratitude and appreciation to the125 people who had a significant role in this study: especially to the test subjects, Dee O'Hara, manager of the Human Research Facility, and Edith Crofoot and the nursing and aides staff; the exercise testing group from University of California, Davis; Todd Trowbridge, Dave McKenzie, and Gene Myers; the dietitions, Robin Williams and Victoria Major, and the food preparation staff; the medical monitor Ralph Pelligra; the Bionetics Corp. personnel managers Gail Bennet-Hiley and Ranita Dalton; the co-investigators and their staffs; the Laboratory for Human Gravitational Physiology support and technical staff (Jeff Ball, Victor D'Aloia, Sally Greenawalt, Teresa Hutchinson, Linda Kirby, Sandra Lewis, Joann Meredith, Andrea Ertl, and Joan Silver), David Ludwig for statistical consultation, and Bridget Eller, Shannon Watenpaugh, and Angela Hardesty for manuscript preparation.

This work was supported by NASA Tasks 199-21-12, 199-22-12, 199-22-22, 199-22-32, 199-22-44, NAG2-410, and Army Task MRDC-3A161101A-91C.

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Knee-Joint Proprioceptive Sense-Response during 30-Day 6° Head-Down Bed Rest with Isotonic and Isokinetic Exercise Training

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Abstract

Bernauer EM, Walby WF, Ertl AC, Dempster PT, Greenleaf JE. Knee-joint proprioceptive sense-response during 30-day 6° head-down bed rest with isotonic and isokinetic exercise training. Med. Sci. Sports Exerc. 1994.

To determine if daily isotonic exercise (ITE), or isokinetic exercise (IKE) training coupled with daily leg proprioceptive training, would influence proprioceptive sense-responses during bed rest (BR), 19 men (36 ± SE 2 yr, 178 ± 3 cm, 76.5 ± 2.6 kg) were allocated into a no-exercise (NOE) training control group (N = 5), and isotonic exercise (ITE) (N = 7) and isokinetic exercise (IKE) (N = 7) training groups. Training was conducted during BR for two 30-min periods/d 5 d/wk. Only the IKE group performed proprioceptive training for 2.5 min with each lower extremity before and after the daily training sessions; proprioceptive testing occurred weekly for all groups. There were no significant differences in proprioceptive sense-response scores in the pre-BR ambulatory period between the three groups. Knee extension and flexion tracking responses were unchanged with NOE during BR, but they were statistically significantly greater (*) after BR in both exercise groups when compared with NOE responses: extension: NOE 80.7 ± 0.7%, ITE 82.9* ± 0.6%, IKE 86.5* ± 0.7%; flexion: NOE 77.6 ± 1.5%, ITE 80.0 ± 0.8% (NS), IKE 83.6* ± 0.8%. Although proprioceptive sense was unchanged during BR with NOE, both ITE and especially IKE training when combined with daily proprioceptive training, significantly improved knee proprioceptive sense-responses after 30 days of bed rest.

Introduction

Proprioceptive sense (or awareness) has been defined as "perceived sensations about the static position or velocity of movement (whether imposed or voluntarily generated) of those parts of the body moved by skeletal muscles; and perceived sensations about the forces generated during muscular contractions, even when such contractions are isometric, plus the vestibular sensation and inputs from muscles and joints that are not necessarily perceived" (ref. 11). The role of proprioception in basic motor function is controversial with respect to the functional roles of joint mechanoreceptors and muscle spindle receptors (refs. 4, 10, and 11). The choice of passive versus active muscle motion and position sense, and interaction of speed and range of motion, have added to the ongoing discussion (refs. 2, 9, and 12). Proprioceptive information can be utilized to correct velocity and timing errors induced by sudden perturbations of resistance during multijoint movement (ref. 3). Proprioceptive sensory ability decreases with tissue atrophy following injury and immobilization (refs. 4 and 5). Rehabilitation of an injury can restore range of motion and strength, but may not restore proprioception sense.

Astronauts will be required to spend ever increasing periods of time in microgravity, and Watt et al. (ref. 13) reported degradation of limb position proprioception immediately after eight days of weightlessness. More astronauts will perform lengthy periods of extravehicular activity involving physical work during construction of the space station and microgravity-deconditioned pilots land the space shuttle manually. Any decrease in proprioceptive sense might cause a decrement in their ability to perform these important motor tasks. Thus, the purpose of the present study was to determine the effect of isotonic (dynamic) and isokinetic lower extremity exercise training on knee proprioceptive sense-response during 30 days of 6° head-down bed rest.

Methods

Informed, written consent was obtained from 19 men (32–42 yr) who had passed a comprehensive examination that included a complete medical history, physical examination, treadmill test, and standard laboratory biochemical analyses. All were non-smokers and none reported taking nonprescribed medication. The overall study, conducted in the Human Research Facility at Ames Research Center, involved a 7-d ambulatory control period, 30 d of 6° head-down bed rest (BR), and a 4.5-d ambulatory recovery period.

The subjects were allocated into three groups (table 1): (a) no exercise (NOE) training control (N = 5), (b) isotonic exercise (ITE) training (Quinton Imaging/Ergometer Table, model 846T, Seattle, WA 98121) (N = 7) and, (c) an isokinetic exercise (IKE) training regimen (N = 7) which included proprioceptive training and testing on a computer controlled isokinetic ergometer (LIDO, Loredan Biomedical Inc., Davis, CA 95617). The IKE group's daily training regimen is presented in figure 1(a), and the ITE and IKE groups' weekly training and testing protocols in figure 1(b). One 30-min IKE training session performed with each leg consisted of 2.5-min warm-up, five maximal extension-flexion repetitions in 10 s followed by 50 s rest (performed 10 times), and a 2.5-min cool-down period (within 15 min). The 2.5-min warm-up and cool-down periods, performed in the a.m. and p.m., were devoted to proprioception training (PT) of both extension and flexion with the right and left knees (fig. 1(b)). The other groups (NOE, ITE) did not engage in daily proprioceptive training as they were controls. All groups had four practice sessions, eight repetitions of the 2.5 min proprioceptive routine, during the control period before control day minus 5 (C – 5); this PT routine was performed once during the warm-up period of the weekly muscular strength test (day 6, LIDO peak) which consisted of one bout of five maximal repetitions in 10 s.

Table 1. Anthropometric and physiologic baseline data forthe three groups

	Age,* yr	Ht.,* cm	Wt.,* kg	S.A.,* m_2	Fat, %	Leg total strength,* Newton-m
			No exercise (N = 5)			
X	36	177	74.6	1.91	15.5	646
±SE	2	2	5.3	0.06	2.4	38
			Isotonic exercise (N = 7)			
X	36	178	80.2	1.98	19.9	714
±SE	1	3	1.5	0.04	2.2	42
			Isokinetic exercise (N = 7)			
X	36	177	74.3	1.91	11.0	704
±SE	2	3	2.4	0.05	2.0	38

*Measured before the bed rest ambulatory control period.
Measured on ambulatory control day 3.

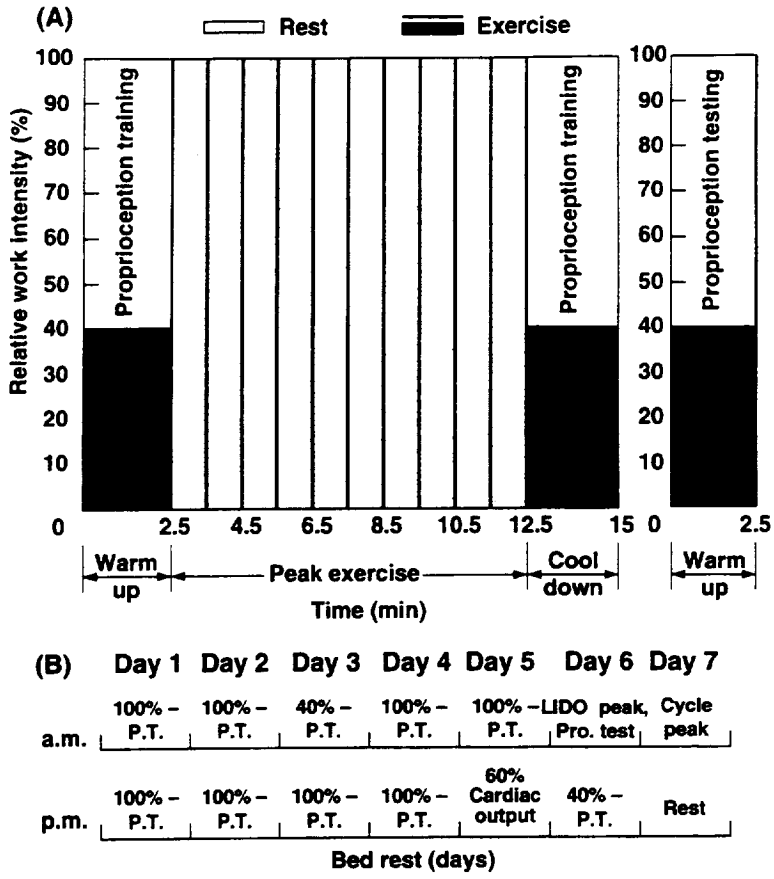

Figure 1. (a) Daily isokinetic exercise training protocol; (b) weekly testing schedule for the isokinetic and isotonic training groups: PT = proprioceptive training only for the isokinetic group. Proprioceptive testing (pro test) for all groups occurred on day 6. The 100% indicates 60 min/d training for both exercise groups.

One unit of the LIDO system houses the torque or force measuring system (fig. 2-1); another the controllable movement system (fig. 2-2) where a rotary load produced by the main shaft pushes oil through electrically-controlled valve openings. An adjacent dedicated micro-controller senses shaft position and torque and, with a combination of prediction and serve techniques, makes shaft velocity relatively independent of torque (i.e., isokinetic operation). A serial data link provides two-way communication between the torque-sensing unit (figs. 2-1, 2) and an IBM (model AT) personal computer (fig. 2-4). A bar, attached to the torque shaft, has a slide-wire unit to which the subject's ankle is bound with a velcro strap. This limb position measuring system (fig. 2-3) slides along the bar as the knee rotates; the constantly changing slide wire length is sensed in the torque unit and provides lever-arm length for calculation of force and work. Full excursion and retraction of the bar is indicated by arrows on the visual biofeedback display (fig. 2-5).

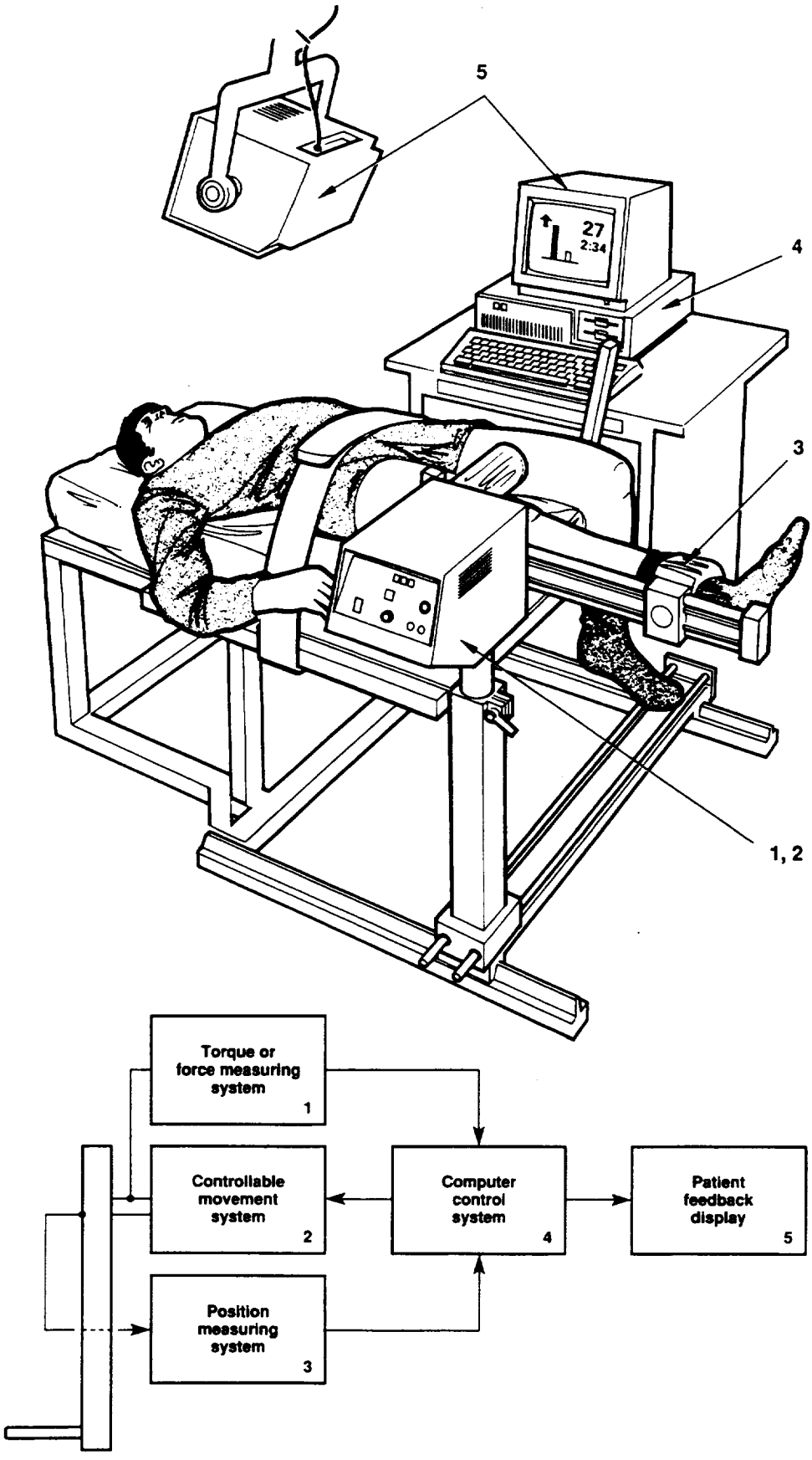

Figure 2. LIDO isokinetic system components used for daily exercise and proprioceptive training and testing.

This basic system was modified for proprioceptive testing by inclusion of additional software which introduced random perturbations into the load (resistance) of the torque unit. Load development is generated by controlling valve openings as a function of limb position during pre-proprioceptive exercise. Then these valve openings are duplicated during proprioceptive testing and training with superimposition of random perturbations. These perturbations may be considered as a noise with a spectral content, where lower frequency components are of higher amplitude than higher frequencies, and energy content decreases as the inverse square of frequency. In this proprioceptive mode neither torque nor velocity is controlled by the LIDO, only resistance to movement. Velocity and torque are controlled by the subjects depending on their ability to coordinate and respond to the perturbations. The subjects followed a dynamically expanding (representing knee extension) and contracting (representing knee flexion) bar-graphed video display moved randomly by the computer (fig. 2-5). They were requested to follow the moving bar-graph with a horizontal line on the display, the movement of which was controlled by their flexion-extension movements, at a speed of 60°/s. Thus limb position as a function of time, not velocity, was tracked and scored.

Scoring was based on the integrated error between the computer generated video moving bar graph—reflecting knee joint (leg) position (heavier line), and the subject's horizontal video line tracking response—reflecting knee joint torque (lighter line)—as presented in a typical 5 s analog display (fig. 3). Two left leg position-torque time curves are shown. An error value (in degrees), obtained from the difference between the computer-generated position (fig. 3, heavy line) and the subject's tracking response (not shown), was calculated by Fourier analysis for each flexion-extension excursion. Five excursion error values were averaged to obtain the final error score presented as a percentage of correct (100) responses (fig. 4). Higher scores indicated smaller errors.

Calibration of the LIDO digital head on three separate days during the pre-ambulatory control period revealed similar variability. Weights were placed on the calibration arm (attached to the digital head) and allowed the weight to fall through 180° five times. Allowing the weights to fall in the opposite 180° arc indicated extension torque. The mean errors (measured torque) for the flexion and extension calibrations were not different; the correlation coefficient between measured and expected torque was 0.99. More comprehensive discussions of procedures and methods for the entire bed rest study have been published (refs. 7 and 8).

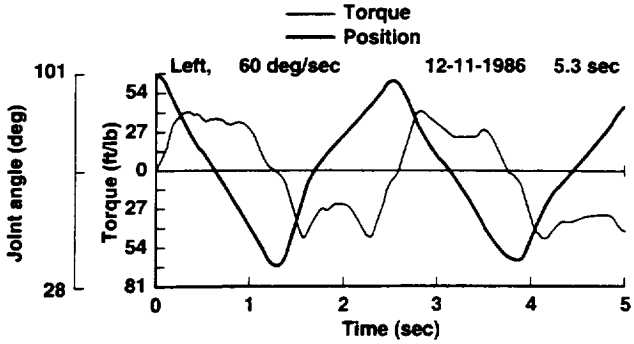

Figure 3. Typical analog tracing of proprioceptive output. The position curve (heavier line) is that of the left leg responding against a velocity of 60°/sec when tracking the moving bar on the video display. The test started with the leg at full flexion at a joint angle of 101° and moved to full extension at 28° below the horizontal (0°). The torque curve (lighter line) is the force of the subject's response during tracking; a trace of the tracking is not shown.

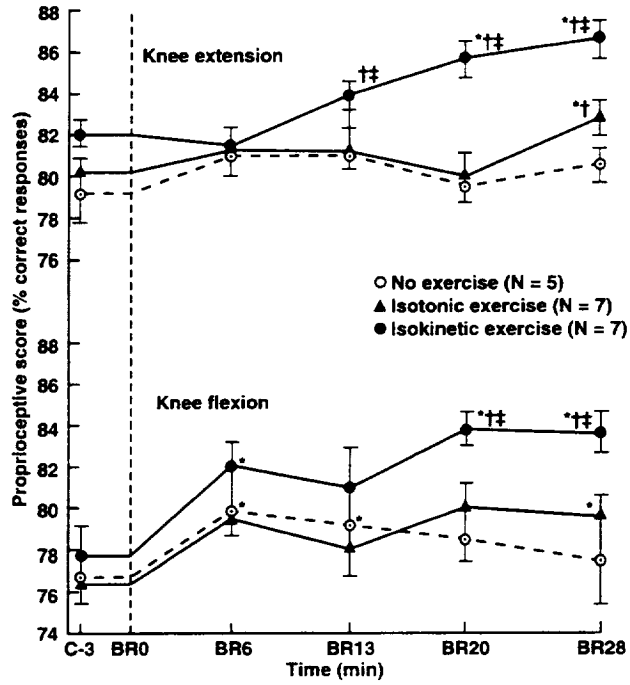

*Figure 4. Mean (±SE) proprioceptive response scores for extension and knee flexion during ambulatory control (C – 5) and weekly during bed rest for the three groups. *P < 0.05 from corresponding C – 5, P < 0.05 vs. no exercise, P < 0.05 vs. isotonic group.*

The data were analyzed with appropriate dependent or independent t-tests (HP-65 stat Pac-1, Hewlett-Packard, Cupertino, CA 95014). Non-significant differences were denoted by NS. Even though there were statistically significant differences between some right and left limb

proprioception scores, as determined by a pooled paired t-test, data from right and left limbs were added so comparisons could be made between combined extension and combined flexion responses. This procedure corrected for variations in dominant and non-dominant lower extremity strength and coordination.

Results

The only difference in proprioceptive tracking responses during the ambulatory control (C – 5) period among the three groups was for knee extension: IKE vs. NOE (fig. 4). Proprioceptive responses for NOE extension and flexion tended to increase during BR 1, but they remained or returned to ambulatory levels by BR 4. There were statistically significant scores increased during BR in the IKE group with peak levels occurring at BR 3 for flexion ($df = 13$, $P < 0.001$) and BR 4 for extension ($df = 13$, $P < 0.001$). Scores for IKE were significantly higher than those for NOE for both extension and flexion in BR 3 and BR 4 (fig. 4). At BR 4 the ITE extension score ($86.5 \pm 0.7\%$) was significantly higher than the NOE score ($80.7 \pm 0.7\%$). At BR 4, both exercise groups' flexion and extension responses were higher ($P < 0.05$) than their respective control (C – 5) scores, while the NOE flexion and extension scores were unchanged. Percent changes (BR 4 vs C – 5) in proprioceptive extension scores for the NOE, ITE, and IKE groups were +2.0 (NS), +3.5 ($P < 0.05$), and +5.6% ($P < 0.05$), respectively; and for flexion were +1.6 (NS), +4.4 ($P < 0.05$), and +7.2% ($P < 0.05$), respectively. In general, the mean extension score ($N = 5$ data points) for each group was higher ($P < 0.05$) when compared to corresponding flexion data. Thus, in non-immobilized subjects proprioceptive sense-responses were not degraded during BR without exercise training, were improved significantly only at the end of BR in the isotonic group, but were improved significantly during BR in the isokinetic group.

Discussion

Daily lower extremity proprioceptive training by the IKE group significantly increased their response scores over that of the NOE group and, to some extent, over that of the ITE group. There was some improvement in proprioceptive tracking at the end of BR from the non-specific exercise training performed by the ITE group. This would lend support to the hypothesis that general exercise training can increase proprioceptive performance (ref. 1).

The proprioceptive test involved responding to sudden perturbations in torque imparted to the lower extremity by the LIDO ergometer. Muscular training resulting from ballet dancing increased the dancer's ability to detect slower angular velocities of knee joint motion (ref. 1). However, the dancers were significantly poorer at detecting static knee position than the control group. Barrack et al. suggested that the differences between these groups was most likely due to an increase in muscle spindle sensitivity (gain) which occurs with ballet training. Perhaps the non-specific muscular training provided by the daily isotonic exercise in our subjects also enhanced spindle sensitivity which facilitated their ability to perform this velocity-based proprioceptive task. The remaining difference between improvement of the isotonic group, and the greater improvement in the isokinetic group, was probably due to the specific daily proprioceptive practice and additional familiarization with the LIDO ergometer by the isokinetic group.

It was not possible to determine if the difference in proprioceptive responses between the exercise groups was due to changes in muscle spindle response alone, or to a combination of improved proprioception and learning via visual feedback enhancement. Proprioceptive information alone, i.e., without visual feedback, can correct up to 95% of velocity and timing errors associated with sudden perturbations in resistance during a multijoint movement sequence (ref. 3). Since our experimental design focused on position (tracking) errors associated with sudden changes in torque, it cannot be determined if either exercise mode would have influenced the muscle spindles' ability to detect timing errors associated with these perturbations.

Proprioceptive sense-response decreases significantly in muscles atrophied by injury and immobilization, and recovers during rehabilitation (refs. 4 and 5). Perhaps 2.5-min per week of proprioceptive testing and general body movement provided sufficient stimuli to maintain proprioceptive sense-response levels in the NOE group. The subjects were not immobilized during BR: they could move freely in lateral directions while in bed and were moved via guerney to other locations for their daily exercise training, showering, and testing. Also, the NOE group maintained stable body weight ($= -1.01 \pm 0.81$ kg,NS) during BR by consuming $2{,}678 \pm 75$ kcal/d. The increased proprioceptive sense-response in the isotonic group must have involved additional stimuli from that provided by the exercise training; e.g., maintenance of or increased blood flow in the lower extremity muscles, or perhaps maintenance or enhanced neuromuscular coordination.

Some astronauts have exhibited altered proprioceptive function in microgravity. Proprioceptive illusions, perceived movement of stationary walls, floor, or horizontal surfaces, were experienced by one astronaut

while performing arm and knee bends (ref. 13). The first illusion, which occurred only inflight with eyes closed, was a feeling that a wall was moving toward him when his arms were flexing; but there was no feeling that the wall was moving away during arm extension. This illusion was present with eyes closed and open 2 hr after landing and disappeared within 24 hr. The second illusion occurred during deep knee bends only after landing and felt as if the floor was oscillating like a trampoline. It was present with eyes closed and open. Like the first illusion, he could "feel" the floor moving but he couldn't see it moving. Thus, in some astronauts the ability to separate self-generated from externally-generated limb movements is compromised for up to 24 hr postflight, the degraded proprioceptive function reduces awareness of the position of a relaxed limb, and muscular contractions improve somewhat the diminished proprioception.

Although there was no proprioceptive degradation in the NOE group, it is clear that daily isotonic exercise training, and especially daily isokinetic exercise training plus proprioceptive training, can improve normal proprioceptive ability for detecting lower limb velocity errors during bed rest. This enhanced proprioception sense-response induced by isotonic and isokinetic exercise training during bed rest may be applicable for assisting recovery of bedridden patients and for assisting astronauts in the performance of their physical tasks during exposure to microgravity.

Acknowledgments

The authors express their warm gratitude and appreciation to the 125 people who had a significant role in this study: especially to the test subjects, Dee O'Hara, manager of the Human Research Facility, and Edith Crofoot and the nursing and aides staff; the exercise testing group from University of California Davis; Todd Trowbridge, Dave McKenzie, and Gene Myers; Joe Forma for software formulation; the dietitions, Robin Williams and Victoria Major, and the food preparation staff; the medical monitor Ralph Pelligra; the Bionetics Corp. personnel managers Gail Bennet-Hiley and Ranita Dalton; the co-investigators and their staffs, especially Bonnie Rosenberg and Kristen Lindseth-Gomez for performance and mood testing assistance; the Laboratory for Human Environmental Physiology support and technical staff (Jeff Ball, Victor D'Aloia, Sally Greenawalt, Teresa Hutchinson, Linda Kirby, Sandra Lewis, Joann Meredith, Andrea Ertl, and Joan Silver), and Bridget Eller and Angela Hardesty for manuscript preparation.

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Exercise-training protocols for astronauts in microgravity

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GREENLEAF, J. E., R. BULBULIAN, E. M. BERNAUER, W. L. HASKELL, AND T. MOORE. *Exercise-training protocols for astronauts in microgravity.* J. Appl. Physiol. 67(6): 2191–2204, 1989.—The question of the composition of exercise protocols for use by astronauts in microgravity is unresolved. Based on our knowledge of physical working requirements for astronauts during intra- and extravehicular activity and on the findings from bed-rest studies that utilized exercise training as a countermeasure for the reduction of aerobic power, deterioration of muscular strength and endurance, decrements in mood and cognitive performance, and possibly for bone loss, two exercise protocols are proposed. One assumes that, during microgravity, astronaut exercise physiological functions should be maintained at 100% of ground-based levels; the other assumes that maximal aerobic power in flight can be reduced by 10% of the ground-based level. A recommended prescription for in-flight prevention or partial suppression of calcium (bone) loss cannot be written until further research findings are obtained that elucidate the site, the magnitude, and the mechanism of the changes. Hopefully these proposed exercise prescriptions will stimulate further research and discussion resulting in even more efficient protocols that will help ensure the optimal health and well-being of our astronauts.

isotonic exercise; isometric exercise; isokinetic exercise; bed rest; weightlessness; astronaut energy metabolism

WHEN THE United States' Space Station Freedom is fully operational, because of its size, the occupants will be able to live and work in it with few, if any, physical constraints. Maintenance of normal ambulatory body weight in crewmembers (91) and in unrestrained bed-rested men (29, 30) requires 2,800–3,100 kcal/day, the range necessary for maintenance of body weight in normal ambulatory men on Earth. Therefore, it is highly probable that the requirements for energy utilization, including physical exercise and exercise training, will be essentially the same in microgravity as in the eugravitational field (60). It would seem logical and prudent for those who must function unerringly in the hazardous space environment to acquire and maintain a sufficient level of body speed, power, strength, endurance, and cognitive performance (i.e., physical fitness) to perform daily tasks efficiently with sufficient reserve capacity to optimize survival in emergency situations. The question of optimal exercise prescriptions (involving type, frequency, duration, and intensity) to be used by astronauts on the ground before flight, in flight, and during postflight recovery is unresolved. To date there has been no structured or mandatory exercise-training program to assist astronauts in this important phase of their ongoing flight training program. Some investigators, however, have suggested that astronauts should not engage in preflight endurance training (50) and that this type of training may adversely affect the blood pressure control system, resulting in decreased postflight orthostatic tolerance (81).

As time of exposure to microgravity lengthens, appropriate exercise training regimens will probably become more important. On short flights (<15 days) few if any of the body systems affected by microgravity are compromised severely, so intensive exercise training has not been necessary as a required countermeasure (69, 70). It is still an open question whether an attempt should be made to maintain all physiological systems at the eugravitational level in all astronauts during prolonged exposure (>30 days) to microgravity. How much is enough? Would deterioration of mental function follow deterioration in physiological function?

Our working hypothesis is that the types of exercises

(isotonic, isometric, isokinetic) used to acquire and maintain physical fitness on the ground will be the same types required to maintain fitness during exposure to microgravity. The undecided aspects of the training program are type, intensity, duration, frequency, and specificity. An example of the latter is the probable (but not confirmed) greater selective decrease in function in microgravity of the antigravity elbow and knee extensor muscles compared with function of the antagonistic flexor muscles (79).

The purposes for this paper are *1*) to review the physical working requirements for astronauts during intra- and extravehicular activity; *2*) to review briefly the important and applicable findings from microgravity simulation (mainly bed rest) studies regarding the use of exercise training as a countermeasure for reduction of aerobic exercise capacity, orthostatic intolerance, deterioration of muscular strength and endurance, adverse changes in mood and cognitive performance, and possibly for bone loss; *3*) to review the pertinent basic data for the formulation of exercise prescriptions; and *4*) from the results of *1*, *2*, and *3*, to present suggested exercise prescriptions for use in microgravity conditions.

ASTRONAUT PHYSICAL WORK REQUIREMENTS

Intravehicular Activity

Apollo. Exercise metabolic and cardiovascular responses have been measured only preflight and postflight from the first five (7–11) and final four (14–17) Apollo flights (67, 69, 70). Stress tests were not conducted after flights 12 and 13 because of postflight quarantine requirements. Submaximal cycle ergometer tests were conducted by measuring oxygen uptake ($\dot{V}O_2$) at heart rates of 120, 140, and 160 beats/min at 6, 9, and 12 min, respectively, during the increasing exercise loads. The 160-beats/min heart rate results from an absolute exercise load that is equivalent to a relative $\dot{V}O_2$ of ~75% of the peak $\dot{V}O_2$. The general findings from Apollo 7–11 astronauts ($n = 15$) were that the mean $\dot{V}O_2$ at 160 beats/min decreased from the preflight level of 2.44 ± 0.09 to 1.93 ± 0.09 (SE) l/min ($\Delta = -21\%$, $P < 0.001$) on the 1st recovery day, and it was 2.34 ± 0.13 l/min ($\Delta = -4\%$, NS) by the 2nd recovery day, 24–36 h postflight (67, 70). Comparable results from Apollo 14–17 astronauts ($n = 12$) were that $\dot{V}O_2$ at 160 beats/min decreased from the preflight level of 2.68 ± 0.14 to 2.23 ± 0.12 l/min ($\Delta = -17\%$, $P < 0.05$) on the 1st recovery day and was 2.49 ± 0.11 l/min ($\Delta = -7\%$, NS) 24–36 h postflight (69, 70). Thus the magnitude of the reduction and rate of recovery of exercise capacity of some Apollo astronauts were similar. The 17–21% reduction in submaximal $\dot{V}O_2$ during these short-term flights (<15 days) was of the same magnitude as the reduction in peak $\dot{V}O_2$ in middle-aged men undergoing −6° head-down bed-rest deconditioning between 21 and 30 days without remedial exercise (29).

Skylab. The type, duration, and frequency of exercise training undertaken by the Skylab astronauts preflight and during the three missions (II, 28 days; III, 59 days; IV, 84 days) were not specified as a basic flight requirement; i.e., there was no mandatory exercise program (71). Exercise facilities on the ground consisted of a quarter-mile track and a well-equipped gymnasium with weight-training equipment, racket courts, and cycle ergometers. In-flight exercise equipment on Skylab II included only a cycle ergometer and an Exer-Gym isometric friction rope-pull device. A Mini-Gym isokinetic device and tension springs were added on Skylab III. A Teflon-coated inclined plate was added on Skylab IV: the crewmen were tethered from the waist and over their shoulders to the floor and slid stocking-covered feet over the surface as though they were walking or jogging on a treadmill (71).

During the 18-day preflight isolation period the Skylab II crew mainly rode the cycle ergometer and played racquetball. The Skylab III crew ran 2–7 miles twice per week, rode the ergometer, and lifted weights but did not play racquetball. The Skylab IV crew ran more frequently, used the ergometer minimally, and did not play racquetball or lift weights (71). The total quantity of in-flight exercise training increased progressively during succeeding missions: 0.5, 1.0, and 1.5 h/day on missions II, III, and IV, respectively. The Skylab II crew used only the ergometer (isotonic exercise); the mission III crew used the ergometer, Exer-Gym (isometric exercise), springs (isotonic exercise), and the Mini-Gym (isokinetic exercise); and the mission IV crew used all the above devices plus the treadmill (isotonic exercise). The only quantitative data of in-flight exercise training were obtained from the ergometer sessions. The means were 31, 65, and 71 $W \cdot min \cdot kg^{-1} \cdot day^{-1}$ for the respective missions of 28-, 59-, and 84-days duration. The doubling of the quantity of ergometer exercise was associated with better maintenance of submaximal $\dot{V}O_2$ capacity in flight and faster recovery postflight on the last two missions (71, 80).

Exercise metabolism was measured preflight, in flight, and postflight during the Skylab missions with precision mass spectrometry (60, 61, 68, 71). Peak $\dot{V}O_2$ was measured in the Skylab crews preflight, but since there was no organized effort to measure it during or after flight, submaximal $\dot{V}O_2$ was measured instead on the ergometer at a heart rate of 160 beats/min (~75% peak $\dot{V}O_2$). Mean preflight submaximal $\dot{V}O_2$ for the nine crewmen was 36 ± 2 $ml \cdot min^{-1} \cdot kg^{-1}$ (range 28–46 $ml \cdot min^{-1} \cdot kg^{-1}$) (71). The extrapolated mean peak $\dot{V}O_2$ would have been ~45 $ml \cdot min^{-1} \cdot kg^{-1}$.

The in-flight exercise capacity test was performed for 5 min each at ~25, 50, and 75% of their preflight peak $\dot{V}O_2$ using the cycle ergometer (where load was independent of pedaling rate). Results from Skylab II indicated no change in resting metabolism during flight, and a small nonsignificant decrement (by 0.2–0.3 l/min) in $\dot{V}O_2$ with performance of the three exercise levels (60). If similar absolute exercise loads were used both preflight and in flight, these observations suggest that peak $\dot{V}O_2$ were decreasing during flight. The exercise heart rate responses at the 75% load postflight in missions II and III (61, 64) tend to substantiate this hypothesis. Postflight exercise heart rate responses after mission II were still elevated after 20 days, but this elevation had returned to normal by the 4th day after Skylab III. There were no changes in the postflight exercise (75%) heart

rate responses of the Skylab IV crew, suggesting they not only maintained, but probably increased somewhat, their aerobic power during flight (71). However, estimation of aerobic power from changes in heart rate is complicated by factors such as microgravity-induced hypovolemia, changes in vascular and cardiac dynamics, and motivational factors. One firm conclusion is that exercise capacity was maintained better with succeeding flights coincident with longer exercise periods and more diverse modes of exercise. Care must be taken in ascribing the maintenance of aerobic power in the mission IV crew to the additional work on the "sliding treadmill," since there was increased utilization of all exercise devices compared with mission III participation. The crew also believed (subjectively) they had increased their aerobic power in flight because of the perceived decrease in effort required and the increased ease with which they accomplished their periodic exercise testing as their 84-day flight progressed (G. Carr, personal communication).

Isokinetic strength and endurance were measured at 18 days preflight and at 5 days postflight on a Cybex dynamometer. After a thorough warm-up, peak torque (mean of 10 repetitions) was measured for elbow (arm) and knee (thigh) flexions and extensions at a rate of 45°/s (76). Compared with Skylab II, results from mission III showed less decrement in postflight peak torque for the arm but the same or greater decrements in peak torque values for the thigh (Table 1). The magnitude of the decrease in thigh strength was about twice that of the arms. In mission IV the mean decreases in both limb strengths were about equal, and the thigh decreases were substantially less than those during the first two missions reflecting perhaps the increased duration and intensity of leg exercise training. These 5–6% reductions in peak torque in the arms and thighs were similar to those measured in men who underwent no remedial exercise training during 30 days of −6° head-down bed-rest deconditioning (28).

Space Shuttle. As mentioned previously, there is no structured preflight exercise training program for Space Shuttle astronauts. The majority maintain good physical condition through self-directed weight- and aerobic-training activities consisting of running-jogging, cycling, racquetball, and squash. Although normal living and working in microgravity is not demanding physically, maintaining good physical fitness increases the astronauts' confidence and mental fitness to meet unexpected emergency situations; e.g., extravehicular activity (EVA), egress, or escape (T. Moore, personal communication).

TABLE 1. *Mean percentage changes in peak torque of the right arm and right thigh flexor and extensor muscle groups after the Skylab missions*

	Skylab II (28 days)	Skylab III (59 days)	Skylab IV (84 days)
Arm (elbow)			
Flexors	−8	−3	−0
Extensors	−10	0	−10
Mean	−9	−2	−5
Thigh (knee)			
Flexors	−10	−19	−14
Extensors	−20	−21	+2
Mean	−15	−20	−6

Values are in percent (from Ref. 80).

In-flight exercise has been limited to use of the nonmotorized passive treadmill where the astronauts lean forward and push against movable treads. The effect approximates jogging or running uphill on a slight grade. The treadmill was first flown on the third Space Shuttle flight (STS-3) and has flown on every subsequent Space Shuttle mission. There is no mandatory in-flight exercise program, hence the large variability in use of the treadmill. The Space Shuttle pilots are the most compulsive users to ensure maintenance of leg strength and endurance for rudder and brake pedal operation during reentry and landing. Heart rates of 140–150 beats/min have been reported during treadmill exercise (T. Moore, personal communication). No specific muscle-exercising devices are flown because of the minimal requirements for intravehicular physical work.

Extravehicular Activity

Although intravehicular metabolic function had been measured directly by mass spectrometry (60), it was not possible to measure $\dot{V}O_2$ directly during EVA, so energy utilization had to be estimated by indirect methods discussed below.

Gemini. Energy utilization during EVA was limited by the heat removal capacity of the suit's life support system. The upper limit was 225–250 kcal/h. Exercise rates >250 kcal/h ($\dot{V}O_2$ ~0.8 l/min) caused progressive increases in body temperature, and the astronauts reduced their working rates until they felt comfortable.

Apollo. Greater exercise loads during EVA were permitted by the use of a liquid cooling garment worn next to the skin. Body heat was transferred from the skin to the cool plastic tubing by conduction. The heat removal capacity of this suit was increased to ~500 kcal/h (89). The average metabolic rate of 12 astronauts (Apollo 11, 12, and 14–17), measured by temperatures of the incoming and outgoing suit cooling liquid, during 28 lunar-surface EVA sorties (involving scientific package deployment, geological station activity, working overhead, and lunar rover vehicle operations) was 235 ± 5 (SE) kcal/h; average time of these EVAs was 5.7 ± 0.5 h. The average speed of walking for each 2.9 km of lunar surface covered was 2.4 km/h with a mean metabolic rate of 300 kcal/h. Results from a kinematic analysis showed that manipulative tasks were conducted in the EVA suit more rapidly than at eugravity, but at a greater metabolic rate. This was probably due to the hobbling effect of the pressurized suit.

Estimated average metabolic rate during microgravity EVA in seven Apollo astronauts (flights 9 and 15–17) was <242 ± 59 (SE) kcal/h ($n = 6$), and average duration of EVA was 1.05 ± 0.12 h (89). The EVA on these flights consisted of one astronaut retrieving three film cannisters while another astronaut stood in the spacecraft hatch and observed.

Skylab. Microgravity EVA during Skylab missions was similar to that during Apollo flights. Measurements of metabolic rates were estimated only from the tempera-

ture differential of liquid in the cooling garments and from heart rates (89). The latter were compared with heart rate data taken from the in-flight ergometer tests. These EVAs included erection of solar panels, canopy, and an antenna and replacement of a gyro package. Average EVA time for 19 sorties with the nine men was 4.2 ± 0.7 h (range 0.6–6.9 h), and the metabolic rate was 238 ± 12 kcal/h. The greatest load (500 kcal/h) occurred on the first EVA of Skylab I, when a restraint strap on the solar panels was being cut (89). Data from Russian cosmonauts were also within these ranges of energy expenditure (1, 48, 84, 88), and rectal temperatures (T_{re}) reached 37.8°C during EVA from the Salyut-6 station (1).

The crew reported that it was easier to maneuver in microgravity EVA than during water immersion in eugravity. It was clear here also that the upper limit of physical activity was determined by the heat removal capacity of the suit and not by the physical working capacity of the astronauts. Thus the self-paced exercise loads of astronauts during microgravity and lunar surface EVA were ~240 kcal/h; the rate during Moon walking was 300 kcal/h (89).

Whittle and colleagues (92, 93) have performed some very interesting biostereometric studies on the Skylab astronauts involving three-dimensional measurements of body form from which various volumes were calculated. From the volume changes in the leg segments, the duration and energy cost of the in-flight exercise training, and caloric intakes, they have concluded that an exercise load of 80–100 $W \cdot min \cdot kg$ lean body $mass^{-1} \cdot day^{-1}$ would be necessary to prevent in-flight muscle atrophy of presumably the thigh and leg muscles. This represents 30–60 min of hard cycling daily. Sixty minutes per day of hard intermittent leg cycling (60–90% of peak $\dot{V}O_2$) maintained peak $\dot{V}O_2$ in seven men during 30 days of −6° head-down bed rest (29). A second conclusion was that caloric intakes of 47–51 $kcal \cdot day^{-1} \cdot kg$ lean body $mass^{-1}$ (2,880–3,121 kcal/day) were required to maintain lean body mass and fat content. These levels of caloric intake agree nicely with those intakes required to maintain body weight in prolonged-bed-rested men (29, 30, 37).

Space Shuttle and Space Station. The total heat removal capacity on the current EVA suit is ~2,513 kcal (10,000 BTU), and the greatest rate is 503 kcal/h (2,000 BTU/h) (H. Vykukal, personal communication). The mean steady-state operational range is 213 kcal/h (850 BTU/h), which is somewhat lower than the 235- to 240-kcal/h range utilized by the Apollo and Skylab crews. The upper limit of 503 kcal/h, equivalent to $\dot{V}O_2$ of ~1.7 l/min, is only half of the peak aerobic capacity of 3.4 l/min (45 $ml \cdot min^{-1} \cdot kg^{-1}$) with leg exercise, which is about the average for the total astronaut corps. Constant leg work at this level could be continued for no more than 5 h. Since peak $\dot{V}O_2$ with dynamic upper body (arm) exercise is ~70% of peak $\dot{V}O_2$ with legs, 50% of peak $\dot{V}O_2$ with legs is equivalent to ~70% of arm peak $\dot{V}O_2$, which may be close to the limit for heat removal for 5 h. Fatigue may stop the arm exercise sooner.

There have been 13 two-crewmember EVAs during previous Space Shuttle flights. The physical demands during these EVAs varied and depended on the EVA mission requirements; these have included testing of tools and equipment, satellite retrieval and repair, and simulated space station construction. Astronauts' subjective ratings of perceived exertion during the EVA have ranged from relatively easy to extremely difficult. The average metabolic rate for those 26 EVAs was 199 kcal/h, and the average duration was 5.5 h (T. Moore, personal communication). Since most EVA work is performed with the arms, forearms, and hands, with additional work necessary to overcome the elastic recoil of the suit pressure of 4.3 psi, significant upper body muscle fatigue can occur. The almost exclusive use of upper extremity muscles will result in lower heat production than if the larger lower extremity muscles were used. Consequently the space suit that utilizes liquid cooling and ventilation appears to function quite efficiently. There have been no subjective complaints of astronauts overheating during Space Shuttle EVAs.

Exercise thermoregulation in eugravity is such that the equilibrium level of T_{re} during isotonic exercise, at a load equivalent to 50% of the peak $\dot{V}O_2$, is 38.0 ± 0.1°C and is independent of the absolute $\dot{V}O_2$ (4, 34, 73). At the same relative $\dot{V}O_2$ (i.e., 50%), these different aerobic powers will be reflected in heart rate differences among subjects but not in core temperatures (34). The greater heat production in subjects with higher aerobic power is dissipated via greater heat loss, mainly by evaporation (27). Thus, astronauts with higher peak $\dot{V}O_2$ will be able to work at higher absolute energy levels ($\dot{V}O_2$), but their greater mandatory heat production and dissipation loads will limit working time because of the suit's finite heat removal capacity.

The type of exercise training performed during 14 days of bed rest affects the core temperature response to supine dynamic exercise. The equilibrium level of T_{re} during supine isotonic ergometer leg exercise is approximately inversely proportional to the intensity level of exercise training during 14 days of horizontal bed-rest deconditioning (38). Isometric exercise training augments the hyperthermic response to exercise. Compared with the equilibrium level of T_{re} during ambulatory control supine exercise (37.50°C), the comparable levels after isometric (37.92°C), isotonic (37.72°C), and no exercise training (37.75°C) were all elevated. The greatest difference in T_{re} was 0.42°C after the isometric-training regimen. The mechanism appears to be a proportional reduction in tissue heat conductance, which may be caused, in part, by hypovolemia and by a decrease in peripheral vascular function (21, 38). It appears that a penalty must be paid in higher exercise core temperature as a result of the various exercise-training regimens employed during bed-rest simulations. It is not known whether this excessive exercise-induced hyperthermia occurs in astronauts in microgravity.

EXERCISE TRAINING AS A COUNTERMEASURE

The purpose for the use of countermeasures is ostensibly to permit astronauts to function productively, perhaps not necessarily normally, during exposure to microgravity. Major factors that could impair performance

during long-term exposure to microgravity are increased risk of fracture on return to eugravity or partial gravity; decreased aerobic power, muscular strength, and endurance (fatigue); and deterioration in mood and psychological state (faulty decision making). The adverse consequences of all these factors, plus orthostatic intolerance (tendency to faint), could be accentuated when microgravity-acclimated astronauts are exposed to increased gravitational fields (e.g., Moon 0.2 G, Mars 0.4 G, Earth 1.0 G, and reentry accelerations >1.0 G). The major question that arises when prescribing various countermeasures is, How much is enough? Is it necessary to maintain all body systems and functions at the eugravitational level? Is it possible to do so? If it is necessary and possible, what are the penalties in time, possible injury, and astronaut morale? And finally, are there adverse consequences for full maintenance? Since it is almost certain that various kinds of exercise-training protocols (prescriptions) will be used as countermeasures in prolonged flights, it is necessary to try to determine what, if any, adverse consequences might occur in physical (aerobic) performance, orthostatic tolerance, muscular strength and endurance, bone integrity, and psychological performance.

Aerobic Power

Changes in peak $\dot{V}O_2$ have been measured many times before and after prolonged bed rest (36, 39), and the results have been reviewed recently (12). The general consensus is that nearly all types and durations of exercise-training regimens performed during bed rest will attenuate the decrease in aerobic power. In only five studies (10, 29, 62, 66, 77), however, has complete information been reported where meaningful quantitative comparisons can be made between exercise type, duration, and intensity and the effect of exercise training on the level of maintenance of aerobic power (Table 2). In only two studies (10, 29) were positive training responses reported; i.e., peak aerobic power was higher after than before bed rest. The mean increase in peak $\dot{V}O_2$ of 16% in four untrained subjects who exercised for 30 min/day (Table 1) on a horizontal bed that moved laterally between two vertical trampolines was remarkable (10). A second group of untrained subjects from the same study who exercised in the horizontal position on a cycle ergometer at 31 ml $O_2 \cdot min^{-1} \cdot kg^{-1}$ increased peak $\dot{V}O_2$ by 8.5%. In contrast, eight other subjects who endurance trained before bed rest were not quite able to maintain their peak aerobic power ($\Delta = -4.6$ to -6.6%) during bed rest despite more intensive in-bed exercise training (Table 2). Thus, previously untrained subjects improved their aerobic power during bed rest while previously trained subjects could not, even though their training intensity during bed rest was greater than that of the untrained group. The fact that untrained men have a greater range for increasing their aerobic power (90) may be a partial explanation for these findings and for those of Rodahl et al. (66). In the latter study four men (peak $\dot{V}O_2$ 2.5–3.2 l/min) essentially maintained aerobic power during 24 days of bed rest while undergoing exercise training loads of only 100 W (600 kg-m/min) for 1 h/day

TABLE 2. *Effect of exercise training during bed rest on aerobic power*

Ref.	*n*	Age, yr	Exercise Test: Device	Exercise Test: Position	Mean Peak $\dot{V}O_2$: l/min: Before	Mean Peak $\dot{V}O_2$: l/min: After	Mean Peak $\dot{V}O_2$: l/min: %Δ	Mean Peak $\dot{V}O_2$: ml·min^{-1}·kg^{-1}: %Δ	Days	Bed-Rest Training Schedule: Device	Position	m/day	Intensity	Remarks
Chase et al. (10)	4	22–26	Cycle ergometer	Sitting	3.19	3.42	+7.2	+8.5	15	Cycle isotonic	Horizontal	30	31 ml·min^{-1}·kg^{-1}	
	4	21–24	Cycle ergometer	Sitting	2.96	3.42	+15.5	+16.4	15	Trampoline isotonic	Horizontal	30	31 ml·min^{-1}·kg^{-1}	
	4	21–25	Cycle ergometer	Sitting	3.17	2.92	−7.9	−4.6	30	Trampoline isotonic	Horizontal	45	75% peak $\dot{V}O_2$	Conditioned 5 wk before bed rest
	4	21–22	Cycle ergometer	Sitting	3.51	3.19	−9.1	−6.6	30	Trampoline isotonic	Horizontal	15	75% peak $\dot{V}O_2$	Conditioned 5 wk before bed rest
Miller et al. (62)	6	18–21	Treadmill	Standing	2.91	2.28	−21.6	−19.5	28	Cycle isotonic	Horizontal	60	Light	HR 88–126 beats/min $\dot{V}O_2$ 0.8–0.94 m
Stremel et al. (77)	7	19–22	Cycle ergometer	Horizontal	3.80	3.45	−9.2	−7.3	14	Cycle isotonic	Horizontal	60	68% peak $\dot{V}O_2$	Continuous exercise 30 m A.M./30 m P.M.
	7	19–22	Cycle ergometer	Horizontal	3.77	3.59	−4.8	−3.7	14	Foot bar isometric	Horizontal	60	21% peak force	Intermittent leg extension 30 s exercise/30 s rest
Greenleaf et al. (29)	7	32–42	Cycle ergometer	Horizontal	3.13	3.14	+1.4	+2.6	30	Cycle isotonic	−6° head down	60	90% peak $\dot{V}O_2$	60–90% intermittent exercise
	7	32–42	Cycle ergometer	Horizontal	3.24	2.90	−10.2	−9.1	30	Lido isokinetic	−6° head down	60	Peak intensity	Intermittent exercise: 10 s exercise/50 s rest
Rodahl et al. (66)	2	19–20	Cycle ergometer	Sitting	3.0	2.8	−6.7	−1.4	24	Cycle isotonic	Horizontal	60	600 kg-m/min	
	2	18–19	Cycle ergometer	Sitting	2.8	2.8	0.0	0.0	24	Cycle isotonic	Sitting	60	600 kg-m/min	

All subjects were male. $\dot{V}O_2$, O_2 uptake.

(Table 2). Performance of intermittent cycle ergometer leg exercise (60–90% peak $\dot{V}O_2$) for 60 min/day changed peak $\dot{V}O_2$ by +2.6% (NS) in seven men who were moderately trained before bed rest (29). This integrated exercise regimen was just below the level for injury. In the same study the post-bed-rest $\dot{V}O_2$ was decreased by 9.1% ($P < 0.05$) in the isokinetic-training group and by 18.2% ($P < 0.05$) in the no-exercise-training control group (not shown on Table 2).

Thus, high-intensity (75–90% peak $\dot{V}O_2$) isotonic exercise training for 1 h/day will maintain aerobic power in moderately trained subjects during prolonged bed rest. However, if the prescription for the equilibrium level of aerobic power during microgravity can be lowered to 90% of pre-bed-rest flight levels, then intensive isokinetic exercise training can be used to "maintain" not only muscular strength and endurance but also the 90% level of aerobic power.

Orthostatic Tolerance

Orthostatic is defined as "of, relating to, or caused by erect posture" (25), so responses to lower body negative pressure and acceleration are not discussed. The practical problem is to devise maintenance and/or remedial procedures that will allow deconditioned astronauts to overcome the tendency to faint when exposed to increased gravitational fields or the upright posture. Since it is almost certain that various exercise-training regimens will be used as countermeasures in microgravity, it is necessary to determine whether these regimens result in accentuated orthostatic intolerance.

There is some evidence from cross-sectional studies that ambulatory endurance-trained men have significantly lower tilt-table tolerance, but a much greater number of investigators have concluded that these men have unchanged or somewhat higher tolerances (13, 14, 22, 23, 35). The major question is whether the exercise training per se modifies tolerance. Results from short-term (12 days, isotonic exercise) and long-term (6 mo, isotonic and isometric exercise) longitudinal training studies indicate no significant change (in one case an increase) in tolerance to 60- to 90-min sessions of head-up tilt when the subjects were tested hydrated and euthermic (33, 35). In addition, the reduced tilt tolerance after bed rest was not altered by exercise training during bed rest with changes in peak $\dot{V}O_2$ from 0 to −20% (41).

On the other hand, there is other evidence that suggests greater intolerance during tilting in dehydrated men after they were heat acclimated and exercise trained; i.e., the acclimation accentuated the intolerance with a possible interaction with the dehydration (31, 32). These findings, and those indicating that some endurance-trained men have a more labile blood pressure control system and significantly lower orthostatic tolerance (22, 43, 81), indicate an incomplete understanding of the effects of exercise training and heat acclimation on the control of blood pressure and its interaction with orthostatic tolerance.

MUSCULAR STRENGTH AND ENDURANCE

Ambulation

There is no doubt that muscular strength and endurance are increased by exercise training in normal ambulatory subjects (4). The mechanism(s) of the increase is not entirely clear but involves adaptive responses to increased muscular tension. Some of these responses are increased protein synthesis leading to a greater number of cellular myofibrillar contractile elements (actin and myosin); increased cellular water and potassium content; increased mitochondrial enzyme activity resulting in more efficient energy transformation from pyruvates and fatty acids; increased capillarization, blood flow, and oxygen delivery to muscle cells; and increased "psychological threshold" so that more muscle cells are activated (recruited) during a contraction.

An essential compound in this process is water. Results from a study (9) where maximal isometric strength and isotonic leg endurance (ergometer) were measured after 3 days of acute dehydration (2,887 kcal/day, 1,066 ml H_2O/day) and 3 days of starvation (no food or water) indicated mean strength losses (left and right shoulder extension, elbow flexion, and knee extension) of 9.7–10.4% with dehydration and starvation; the hydrated control group mean loss was 7.5% caused, in part, by the high-protein diet. Endurance to number of sit-ups in 2 min decreased significantly by 9% with dehydration and by 13% after starvation. There were similar reductions in ergometer endurance. It is clear that muscular endurance is decreased in dehydrated ambulatory subjects (26).

Bed Rest

The mean percent changes in maximal isometric strength for various muscle groups after 7–120 days of bed rest are presented in Table 3. In general, there were decreases in strength of all muscle groups during bed-rest deconditioning. The greatest apparent increase in strength was by 2% after isotonic exercise training for 120 min/day during 70 days of bed rest (95). The mean decreases in strengths (−6 to −8%) in the smaller muscle groups (handgrip, forearm, and arm) were only half of the mean decreases in the larger muscle groups (−11 to −24% in the back, abdomen, thigh, and leg). There appears to be a significant progressive decrease in handgrip strength with increased duration of bed rest without remedial exercise. Data from Table 3 are plotted in Fig. 1*B* against duration of bed rest. There is a progressive decrease in strength in both small and large muscle groups with increasing duration of bed rest without remedial exercise (Fig. 1). On the other hand, during bed rest with remedial exercise, the range of strength changes was only +2 to −11% (Table 3). Thus, with the exception of abdominal and handgrip strengths, cycle ergometer exercise training during bed rest essentially maintains strength in all other muscle groups (Table 3, Fig. 1). Furthermore, the significant reduction in handgrip endurance, at 40% of pre-bed-rest maximal handgrip force during bed rest with no remedial exercise, was eliminated with 1 h/day of isotonic (cycle ergometer) and isometric leg exercise during 14 days of bed rest (40). In some cycle

TABLE 3. *Mean percentage changes in maximal strength of various muscle groups after bed rest*

Ref.	Bed-Rest Exercise Schedule						%Change in Muscle Group Strength							
							Small			Large				
	No. subjects	No. days bed rest	Exercise duration, min/day	Exercise type	Exercise position	Strength measure, days	Hand grip	Forearm	Arm	Back	Abdomen	Thigh	Anterior leg	Posterior leg
Friden et al. (24)	14	7	None	None		7	−5					−5		−7
Trimble et al. (85)	8	7	None	None		7	0							
Kozlovskaya et al. (51)	18	14	None	None		16							−9	−16
Greenleaf et al. (40)	7	14	None	None		15	0							
			60	ITE*	Sup	15	−1							
			60	IME	Sup	15	+1							
Taylor et al. (79)	6	21	None	None		22	−3			−8				
Birkhead et al. (7)	2	24	60	ITE*	Sup	25			−2					
Birkhead et al. (6)	4	42	None	None	Sup	43			−5					
Deitrick et al. (18)	4	42–49	None	None		43–50	0	−7	−9	0	0		−13	−21
Kakurin et al. (47)	3	62	None	None		63				−19				
	3	62		ITE*	Sup	63				−8				
Yeremin et al. (95)	1	70	None	None		72		−27	−28	−39	−48	−36	−57	−37
	3	70	120	ITE*	Sup	72		+1	+1			−2	−11	+1
	3	70	120	ITE†	Sup	72		+2	+1			−2	−6	−2
Panov et al. (64)	1	72	None	None		11	0							
						22	−2							
						36	−8							
						44	−12							
						64	−27							
Krupina et al. (54)	10	120	None	None		95	−27							
Grigor'yeva et al. (42)	14	120	None	None		120							−39	−34
Mean							−6	−8	−7	−15	−24	−11	−22	−17

All subjects were males. Sup, supine position; ITE, isotonic exercise (* cycle, † treadmill); IME, isometric exercise.

ergometer tests, the arms were used for stabilization, which may have induced a training effect. Thus, leg exercise training may assist with maintaining handgrip endurance.

The few data available on maximal isokinetic strength during bed rest (Fig. 1*A*) indicate greater strength increases in the grip, forearm, and arm muscles and about the same levels of decreases in strength of the leg muscles compared with the classical isometric data.

Bed Rest, Immersion, and Microgravity

Percent changes in strength of the anterior tibial (ankle dorsal flexion) and triceps surae (ankle plantar flexion) muscle groups have been measured isokinetically at four velocities (0, 60, 120, and 180°/s) before and after 7 days in microgravity and immersion (Fig. 2), 110 and 237 days in microgravity (Fig. 3), and 120 days of head-down bed rest and 110–237 days in microgravity (Fig. 4). Classical maximal isometric strength is measured at 0°/s on the isokinetic ergometer because the joint does not move. With the 7-day exposures both plantar and dorsal flexion strengths were not significantly reduced at all velocities measured after microgravity, but they were significantly reduced (~60%) after immersion (Fig. 2). The exercise training during microgravity probably assisted with maintenance of strength. The only significant differences in leg muscle strengths between 120 days of bed rest and 110–237 days in microgravity were the significantly lower values (by 12 and 14%) for bed-rest plantar flexion strengths at 0 and 60°/s, respectively (Fig. 4). Leg exercise training during flight possibly helped reduce the loss of strength. From the similarity of these two respective pairs of curves and those obtained from the two extended microgravity exposures (Fig. 3), it can be concluded that there is no greater loss of plantar flexion strength in the triceps surae (antigravity) muscles compared with the dorsal flexion (anterior tibial) strength.

CALCIUM LOSS AND BONE MINERAL CONTENT

Ambulation

The effects of exercise training in normal ambulatory subjects on calcium metabolism and the bone mineral content (BMC) of various bones have been studied extensively. Results from cross-sectional studies indicate that, in general, people who undergo exercise training have larger and more dense bones than those who do not exercise (17, 46). The fact that this greater BMC can be

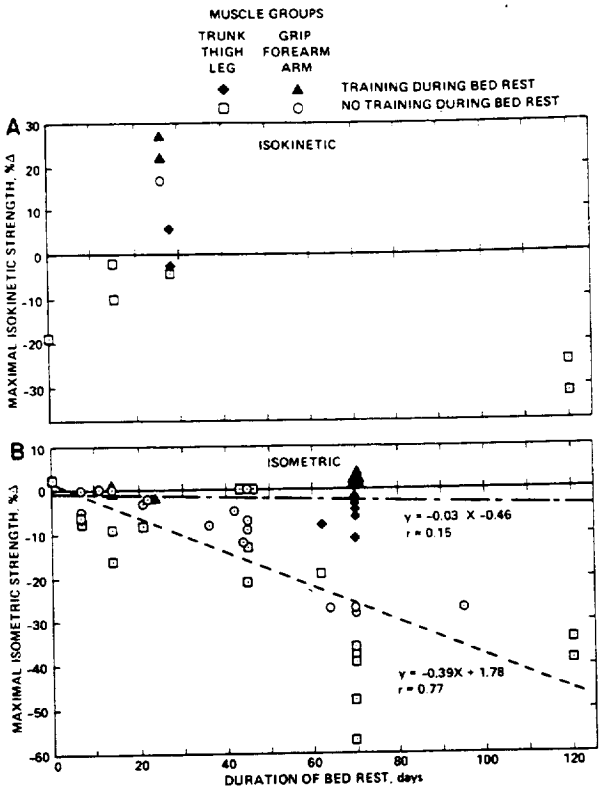

FIG. 1. Mean percent changes in maximal isokinetic strength (*A*) and maximal isometric strength (*B*) in larger (trunk, thigh, leg) and smaller (grip, forearm, arm) muscle groups with and without exercise over 120 days of bed rest.

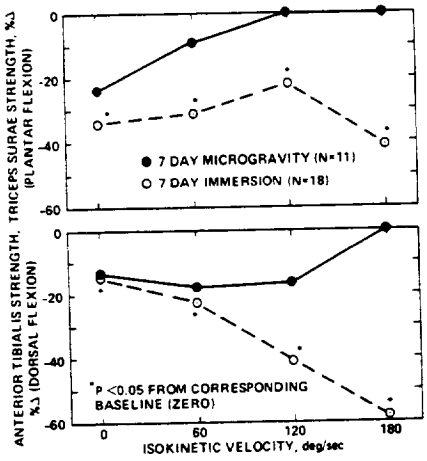

FIG. 2. Mean percent changes in plantar and dorsal flexion isokinetic strengths (0–180°/s) after exposure to 7 days of microgravity and 7 days of dry immersion. [Redrawn from Kozlovskaya et al. (51).]

at least partially accounted for by the strain of exercise has been reported in longitudinal exercise-training studies. Training of moderate intensity in women (29–81 yr) can increase BMC by 1.5–3.5%/yr, and it can also decrease by 1.5–3.5%/yr in nonexercising control subjects (11, 53, 75, 76). There appeared to be a similar rate of increase in BMC in women (29–62 yr) who ran 42 km/wk for 2.5 yr (49). Also, total body calcium content, measured by neutron activation, increased significantly in postmenopausal women who exercise trained for 3 h/wk (2). It is generally agreed that force levels generated

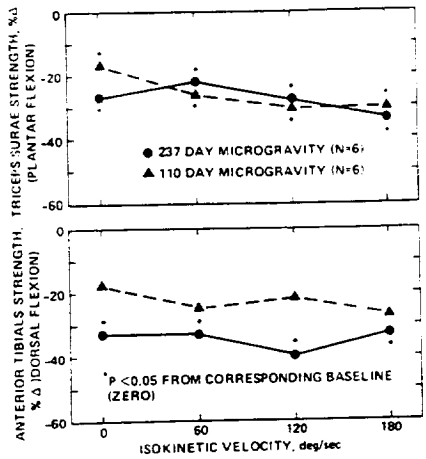

FIG. 3. Comparison of mean percent changes in plantar and dorsal flexion isokinetic strengths (0–180°/s) between 110 and 237 days of exposure to microgravity. [Redrawn from Grigor'yeva and Kozlovskaya (42).]

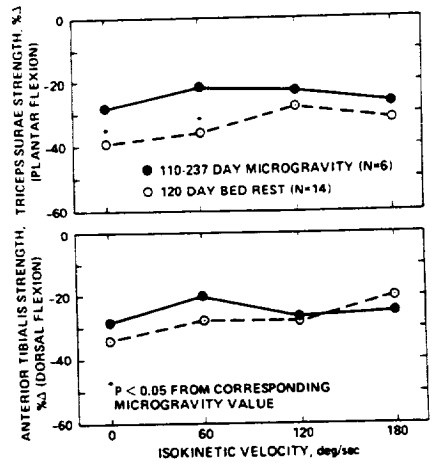

FIG. 4. Comparison of mean percent changes in plantar and dorsal flexion isokinetic strengths (0–180°/s) between exposures to 120 days of bed rest and 110–237 days of microgravity. [Redrawn from Grigor'yeva and Kozlovskaya (42).]

throughout the skeletal system by daily activity are required to maintain the bony framework (55, 59) and also for the integrity of its parts (i.e., bones, muscles, tendons, and ligaments). From an intensive research effort, Tipton and colleagues (82, 83) have concluded that the mechanical strain from exercise and muscular contractions is important for maintaining and repairing ligaments and the junctions between ligaments and tendons and bones.

Thus, in normal ambulatory people, the mechanism for the maintenance or increase of BMC resulting from aerobic exercise training involves *1*) increased general body and presumably bone circulation and metabolism, *2*) increased pressure on bones during the standing posture, *3*) increased intermittent impact loading on bones from running or hitting tennis balls (46), and *4*) increased mechanical forces on bones from contracting muscles when maintaining quiet posture and particularly during exercise. These factors are not mutually exclusive.

Bed Rest

As with aging, the deconditioning (acclimation) responses during prolonged bed rest without countermeasures include a loss of BMC and total body calcium (19, 30, 74). The average daily calcium losses (urine plus fecal) in bed-rested subjects whose diets were controlled were 170 mg/day for 28 days = 62 g/yr (57), 123 mg/day for 35 days = 45 g/yr (56), 243 mg/day for 35 days = 89 g/yr (91), 236 mg/day for 42–49 days = 86 g/yr (18), 157 mg/day for 140 days = 57 g/yr (74), and 221 mg/day for 252 days = 81 g/yr (19) (mean 70 g/yr). Seventy grams of calcium per year (5.8 g/mo) represents ~5.8% of the 1,200 g of total body calcium. The mean calcium loss in 10 men bed rested for 100 days was ~5 g/mo (A. I. Grigor'yev, unpublished data).

Since >99% of body calcium is in bone, the skeleton is the obvious source of the calcium loss, but the etiology of this loss is not clear. Because vigorous exercise training for 1 h/day during bed rest has no effect on the increased rate of urinary calcium loss (30, 66), any decreased energy metabolism during bed rest does not appear to be a major contributory factor. Thus the hypercalciuria could be the result of *1*) the reduction in hydrostatic pressure within the cardiovascular system and/or *2*) the large reduction in axial pressure and muscle forces that load the axial skeletal and bones of the lower limbs during ambulation. Various exercise training regimens that activate thigh and leg muscles, performed in the supine or sitting positions during bed rest, have had no effect on reducing the rate of hypercalciuria or bone density losses (30, 66, 74). On the other hand, Whedon et al. (91) found that the total urinary calcium losses in three men during immobilization in plaster casts in an oscillating bed was only 51% of the losses for the same period of time during immobilization in a stationary horizontal bed. So the slight axial loading and probable cardiovascular stimulation reduced the hypercalciuria. Therefore, weight bearing, rather than moderate-to-heavy leg exercise training, appears to be more important in attenuating the bed-rest-induced hypercalciuria. Quiet sitting for 8 h/day in conjunction with 16 h/day of bed rest did not influence urinary calcium output, but 3 h/day of quiet standing did (45). In the standing position the forces that load the bones vary as postural muscles attempt to maintain balance. In addition, during upright posture there is an accompanying increase in hydrostatic fluid pressure in the lower limbs. So the latter cannot be ruled out as a probable contributory factor for the maintenance of bone integrity. Blood flow through bones during bed rest has not been measured, but the hypoxia of simulated altitude exposure (3,050 and 3,660 m) significantly reduces bed-rest-induced urinary calcium and phosphorus losses (57). All attempts to maintain bone integrity during bed rest involving dietary and vitamin supplements, physical exercise, impact loading, static and intermittent longitudinal compression, and lower body negative pressure have failed to maintain BMC (70) possibly because the impact loading and longitudinal compression treatments have not been applied with sufficient duration and intensity.

However, from measurements of X-ray densitometry in three subjects, Krasnykh (52) reported that aerobic treadmill-exercise training (1 h/day for 30 days presumably conducted in the supine position) plus exposure to lower body negative pressure (LBNP) (2.5 h/day for the last 5 days of horizontal bed rest) reduced the loss of calcaneal density from $-11.9 \pm 0.5\%$ in the control group to $-7.4 \pm 1.5\%$ ($P < 0.05$) in the exercise-LBNP group. A third group given daily muscle electrical stimulation for 60 min/day showed no significant change in calcaneal or finger bone density. Kakurin et al. (47) studied tibial density (X-ray) in men bed rested horizontally for 62 days. They compared density of three men given isometric and intensive leg cycle ergometer exercise (1,000 kcal/day) with that of a sedentary bed-rested control group. Mean bone density of the control group decreased by 15% (range 10–21%), whereas that of the exercise group decreased by 5% (range 2–7%). Statistical significance was not possible to calculate. Even with the relatively large variability in X-ray densitometry, these findings suggest a positive influence of moderately hard aerobic exercise training on the loss of BMC during bed rest. On the other hand, Arnaud et al. (3) found no significant changes in the mean density of the lumbar spine (L_1–L_4) or the middle of the nondominant radius, measured by dual-photon absorptiometry and single-photon absorptiometry, respectively, in middle-aged men undergoing strenuous cycle ergometer leg exercise training (7 men, 1 h/day), isokinetic leg exercise training (7 men, 1 h/day), or no exercise training (5 men) during 30 days of $-6°$ head-down bed rest (29). Also, results obtained from iliac crest biopsies, taken during a recent 120-day study of $-5°$ head-down bed rest on 20 middle-aged men, indicated no significant changes in bone mass parameters (trabecular volume, mean cortical thickness, or mean trabecular plate thickness, density, and separation) in the nontreatment control group or in other groups subjected to isotonic-isokinetic exercise training, to potassium diphosphonate supplementation, or to exercise plus supplementation (86). Since only Kakurin et al. (47) have reported reduced bone density losses in leg (tibial) bones accompanying leg exercise training, it is possible that bone hypertrophy is localized in those bones subjected to direct muscular stress, e.g., humeral hypertrophy in the dominant arm of tennis players (46). Most investigators have treated one body location (i.e., leg exercise) and measured bone parameters in another (i.e., spine or arm). The fact that nutritional supplements have failed in essentially all trials to attenuate the loss of BMC during bed rest without and with supplemental exercise regimens indicates the mechanism is elsewhere, i.e., not caused by dietary deficiencies. The moderately suggestive evidence to date points to axial pressure (standing upright) and physical exercise as the two most useful countermeasures during bed rest. The problem is to determine the kind and magnitude of forces acting on the human skeleton in normal ambulation (mechanical and orthostatic) and then to devise appropriate countermeasures for use in microgravity. Since adequate bone integrity can be maintained in ambulatory people without exercise-training regimens, any effect of exercise

during bed rest would probably act via application of mechanical stress to the bones.

Microgravity

The few data from cosmonauts after spaceflight showed no abnormalities in calcaneal amino acid composition or inorganic content in three deceased crewmembers after their 28-day flight (65). More recent photon absorptiometry data from cosmonauts after 75–184 days in flight indicted a decrease of calcaneal mineral content of 0.9–9.8% in six crewmen that reached a plateau at ~90 days of flight (78, 87).

MOOD AND PSYCHOLOGICAL PERFORMANCE

Exercise and exercise training induce "affective beneficence" on the psychological state of most participants: those who undertake chronic physical training exhibit decreases in anxiety and depression as well as increases in self-esteem (63). Bed-rest confinement and confinement in ambulatory subjects can induce changes in psychological states. Chronic partial confinement in a nuclear submarine for 70 days resulted in a 7% decrease in peak $\dot{V}O_2$ in eight men who did not perform exercise training, but there was no change in the scores from a battery of cognitive performance tests (5).

The psychosocial effects of exposure to long-duration bed rest have been reviewed recently by Winget and DeRoshia (94). The general conclusion from this review and material in other compendia (36, 39) is that the combination of semiconfinement and semi-isolation results in altered mood and psychosocial states. Semiconfinement indicates a reduced level of body movement and exercise (hypokinesia), so one hypothesis suggests that the supposed reduction in energy expenditure due to inactivity during bed rest contributed to the altered psychosocial states. Since 2,800–3,100 kcal/day are required to maintain body weight during bed rest (29, 30) without or with exercise training, respectively, it is doubtful whether adverse psychosocial responses are due to inactivity unless the subject is severely confined. However, inactivity may change the metabolic efficiency. Conversely, hypocaloric intake will aggravate the bed-rest-induced hypovolemia, and the ensuing dehydration could accentuate irritability as it does in ambulatory subjects.

Deitrick et al. (18) studied four men for 42 and 49 days of bed rest, and relatively complete immobilization was achieved by Whedon et al. (91) in three men who were confined within bivalved plaster casts covering the pelvic girdle and legs for 23 h/day for 35 days during horizontal bed rest. They concluded that the severity of the adverse psychosocial responses varied according to each subject's personality traits; e.g., some subjects reacted to confinement with indications of dependency while others exhibited aggressiveness. The most severe reactions occurred early in the control period, the first 2 days of bed rest, and the first 2 days after cast removal, i.e., during protocol changes. Also, the number and intensity of the psychosocial reactions were greatly attenuated in the same subjects after a second similar bed-rest experiment (91). Maslov (58) has characterized the disturbances during bed rest (increased irritability and fatigue, reduced ability to work, inclination to argue, and slight depression) into four stages: *stage 1* (*days 1–2*), the starting condition characterized by high spirits and enthusiasm; *stage 2* (*days 3–6*), a period of physical discomfort; *stage 3* (*days 10–20*), a period of adaptation where physical discomfort essentially disappears and mental states are calm and even; and *stage 4* (*day 20* onward), a period of occurrence of asthenic symptoms characterized by restlessness, increasing monotony, and irritability, shallow sleep, and difficulty in concentrating. It was concluded that the severity of these signs and symptoms appeared to be reduced (no data) in the three subjects performing exercise training (duration and intensity not specified) during bed rest. The hypervolemia associated with exercise training may have attenuated the bed-rest-induced hypovolemia and alleviated some of the dehydration-induced irritability. Subjects who had participated in bed-rest experiments previously had attenuated psychosocial reactions (58).

Other investigators who measured and observed psychosocial reactions in bed-rested subjects also noted reduced adverse signs and symptoms and better performance and emotional adjustment in those subjects who performed moderate exercise training (8, 72). Results from a recent 30-day, bed-rest study that employed heavy and intensive daily isokinetic and isotonic leg exercise training just below the point of injury showed essentially no effect of either mode of training on the modest increase in mood and psychosocial state measured by an extensive battery of qualitative and quantitative tests (28). In this study a concerted effort was made to ensure optimal subject selection, to provide them with varied and interesting activities, and to foster positive leadership attributes in the nursing staff and all investigators and support personnel so that all participants were working together as one team. Thus, we can conclude that adverse mood and psychosocial responses are not necessarily an inherent part of the bed-rest deconditioning syndrome, that there is an increasingly positive psychological state with each succeeding bed-rest experiment, and that intensive exercise training during bed rest can, but does not always, engender better mental states. However, exercise training may improve mood and mental performance in subjects exposed to a less than optimal psychosocial environment during bed rest.

In summary, in successful bed-rest experiments where subjects receive positive psychological reinforcement and subjects and staff work as a team, it seems there are no adverse consequences from physical exercise training on orthostatic tolerance, muscular strength and endurance, bone integrity, and mood and psychosocial performance. Increased physical fitness improves all these functions with the exception of orthostatic tolerance, which remains unchanged. The one potentially adverse effect is excessive exercise hyperthermia during exposure to microgravity.

DISCUSSION OF EXERCISE PRESCRIPTIONS

Our basic hypothesis is that it is unnecessary to maintain in astronauts, who before flight have above-average

TABLE 4. *Exercise prescriptions for intermediate-duration exposures (15–180 days) to microgravity*

	Pilots	Payload Specialists	Mission Specialists (EVA)
Kind	Isotonic (legs) Isokinetic (legs)	Isotonic (legs) Isokinetic (arms and legs)	Isotonic (legs) Isokinetic (arms)
Device	Cycle ergometer Isokinetic ergometer	Cycle ergometer Isokinetic ergometer	Cycle ergometer Isokinetic ergometer
Intensity	Isotonic (70–100%) Isokinetic MVC*	Isotonic (70–100%) Isokinetic MVC	Isotonic (70–100%) Isokinetic MVC
Duration	Isotonic (20–30 min/day) Isokinetic (10 sets/5 reps MVC/day)	Isotonic (30 min/day) Isokinetic (10 sets/5 reps MVC/day)	Isotonic (30 min/day) Isokinetic (10 sets/5 reps MVC/day)

* MVC, maximal voluntary contraction.

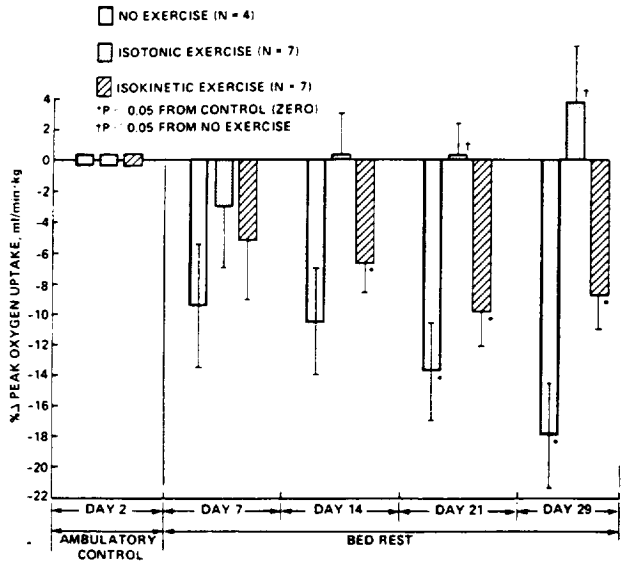

FIG. 5. Mean percent change in peak oxygen uptake during 30 days of −6° head-down bed rest with isotonic (cycle) and isokinetic exercise training. [From Greenleaf et al. (29).]

levels of physical fitness, all physiological systems at the eugravitational level during prolonged exposure to microgravity, especially the physical working capacity. This hypothesis assumes that the astronauts would be relatively well trained when they reached microgravity. The next generation of operational EVA suits is constructed to alleviate most if not all internal resistance to limb movement, particularly in the arms, forearms, and hands, but there may be occasions when great maximal isometric muscular strength is needed. Moderate levels of strength and muscular endurance will be necessary for EVA, and the thermal removal rates of the life support system will limit individual EVA to <8 h. Astronauts with high peak $\dot{V}O_2$ can work at greater loads, and intense exercise training in microgravity may result in excess exercise hyperthermia; the combined result could be greater heat produced for removal by the life support system and reduced EVA time. Thus, very high levels of physical fitness will probably not be necessary for microgravitational work in and about the Space Station and may, in some situations, be a liability.

On the other hand, to be prepared for emergency situations requiring high-intensity and/or long-duration exercise, a prudent and reasonable policy would be for astronauts to maintain a high level of physical fitness, and work rate should be monitored to minimize possible reduced working time during EVA. Also, the emergency egress procedures from the Space Shuttle during or after landing on Earth would require high levels of strength and possibly endurance if injured crewmembers need assistance from healthy crewmembers. There is no reason to maintain excessively high fitness levels in all astronauts during prolonged periods on the Space Station if their work situations do not require it. Perhaps fitness levels can be increased by a more intensive training program a few weeks before returning to Earth in anticipation of landing exigencies.

Prescriptions

Ground based. It is probably inappropriate to recommend specific exercise-training regimens for astronauts to use on the ground to attain and maintain an appropriate level of physical fitness; Frey (22) has presented some potential problems, e.g., reduced orthostatic tolerance of some endurance-trained athletes. A recommended maximal or peak level of $\dot{V}O_2$ would be 50 ml·min^{-1}·kg body wt^{-1} to be maintained by whatever exercise protocols would be acceptable to each crewmember (e.g., cycling, running, swimming). Recommended mean strength peak torque levels for shoulder abduction/adduction and knee flexion/extension would be 60 and 150 N-m, respectively. Both could be maintained by self-selected exercise regimens. Exercise-training adherence is difficult enough even when a variety of exercise and sport regimens is employed. A rigid prescription of specified exercise would probably be counterproductive, but a minimal level of strength and endurance to be maintained by all astronauts would not be an unreasonable requirement.

In flight. Unfortunately, crewmembers in flight will not have access to the variety of exercise equipment and regimens that are available on Earth. Since productive working time in microgravity is at a premium, it is paramount to design efficient exercise prescriptions. One proposed prescription is presented in Table 4. This is an amalgamation of protocols from the authors and the other committee members listed in the acknowledgments. It was designed partly from results of the 1986 30-day bed-rest study conducted at Ames Research Center and partly from the committee members' own experience. The purpose of this prescription was to maintain only ground-based aerobic capacity (peak $\dot{V}O_2$), strength,

and endurance during flight. Our prescription is based on use of the cycle (isotonic) and isokinetic modes of exercise, because muscle soreness and fiber damage may occur more readily with eccentric muscular contractions from forced lengthening that occurs with running (15, 24). After prolonged running, muscle glycogen restoration may take >7 days with excess carbohydrate feeding; glycogen resynthesis is proportional to dietary carbohydrate content after prolonged cycling when the chance for muscle damage from concentric contractions is slight (16). The total time for performing this exercise protocol is ~40 min/day. Note (Table 4) that all crewmembers would perform isokinetic leg exercise; payload specialist both arm and leg isokinetic work; and mission specialists, who undertake EVA, mainly arm isokinetic exercise. If EVA is performed frequently, additional exercise training for these crewmembers may not be necessary. Pilots may need to perform isotonic leg exercise for only 20 min/day. Obviously any in-flight exercise-training protocol would be modified to fit the situation. For example, if pilots need to perform EVA, their training protocol would be modified accordingly.

If exercise time becomes critical, an alternative protocol would require <30 min/day. If it could be established that preflight aerobic capacity could be allowed to decrease by ~10% during flight, then performance of only isokinetic leg training [10 sets of 5 maximal voluntary contractions of the thigh muscles (flexion and extension at each knee at a velocity of 100°/s)] once each day for 6 days/wk would probably maintain aerobic capacity, strength, and endurance within 10% of their respective preflight levels (Fig. 5). This is an argument for increasing and maintaining strength and aerobic capacity by 10–15% before flight, so a 10% reduction during flight could be tolerated without significant adverse effects. Dudley and Djamil (20) have concluded that concurrent isokinetic strength and endurance training does not influence the increase in aerobic power resulting from isotonic endurance training alone. A recommended prescription, exercise or otherwise, for total or partial prevention of in-flight calcium (bone) loss cannot be proposed until further research has determined the site and magnitude of bone losses during eugravity and microgravity deconditioning.

We recognize that such proposed in-flight exercise-training regimens can become boring, and they should be supplemented with varied recreational exercise whenever possible (44). Appropriate preflight indoctrination regarding the purposes, benefits, and varieties of exercise would be helpful in this regard.

We thank Victor A. Convertino, Reggie V. Edgerton, William T. Stauber, and Charles M. Tipton, who kindly contributed material for the formulation of the exercise prescriptions, and Robert Whalen and G. Donald Whedon for constructive comments on the manuscript.

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Orthostatic Responses Following 30-Day Bed Rest Deconditioning With Isotonic and Isokinetic Exercise Training

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GREENLEAF JE, WADE CE, LEFTHERIOTIS G. *Orthostatic responses following 30-day bed rest deconditioning with isotonic and isokinetic exercise training.* Aviat. Space Environ. Med. 1989; 60:537–42.

To determine if intensive isotonic or isokinetic exercise training during 30 d of −6° head-down bed rest (BR) would accentuate orthostatic intolerance, 19 men (32–42 years) were divided into a no-exercise control group (N = 5), and isotonic (Quinton ergometer, N = 7) and isokinetic (Lido ergometer, N = 7) exercise groups. Training was two 30-min periods per day for 5 days per week. Changes (* = $p < 0.05$) in peak $\dot{V}O_2$ uptake (L/min) from control day 2 to BR day 29 were: isotonic +1.4%, isokinetic −10.2%*, no exercise −20.1%*. Changes in resting plasma volume (ml) from control day 1 to BR day 30 were: isotonic −3.7%, isokinetic −18.0%*, and no exercise −17.2%*. A 60° head-up tilt test was administered on control day 1 and BR day 30; the test was terminated at 60 min or when presyncopal signs and/or symptoms occurred. Changes in $\bar{X}$ tilt tolerance were: isotonic, 42 to 34 min (Δ = −8 min*); isokinetic, 53 to 30 min (Δ = −23 min*); and no exercise, 46 to 30 min (Δ = −16 min*). Mean day 30 group tolerances were all significantly lower than day 1 tolerances, but the reductions were not different between groups. Because there was no obvious relationship between type of exercise, exercise energy expenditure, change in peak $\dot{V}O_2$, or change in resting plasma volume and the consistent reduction in post-BR tilt tolerances, it appears that the orthostatic intolerance was due mainly to the reduction in body hydrostatic pressure from the −6° head-down body position, and was not related to the level of physical fitness. Thus, factors other than training status are probably involved.

ORTHOSTATIC INTOLERANCE (a tendency to faint) is a common response of essentially all astronauts when they attempt to stand immediately after landing in the Space Shuttle. The countermeasures used most widely by astronauts have been physical exercise training, pre-reentry fluid loading, and G-suit inflation. However, the effect of physical training and the level of peak oxygen uptake on orthostasis has remained controversial, mainly because of the faulty logic and inappropriate experimental designs of previous research studies. Conclusions that exercise training causes lower tolerances come mainly from four cross-sectional studies where responses were compared in trained and untrained subjects (1). Results from four other studies (2,4,6,12), in which orthostatic tolerance was actually measured before and after a period of exercise training, indicated a significant increase in tilt tolerance in 4 men after 12 d of training (4), and no change in tolerance in 13 men and6 women after 8–12 d of training (2,4,12). In the fourth study, in spite of an increase in peak $\dot{V}O_2$ of 18–22%, there was no significant change in tilt tolerance in 5 previously untrained men after 6 months of intense, general physical training (6). Thus, factors other than training status are probably involved.

To address the practical problem of the effects of exercise training on tilt tolerance following deconditioning of astronauts, we studied orthostatic responses of 19 men who underwent two intensive exercise-training regimens during 30 d of bedrest. We found no significant change in tilt tolerance with exercise training.

PROCEDURES AND METHODS

Informed consent was obtained from 19 men (Table I) selected to match the average age (37 years) and approximate peak $\dot{V}O_2$ (44 ml • min^{-1} • kg^{-1}) of the active astronaut corps. They passed a thorough medical examination which included a medical history, physical examination, and comprehensive biochemical and physiologic tests.

The subjects were housed in the Human Research Facility at Ames Research Center for 42 d: 7 d of ambulatory control, followed by 30 d of −6° head-down bed rest, and then 4.5 d of ambulatory recovery. They were divided selectively into three groups: a no-

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This manuscript was received for review in January 1988. The revised manuscript was accepted for publication in January 1989.

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TABLE I. BASELINE AND BED REST DATA FOR THE THREE GROUPS.

	Baseline					Bed Rest			
							Body Weight		
	Age (years)	Ht (cm)	Wt (kg)	S.A. (m^2)	Fat (%)	Caloric intake (kcal/d)	Day 1 (kg)	Day 30 (kg)	Δ (kg)
					No exercise				
$\bar{X}$	36	177	74.6	1.91	15.5	2678	75.82	74.82	−1.01
±S.E.	2	2	5.3	0.06	2.4	75	4.79	4.14	0.81
					Isotonic exercise				
$\bar{X}$	36	178	80.2	1.98	19.9	2833	79.60	78.74	−0.85
±S.E.	1	3	1.5	0.04	2.2	82	1.71	1.69	0.59
					Isokinetic exercise				
$\bar{X}$	36	177	74.3	1.91	11.0	2890	73.41	73.41	0.00
±S.E.	2	3	2.4	0.05	2.0	75	2.43	2.59	0.52

exercise training control (N = 5) group, an isotonic exercise training (N = 7) group, and an isokinetic exercise training (N = 7) group (Table I). Twelve subjects (Group 1: 4 no exercise, 4 isotonic, 4 isokinetic) were tested from July 1–Aug. 11, 1986, and 7 subjects (Group 2: 1 no exercise, 3 isotonic, 3 isokinetic) were tested from Aug. 19–Sept. 29, 1986.

Diet and clinical procedures: There were 17 different daily menus composed of fresh and frozen foods that were rotated over the 42 d. The prescribed daily caloric intake was 2,800 kcal for the no-exercise group and 3,100 kcal for the two exercise groups. Because of the difficulty in planning meals to allow for exercise periods, lack of appetite due to gastrointestinal disturbances, aversion to some foods, etc., all prescribed food was not eaten. The actual measured intakes were 2,678 ± 75 to 2,890 ± 75 kcal/d (Table I). Percentages by weight of protein, carbohydrate, and fat were 20–21%, 62–63%, and 18%, respectively. Daily electrolyte contents were 5.4–5.6 g Na, 4.8–4.9 g K, 1.3 g Ca, and 1.8–1.9 g P. Water and other fluids were consumed ad libitum. Body weight was measured daily and average group losses during bed rest ranged from 0.00–1.01 kg (Table I). Body fat was calculated from body density measured by underwater weighing.

The subjects were supervised and monitored 24 h/d and room lighting was on between 0700 and 2300 hours daily. All testing, showering, urination, and defecation functions were done in the horizontal or head-down positions. They were allowed to have one pillow, and to rise on one elbow to eat. We have no evidence that any subject assumed a sitting or standing position during bed rest. Only 3 subjects (1 isotonic, 2 isokinetic) were unable to perform all required exercise training due to muscle strains and gastrointestinal distress; they lost only seven 30-min sessions. Findings from the performance-mood tests suggested some fatigue and perhaps mild "overtraining" in the isotonic group.

Exercise testing and training: Pre-bed rest peak $\dot{V}O_2$ uptake was measured by using standard procedures (3) on calibrated Quinton cycle ergometers (model 845) with the subjects in the horizontal position. The continuous exercise test utilized progressively increasing loads (200 kg-m/min) at 60 rpm until a pedaling frequency of 50 rpm could not be maintained. The peak $\dot{V}O_2$ was the mean of the final four 15-s values.

Peak $\dot{V}O_2$ measured during bed rest utilized a work intensity of 40% followed by a load about 400 kg-m/min below peak load for 2 min, then with loads increasing by 200 kg-m/min each 2 min until the subject could not maintain 50 rpm. All three groups were tested weekly during bedrest for peak $\dot{V}O_2$ on the cycle ergometer. All subjects had 5–6 peak $\dot{V}O_2$ tests prior to the ambulatory control period, so they were well-acquainted and comfortable with the testing procedures.

Daily isotonic leg exercise training during bed rest was performed in the supine position for 30-min periods in the morning and afternoon 5 d/week. Subjects warmed up for 7 min at a load equivalent to 40% of peak $\dot{V}O_2$, which was followed by 2 min of exercise at 60, 70, 80, 90, and 80% with each level separated by 2 min at the 40% load. Once the absolute exercise training loads were established in the ambulatory control period, they were used throughout the study.

Daily isokinetic leg exercise training during bed rest was also performed in the supine position for 30-min periods in the morning and afternoon 5 d/week on a Lido Isokinetic Rehabilitation ergometer. Following a 5-min warm-up period, the subjects performed 5 peak knee flexions and extensions (90° arc) in 10 s at a speed of 100°/s and rested for the remaining 50 s. This routine was repeated 10 times and, after a 4-min cooling-down period, it was repeated with the other leg.

Tilt-table tests and plasma volume: Orthostatic testing was performed on ambulatory control day 1 and bedrest day 30 on a motorized Laberne Physical Therapy Treatment table. The protocol consisted of 45 min in the supine position pre-bedrest (control), and in the −6° head-down supine position post-bedrest; the subjects were tilted to 60° within 10–15 s, remaining in that position for 60 min or until the onset of presyncopal signs and symptoms (e.g., nausea, dizziness, sweating, lightheadedness, and tunnel vision), and had at least a 10-min recovery period in the −6° head-down position.

An antecubital vein was catheterized with a 3-cm nylon needle (Quick-Cath, Travenol Lab) 45 min before tilt. The catheter was flushed with Na-heparin and the arm was supported comfortably in a neutral, horizontal position during the 45-min pre-tilt period and for 5 min following tilt. Plasma volume was measured between −15 and −5 min of the control period with the standard Evans blue dye-dilution technique from one 10-min

post-injection blood sample (5). The catheter was cleared by withdrawing 3 ml of blood; then 28 ml of blood were withdrawn—8 ml for the Evans-blue control and 20 ml for other analyses. A weighed syringe contained approximately 5 ml of dye; the dye was injected, and the line was flushed with 5 ml of isotonic saline and 2 ml of Na-heparin. The empty dye syringe was weighed again and the weight of dye injected calculated. Then the subjects were tilted. They stood on a pillow placed on a 7-cm foam cushion which was placed on the footboard. A 15-cm wide canvas belt was secured firmly across the superior iliac crest. About 65% of the subject's weight (measured with a scale) was supported on the footboard. The subject was instructed to remain relaxed during tilting with no conversation except to answer occasional queries regarding his status. Heart rate (Hewlett-Packard cardiotachometer) and manual sphygmomanometric blood pressures were taken periodically during the control and tilting periods. After the 5-min blood sample (20 ml) during tilt, the arm support was removed and the arm was lowered to the normal, relaxed position. The catheter was removed in the recovery period. Total blood volume withdrawn was 65 ml and about 50 ml of saline and Na-heparin were injected. Quadruplicate microhematocrits were spun at 11,500 rpm for 10 min and read on a modified International microcapillary reader (model CR). Raw Hct values were corrected for trapped plasma and whole-body Hct by multiplication with the factors 0.96 and 0.91, respectively. Blood volume (BV) was BV = PV{100/[100 − (Hct × 0.96 × 0.91)]} and red cell volume (RCV) was BV-PV.

The data were analyzed with linear regression, analysis of variance, and the *t* test. The null hypothesis was rejected when $p < 0.05$. Nonsignificant differences were indicated by NS. Variability was expressed as ±S.E.

RESULTS

Tilt tolerance: There was wide variability pre-bed rest control (day 1) and post-bed rest (day 30) tilt tolerances (Table II). Thirteen subjects reached the arbitrary 60-min tolerance during the control test, but only 7 subjects reached 60 min after bed rest. Further, those 7 subjects (2 no exercise, 3 isotonic, 2 isokinetic) tolerated 60 min in both the control and post-bed rest tests (Table II). Mean (±S.E.) tilt-tolerances for all three groups analyzed collectively (N = 19) were 47 ± 5 min in control and were reduced to 32 ± 5 min ($p < 0.05$) after bed rest on day 30 (Fig. 1, Table II). There were no significant differences between the groups' ambulatory tolerances (46, 42, and 53 min) or between their tolerances after bed rest (30, 34, and 30 min).

Heart rate and blood pressure: Mean (±S.E.) heart

TABLE II. INDIVIDUAL TILT TOLERANCES AND HEART RATE AND BLOOD PRESSURE DATA AT REST AND AT TOLERANCE ON CONTROL (DAY 1) AND BED REST (DAY 30).

	Tilt Tolerance			Heart Rate, Day 1			Heart Rate, Day 30			Blood Pressure, Day 1			Blood Pressure, Day 30		
Subject	Day 1 (min)	Day 30 (min)	Δ (min)	Contr (b/min)	Tol (b/min)	Δ (b/min)	Contr (b/min)	Tol (b/min)	Δ (b/min)	Contr (mmHg)	Tol (mm Hg)	Δ (mm Hg)	Contr (mm Hg)	Tol (mm Hg)	Δ (mm Hg)
							No exercise (N-5)								
ALF	26	8	18	64	95	31	82	127	45	127/89	120/92	−7/3	120/100	130/110	10/10
BEL	60	7	53	59	64	5	83	116	33	123/77	124/98	1/21	127/84	150/110	23/26
MUM	60	60	0	65	88	23	80	132	52	110/70	110/78	0/8	113/70	130/100	17/30
SCH	25	16	9	59	60	1	59	75	16	135/88	128/80	−7/−8	121/81	120/98	−1/17
STE	60	60	0	60	80	20	62	120	58	117/81	130/100	13/19	123/84	118/100	−5/16
$\bar{X}$	46	30	16	61	77	16	73	114	41	122/81	122/90	0/9	121/84	130/104	9/20
±S.E.	8	12	10	1	7	6	5	10	8	4/4	4/5	4/5	2/5	6/3	5/4
							Isotonic exercise (N = 7)								
MIN	1	3	2	66	66	0	74	110	36	128/79	128/80	0/1	132/86	140/110	8/24
MON	60	60	0	59	90	31	67	156	89	135/94	130/102	−5/9	130/87	110/100	−20/13
RAN	60	12	−48	58	81	23	59	89	30	119/77	110/92	−9/15	110/75	110/94	0/19
SCO	60	60	0	67	83	16	80	119	39	121/79	114/84	−7/5	121/79	120/100	−1/21
AYA	39	37	−2	60	78	18	65	86	21	129/98	128/102	−1/4	125/90	120/100	−5/10
GRE	11	9	−2	52	70	18	50	120	70	120/79	132/96	12/17	119/77	130/98	11/21
RAW	60	60	0	65	80	17	70	102	32	121/79	120/88	−1/9	129/79	124/100	−5/21
$\bar{X}$	42	34	−7	61	75	18	66	112	45	125/84	123/92	−2/8	124/82	122/100	−2/18
±S.E.	10	10	7	2	4	4	4	9	9	2/3	3/3	3/2	3/2	4/2	4/2
							Isokinetic exercise (N = 7)								
DOR	60	29	−31	40	60	20	59	136	77	131/73	128/80	−3/7	134/79	110/90	−24/11
KAM	60	60	0	56	77	21	63	130	67	121/87	120/102	−1/15	120/78	120/106	0/28
NEL	60	8	−52	52	82	30	61	58	−3	123/73	120/96	−3/23	123/78	120/90	−3/12
NOR	60	30	−30	62	88	26	68	112	44	123/80	116/88	−7/8	121/73	90/60	−31/−13
GOL	60	19	−41	59	64	5	60	100	40	130/82	110/90	−20/8	123/79	120/90	−3/11
MCC	11	4	−7	56	75	19	59	80	21	127/97	118/98	−9/1	123/94	134/98	11/4
STO	60	60	0	47	58	11	52	125	73	108/70	120/90	12/20	110/74	98/90	−12/16
$\bar{X}$	53	30	−23	53	72	19	60	106	46	123/80	119/92	−4/12	122/79	113/89	−9/10
±S.E.	7	9	8	3	4	3	2	11	11	3/4	2/3	4/3	3/3	6/5	6/5
							All groups (N = 19)								
$\bar{X}$	47	32	−15	58	74	18	66	110	44	124/82	121/91	−2/10	122/81	121/97	−2/16
±S.E.	5	5	5	2	3	2	2	6	5	2/2	2/2	2/2	2/2	3/3	3/2

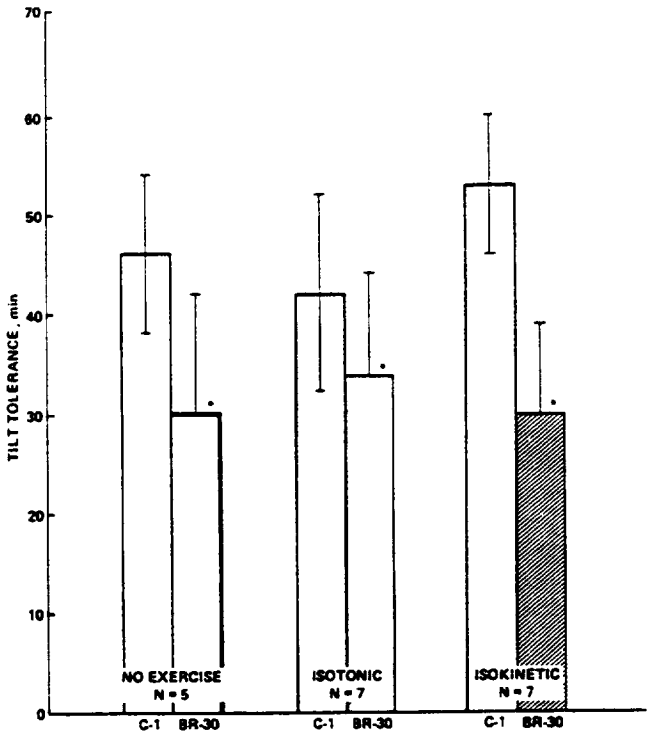

Fig. 1. Mean (±S.E.) tilt tolerances before (C-1) and at the end of bed rest (BR-30) in the three groups. *p < 0.05 from C-1.

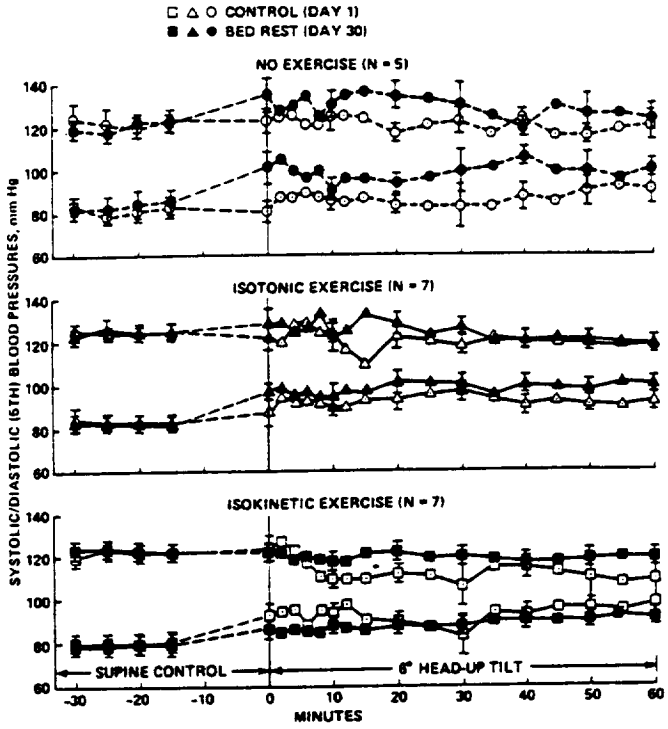

Fig. 3. Mean (±S.E.) systolic and diastolic blood pressures during the supine control and 60° head-up tilt periods before (C-1) and at the end of the bed rest (BR-30) in the three groups.

rates and blood pressures during the supine control and tilt periods are presented in Fig. 2 and 3, respectively. Because individual tolerances were different, the number of subjects included in each mean value decreased progressively as time of tilt lengthened. Mean heart rates in the supine control period ($\bar{X}$ of −25, −20, −15 min) for N = 19 were 58 ± 2 beats/min on day 1 and they increased to 66 ± 2 beats/min ($p < 0.05$) on bed rest day 30 (Fig. 2, Table II). Mean heart rates for all three groups in the first minute of tilt at day 30 were all higher ($p < 0.05$) than their respective rates on day 1 (Fig. 2). These elevated heart rates continued throughout the tilt period. Mean increases in heart rate (N = 19) from rest to tolerance on day 1 were 58 to 74 beats/min ($p < 0.05$), and 66 to 110 beats/min ($p < 0.05$) on day 30 (Table II). The two exercise-training regimens had no significant effect on the resting-to-tolerance heart rates: the mean changes on day 1 were 16, 18, and 19 beats/min, and those on day 30 were 41, 45, and 46 beats/min, respectively (Table II).

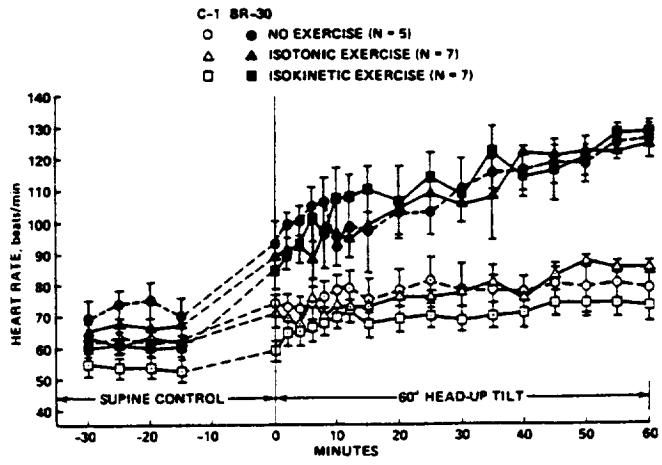

Fig. 2. Mean (±S.E.) heart rates during the supine control and 60° head-up tilt periods before (C-1) and at the end of bed rest (BR-30) in the three groups.

In general, systolic blood pressures were relatively constant during the supine control period and during tilting before (day 1) and after (day 30) bed rest (Fig. 2, Table II). Mean changes (N = 19) from supine control to tolerance on day 1 were 124 ± 2 to 121 ± 2 mm Hg (NS), respectively, and 122 ± 2 to 121 ± 3 mm Hg (NS) on day 30, respectively (Table II). On the other hand, the diastolic pressure rose significantly at tolerance. Mean (±S.E.) changes (N = 19) from supine control to tolerance on day 1 were 82 ± 2 to 91 ± 2 mm Hg ($p < 0.05$), and 81 ± 2 to 97 ± 3 mm Hg ($p < 0.05$) on day 30 (Table II).

Fluid volumes: Resting plasma volume (PV) decreased during bed rest in the isokinetic and no-exercise groups, but was unchanged in the isotonic group. In the isokinetic group, plasma volume decreased from 3665 ± 167 ml on ambulatory control day 1 to 3120 ± 55 ml (−14.2%, $p < 0.05$) and to 2988 ± 109 ml (−18.0%, $p < 0.05$) on bed rest days 8 and 30, respectively (Fig. 4). Similarly, in the no-exercise group, plasma volume decreased from 3401 ± 198 on day 1 to 3017 ± 140 ml (−11.0%, $p < 0.05$) and to 2810 ± 165 ml (−17.2%, $p < 0.05$) on bed rest days 8 and 30, respectively. Corresponding unchanged PVs in the isotonic group were 3255 ± 190 ml (day 1), and 3116 ± 142 ml (−3.8%, NS) and 3111 ± 123 ml (−3.7%, NS) on bed rest days 8 and 30, respectively (Fig. 4).

Red cell and total blood volumes followed plasma

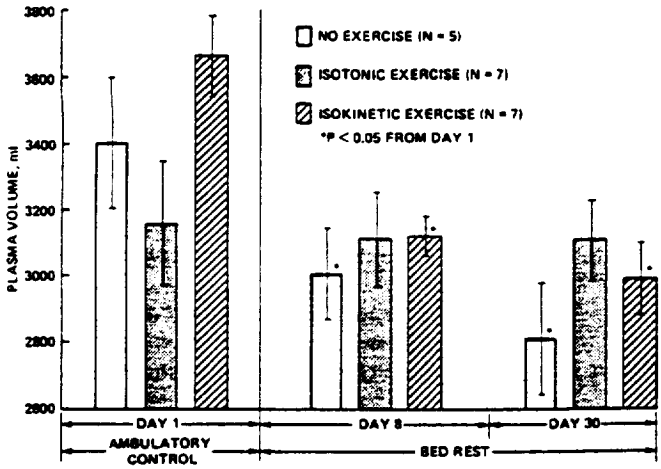

Fig. 4. Mean (±S.E.) plasma volumes before (C-1), during (BR-8), and at the end of bed rest (BR-30) in the three groups. *p < 0.05 from Day 1 (C-1).

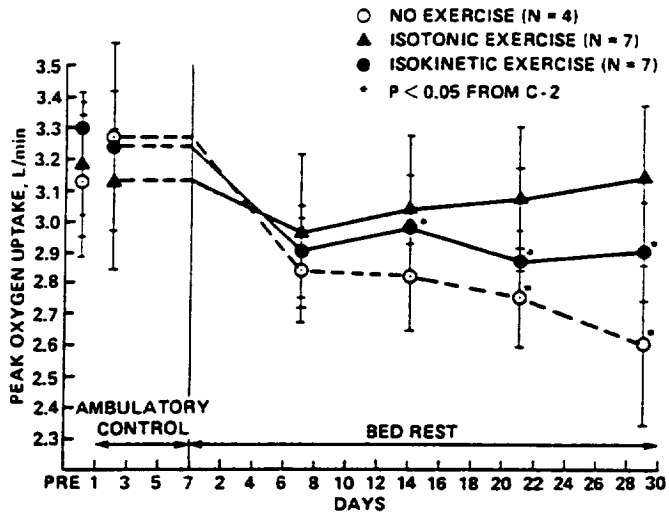

Fig. 5. Mean (±S.E.) peak oxygen uptakes during the precontrol and control (C-2) periods, and weekly during bed rest in the three groups. *p < 0.05 from C-2.

volumes; there were no significant changes in the isotonic group but significant decreases in the isokinetic and no-exercise groups during bed rest (Table III).

Aerobic power: Peak oxygen uptake was maintained at ambulatory control levels during bed rest in the isotonic exercise training group (Fig. 5): it was 3.13 ± 0.29 L/min (38.9 ml • min^{-1} • kg^{-1}) on control day 2 and 3.14 ± 0.23 L/min (40.0 ml • min^{-1} • kg^{-1}) on bed rest day 29 (Δ = +1.4%, NS). The magnitude of the decreases in peak $\dot{V}O_2$ in the isokinetic and no-exercise groups in the same time period was: 3.24 ± 0.17 (44.1 ml • min^{-1} • kg^{-1}) to 2.90 ± 0.16 L/min (40.0 ml • min^{-1} • kg^{-1}) (Δ = −10.2%, $p < 0.05$) and 3.27 ± 0.31 (43.6 ml • min^{-1} • kg^{-1}) to 2.60 ± 0.26 L/min (35.7 ml • min^{-1} • kg^{-1}) (Δ = −20.1%, $p < 0.05$), respectively. The average energy expenditures for each 30-min isokinetic and isotonic exercise regimen were 8.9 ± 0.5 and 18.8 ± 1.6 ml • min^{-1} • kg^{-1}, respectively.

Intercorrelations: Correlation coefficients were calculated with peak $\dot{V}O_2$, tilt-tolerance, and resting plasma volume data before and at the end of bed rest. There was a significant ($p < 0.001$) correlation of 0.85 between peak $\dot{V}O_2$ on ambulatory control day 2 and on bed rest day 29. There was a lower but significant ($p < 0.02$) correlation of 0.54 between tolerance time on control day 1 and bed rest day 30. However, there were no significant correlations between peak $\dot{V}O_2$, tolerance time, and plasma volume for the separate groups or for the combined group (N = 19), suggesting that these three factors are largely independent.

DISCUSSION

The results show clearly that the range in peak oxygen uptake of +1.4% to −20.1% in the three groups during 30 d of −6° head-down bed rest deconditioning had no significant effect on the magnitude of the usual decrease in 60° head-up tilt tolerance following prolonged bed rest. Further, resting plasma volume was unchanged in the isotonic group while it decreased significantly in the other two groups, which suggests that the magnitude of resting hypovolemia is not a major factor determining orthostatic intolerance following prolonged bed rest.

Another factor that might have explained our results is energy expenditure. It must not be assumed, because the no-exercise control group had no formal, daily ex-

TABLE III. MEAN (±S.E.) CALCULATED RED-CELL AND TOTAL BLOOD VOLUMES DURING THE AMBULATORY CONTROL (C-1) AND BED REST (BR-8, BR-30) PERIODS.

	Red Cell Volume						Total Blood Volume					
	Day 1		Day 8		Day 30		Day 1		Day 8		Day 30	
	(ml)	(ml/kg)	(ml)	(ml/kg)	(ml)	(ml/kg)	(ml)	(ml/kg)	(ml)	(ml/kg)	(ml)	(ml/kg)
						No exercise						
$\bar{X}$	2031	27	1941	26	1764*	24*	5433	71	4958	66	4573*	62*
±S.E.	107	1	102	2	73	1	287	4	216	3	213	4
						Isotonic exercise						
$\bar{X}$	2064	26	1959	25	1892	24	5319	66	5075	64	5003	64
±S.E.	174	2	136	2	109	2	362	4	274	4	229	3
						Isokinetic exercise						
$\bar{X}$	2144	29	1961*	27*	1740*	24*	5809	79	5081*	70*	4729*	65*
±S.E.	78	2	81	2	69	1	193	3	106	3	146	2

* $p < 0.05$ from comparable Day 1 value.

ercise training, that they had low energy expenditure. Their mean (±S.E.) daily caloric intake was 2,678 ± 75 kcal/d, and during bed rest they lost 1.01 ± 0.81 kg with no change in body fat content (3). Thus, their daily caloric utilization was essentially that of a moderately sedentary ambulatory man. The two exercise groups worked to the point where any further increase in intensity and/or duration would have probably caused serious injury; only seven 30-min exercise training bouts in 3 subjects (1 isotonic, 2 isokinetic) were lost due to muscle strain (3). Thus, the near-maximal isotonic and isokinetic training regimens with their attendant increases in energy utilization did not influence or ameliorate the orthostatic responses; i.e., heart rates, blood pressures, or truncated tolerances. This means that factors associated with or caused by exercise training intensity have essentially no influence on the decrease in tilt tolerance.

The remaining major stressor is reduction of hydrostatic pressure within the body and the cardiovascular system in particular. Insufficient data were collected to investigate this hypothesis. But Sheldahl *et al.* (11) have found that the headward shift of blood into the thorax during training in water immersion does not alter the normal adaptive responses (mainly cardiovascular) to aerobic exercise training in normal ambulatory subjects.

Direct evidence is accumulating which supports the conclusion that exercise training per se does not cause a reduction in tilt tolerance. Harrison (9) has reviewed the literature thoroughly and concluded that ". . . the presently available information is both qualitatively and quantitatively inadequate to permit any definite statement regarding a possible relationship between aerobic power ($\dot{V}O_{2max}$) and orthostatic tolerance." The supposition that the level of physical fitness, a complex physiological adaptation, can be measured adequately by only one variable—the maximal oxygen uptake—is part of the problem. After a thorough review of the literature, Convertino (1) also concluded there is no association between aerobic fitness and orthostatic tolerance. Results from a recent 4-month training study of 85 men also indicated no relationship between estimated aerobic capacity and heart rate and blood pressure changes during head-up tilt after training (10).

Findings from the four previous studies, where tilt tolerances were measured directly before and after exercise training periods, indicated either an increase in tolerance (4) or no change in tolerance (2,4,6,12). Results from the present study add a new dimension to the finding that training does not affect tilt tolerance in that the training was undertaken by bed rested subjects.

No valid conclusions can or should be drawn at this time from results of cross-sectional studies involving a comparison of the levels of intolerance between various groups of trained and untrained subjects. Merely because a particular group of endurance-trained men exhibit significantly lower tilt-tolerance than a comparable group of untrained men does not mean that the lower tolerance was due to the exercise training per se unless all other pertinent factors had been controlled. That the blood pressure control system is altered in the direction of greater lability and lower resting pressures following some exercise training programs seems well-documented (7). There is sufficient evidence to conclude that some high-endurance subjects have more labile blood pressure control systems; however, many more subjects must be tested before firm conclusions can be drawn. To extrapolate from these findings to the conclusion that their lower tilt-tolerances were caused or resulted from their exercise training is unwarranted. It would be prudent to thoroughly test astronaut candidates who have been highly endurance-trained to determine if they exhibit unusual orthostatic intolerance.

ACKNOWLEDGMENT

The authors express their appreciation to the subjects and to the 125 supporting personnel who had a significant role in this bed rest study; we also thank Jeff Ball, Andrea Ertl, Sally Greenawalt, Teresa Hutchinson, Linda Kirby, Joann Meredith, Margorie Hunt, and Atticus Tysen who collected, tabulated, and analyzed the tilt data.

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Balance and Gait

M. M. Cohen

The ability of astronauts to locomote upon landing after orbital missions is frequently compromised by impairment of postural equilibrium, balance, and gait. It has been assumed that these deficits result from reinterpretation of otolith organ inputs during exposure to microgravity, although there are several other possibilities. For example, the deficits could be due to weakened leg muscles resulting from muscle atrophy, to reduced blood flow to the brain from deconditioning, or to altered neuromuscular control resulting from lack of motor activity of the postural muscles. Some of these hypotheses have been studied in bed-rested subjects where the vestibular system remains functional, although potential effects of muscle atrophy, altered brain blood flow, and degraded neuromuscular control may occur.

Results of these two types of exercise training regimens utilizing independent measures of aerobic work capacity, via changes in peak oxygen uptake (indicators of cardiovascular and metabolic changes), and changes in muscle strength and size (partial indicators of muscle atrophy), were used in evaluate their efficacy in preventing the atrophic and other deconditioning effects of bed rest.

The purpose of this study was (a) to examine the influence of the two types of exercise in preventing or ameliorating changes in posture, equilibrium, and gait (PEG) after bed rest deconditioning, and (b) to test the hypothesis that factors other than reinterpretation of inputs to the otolith organs influence post-bed rest changes in PEG, since these inputs are probably not altered during bed rest as they may be during exposure to microgravity.

Methods

These PEG tests were conducted on ambulatory control days −7 and −2 and recovery days 1 and 4. The tilt-table test was performed on the last day of bed rest (BR 30), one day prior to PEG testing on the first and fourth day of recovery. Upon arising on R + 1, the subjects were allowed to assume the upright position over a 2-hr period before the PEG tests were conducted. In four separate 20-min sessions, each subject was tested for his ability to maintain posture and equilibrium, and to walk a specified course.

Posture and equilibrium tests– Each subject was required to stand with his arms folded over his chest on a force platform (stabilometer) to measure body sway. An ABCDE/EDCBA design was used. Conditions were as follows:

	A	B	C	D	E
Eyes	open	closed	open	closed	open
Target	fixed	fixed	fixed	fixed	moved
Platform	fixed	fixed	moved	moved	fixed

Gait test– Immediately following the initial tests on the stabilometer, each subject was required to walk a standardized course to measure locomotive ability and gait. Eletromyogram (EMG) signals from the anterior tibialis and gastrocnemius-soleus muscles, and signals from foot switches indicated contact with the ground, swing/stance phases of the gait, and timing for each step. Ink pads placed on the soles recorded the path of motion including step width, step length, stride length, cadence, and walking velocity (fig. 1).

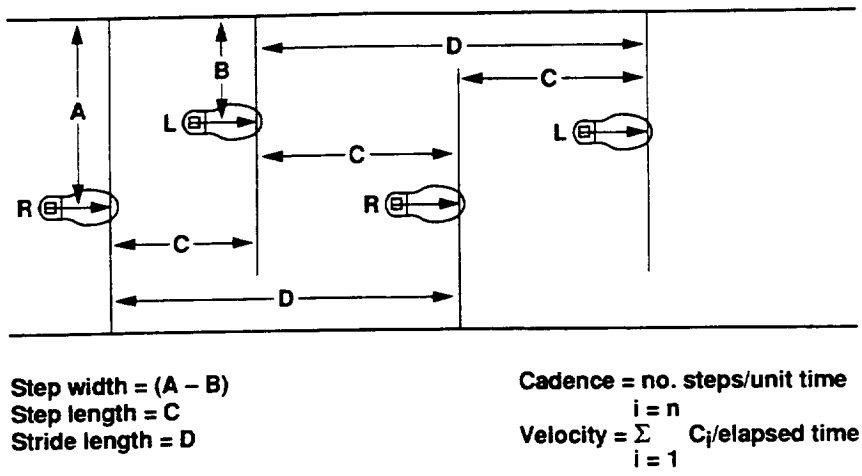

Figure 1. Schematic of gait measurements.

Results and Discussion

Posture and equilibrium tests– Amplitude of body sway was analyzed as a function of the exercise training regimens. The dispersion index, representing the standard deviation of 200 samples of the body's center of gravity (a measure of postural instability), increased by 20% ($P < 0.05$) following the 30-d bed rest period, and returned to pre-bed rest values by the fourth day of recovery. The general increase of postural instability during bed rest was not influenced by either exercise training regimen.

Gait test– On the initial walking attempts following bed rest there were significant ($P < 0.05$) decreases in step length, stride length, and walking velocity in all three groups combined (fig. 2). These changes were not influenced by the exercise training regimens. By the fourth day of recovery all pre-bed rest values were restored. No other significant changes were observed.

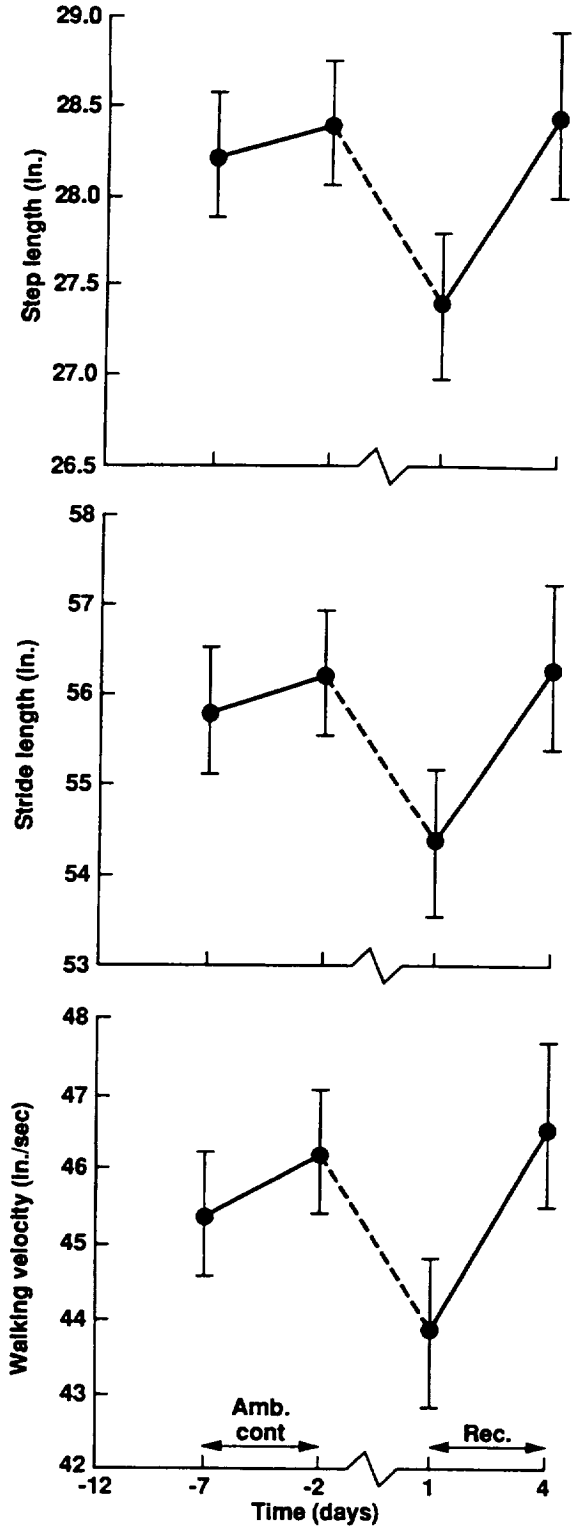

Figure 2. Mean (±SE, N = 19) step length, stride length, and walking velocity during the ambulatory control (days –7 and –2) and recovery (R + 1, R + 4) periods.

Conclusion

Thus, while the bed rest deconditioning resulted in deterioration of body stability and gait parameters, neither intensive isotonic nor isokinetic exercise training during bed rest had a significant influence on posture, equilibrium, or walking gait measurements.

Effect of leg exercise training on vascular volumes during 30 days of 6° head-down bed rest

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GREENLEAF, J. E., J. VERNIKOS, C. E. WADE, AND P. R. BARNES. *Effect of leg exercise training on vascular volumes during 30 days of 6° head-down bed rest.* J. Appl. Physiol. 72(5): 1887–1894, 1992.—Plasma and red cell volumes, body density, and water balance were measured in 19 men (32–42 yr) confined to bed rest (BR). One group ($n = 5$) had no exercise training (NOE), another near-maximal variable-intensity isotonic exercise for 60 min/day (ITE; $n = 7$), and the third near-maximal intermittent isokinetic exercise for 60 min/day (IKE; $n = 7$). Caloric intake was 2,678–2,840 kcal/day; mean body weight ($n = 19$) decreased by 0.58 ± 0.35 (SE) kg during BR due to a negative fluid balance (diuresis) on *day 1*. Mean energy costs for the NOE, and IKE, and ITE regimens were 83 (3.6 ± 0.2 ml $O_2 \cdot min^{-1} \cdot kg^{-1}$), 214 (8.9 ± 0.5 ml $\cdot min^{-1} \cdot kg^{-1}$), and 446 kcal/h (18.8 ± 1.6 ml $\cdot min^{-1} \cdot kg^{-1}$), respectively. Body densities within groups and mean urine volumes (1,752 − 1,846 ml/day) between groups were unchanged during BR. Resting changes in plasma volume (ml/kg) after BR were −1.5 ± 2.3% (NS) in ITE, −14.7 ± 2.8% ($P < 0.05$) in NOE, and −16.8 ± 2.9% ($P < 0.05$) in IKE, and mean water balances during BR were +295, −106, and +169 ml/24 h, respectively. Changes in red cell volume followed changes in plasma volume. The significant chronic decreases in plasma volume in the IKE and NOE groups and its maintenance in the ITE group could not be accounted for by water balance or by responses of the plasma osmotic, protein, vasopressin, or aldosterone concentrations or plasma renin activity. There was close coupling between resting plasma volume and plasma protein and osmotic content. It appears that the ITE training protocol is better than the IKE protocol for maintaining plasma volume during prolonged exposure to BR.

plasma volume; red cell volume; blood volume; body density; water balance

WHEN THE BODY MOVES between horizontal and upright positions, early accompanying responses are fluid shifts from the thorax to the lower extremities and between the vascular and interstitial fluid spaces. The initial transvascular shifts are stimulated mainly by changing hydrostatic pressures within the cardiovascular system. Standing from a horizontal posture causes increased filtration of plasma to the interstitial fluid space, and reclining horizontally after standing induces a reverse flow (23). Fluid shifts and the resulting changes in vascular fluid volume and distribution play important roles in controlling total body fluid volumes during exposure to prolonged bed rest (10, 12, 26), microgravity (11, 12, 21, 24), acceleration (15, 16), and orthostatic stress (7, 16, 20).

Physical exercise training by ambulatory subjects induces a chronic increase in plasma volume (hypervolemia) that appears to be associated with increased activity of the renin-aldosterone system, which promotes increased plasma Na^+ content, and with increases in plasma vasopressin and plasma protein content, which enhance vascular fluid volume (4–6).

Prolonged exposure to bed rest without accompanying intensive physical exercise training results in chronic hypovolemia (14, 26, 27). Moderate continuous isotonic leg exercise (68% of maximal O_2 uptake) for 1 h/day provides some attenuation of the hypovolemia during 14 days of horizontal bed rest; hypovolemia drops from −12.6% with no exercise to −7.8% with isotonic exercise training (16). Smirnova et al. (26) were able to maintain plasma volume at +3.0 ± 9.6% after 120 days of 5° head-down bed rest with an unspecified set of high-speed, rapid-forced, and passive-active extension exercise for gravity muscle groups.

The purposes of the present study were to determine whether near-maximal variable-intensity isotonic and intermittent isokinetic exercise training would maintain plasma volume during 30 days of 6° head-down bed rest and to relate the levels of hypovolemia to body fluid balances. This is the third in a series of reports from this study. The work capacity (13) and orthostatic responses (20) from the interrelationship of these bed rest and exercise countermeasures have been published previously.

METHODS

The subjects were 19 men (aged 32–42 yr) who passed a comprehensive medical examination and, after extensive briefing and discussion, gave their informed written consent to the experimental conditions. All subjects were nonsmokers, and none took nonprescribed medications. They were of average anthropometric composition and working capacity: age, 36 ± 1 yr; height, 178 ± 2 cm; weight, 76.5 ± 1.8 kg; peak O_2 uptake ($\dot{V}O_2$; supine), 3.36 ± 0.12 l/min (44 ± 2 ml$^{-1} \cdot min^{-1} \cdot kg^{-1}$); leg strength, 690 ± 23 N · m (13). No adverse health problems were observed or reported during the study.

Procedure. On the basis of age, peak $\dot{V}O_2$, and strength, the men were divided into three groups: no-exercise training control (NOE; $n = 5$), isotonic (model 846 T, Quinton Imaging/Ergometer Seattle, WA) exercise training (ITE; $n = 7$), and isokinetic (Lido isokinetic ergometer, Loredan Biomedical, Davis, CA) exercise train-

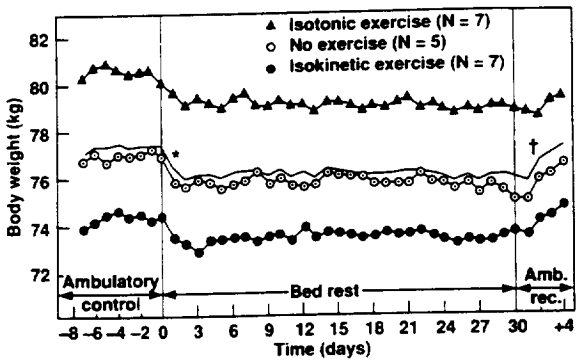

FIG. 1. Daily mean body weights during ambulatory control, bed rest, and ambulatory recovery (Amb rec) periods. Solid line, mean body weight of the 3 groups ($n = 19$). *$P < 0.05$ compared with bed-rest *day 0*; †$P < 0.05$ compared with bed-rest *day 30*.

ing (IKE; $n = 7$). After a 3-mo familiarization period, 12 subjects (4 NOE, 4 ITE, and 4 IKE) entered the Human Research Facility at Ames Research Center for testing in July and August 1986. The other 7 men (1 NOE, 3 ITE, and 3 IKE) were tested in August and September 1986. The protocol was 7 days of ambulatory control with dietary equilibration and collection of control data, 30 days of 6° head-down bed rest, and then 4.5 days of ambulatory recovery (Fig. 1). Sitting ergometer exercise (50% peak $\dot{V}O_2$) was performed for 30 min/day during ambulatory control to retard the semiconfinement deconditioning. The subjects were supervised 24 h/day while in the Human Research Facility, and room lighting was on between 0700 and 2300 h. We have no evidence that any subject stood up during the bed-rest period; all testing, showering, and excretory functions were done in horizontal or head-down positions. The subjects were allowed one pillow and to rise on one elbow to eat.

Diet and anthropometric measurements. The diet was composed of fresh and frozen foods. Seventeen different daily menus were rotated sequentially during each 42-day study. The prescribed daily intake was 2,800 kcal for the NOE group and 3,100 kcal for the ITE and IKE groups. No caloric adjustment was made for body weight. Because of the problem with arranging meals around the exercise periods, dislike of some foods, and occasional gastrointestinal disturbances, all the prescribed food was not consumed (Table 1). Composition of food consumed was calculated from values established by Gebhardt et al. (9). Water and other noncaloric beverages were consumed ad libitum and measured.

Body weight was measured daily (horizontally during bed rest) in the morning after breakfast (Fig. 1). Body fat content was calculated from body density, corrected for residual volume, which was measured before bed rest and on *day 30* of bed rest by underwater weighing (2): body lean mass = 100 − %body fat.

Exercise regimens. Details are presented elsewhere (13, 20). Briefly, the two exercise groups worked for two 30-min periods/day for 6 days/wk, and peak $\dot{V}O_2$ was measured weekly in all three groups with leg exercise on the cycle ergometer. The ITE regimen involved continuous 2-min work bouts at 40% of peak $\dot{V}O_2$ alternating with 2-min work bouts at levels of $\dot{V}O_2$ that increased progressively to 90% of peak $\dot{V}O_2$ (e.g., 2 min at 40%, 2 min at 60%, 2 min at 40%, 2 min at 70%). The IKE regimen employed 5 repetitions/10 s (90–100° range of motion) of maximal knee flexion and extension force at a speed of 100°/s followed by 50 s of rest, for a total time of 15 min. Then the other leg was exercised similarly for 15 min. All exercise training and testing were performed with the subjects in the supine position.

The exercise regimens were designed to maintain peak $\dot{V}O_2$ (ITE) and muscular strength and endurance (IKE) at pre-bed-rest levels after 30 days of bed rest. Although both exercise training regimens were conducted using mainly thigh muscle groups, many trunk, shoulder, arm, and forearm muscles were activated as loads approached peak levels with the ITE regimen, and particularly with IKE regimen, because both flexion and extension movements were of maximal intensity and arms were used for stabilization.

Blood analyses. Plasma total protein concentration was measured with an American Optical refractometer, microhematocrit was measured using heparinized microhematocrit tubes spun for 5 min at 11,500 rpm, and hemoglobin was measured with the cyanomethemoglobin method (Coulter Electronics, Hialeah, FL). Plasma osmolality was measured by freezing-point depression (model 3DII, Advanced Instruments Digimatic Osmometer, Needham Heights, MA). Change in plasma protein and osmotic contents were calculated (28). Plasma vasopressin was measured with a modified radioimmunoassay (25), plasma renin activity with a radioimmunoassay for angiotensin I (New England Nuclear, Boston MA), and plasma aldosterone by radioimmunoassay with a kit (Diagnostic Products, Coat-A-Count, Los Angeles, CA). Plasma volume was measured on *day-7* of the control period and *days 8* and *30* of bed rest with the Evans blue dye dilution technique (3, 17). After the subjects rested for 30 min in the supine position, ~5 ml of the 0.5% aqueous dye solution was injected intravenously (the exact volume was determined by differential syringe weights), and an equilibrium blood sample was withdrawn 10 min later. Blood volume (BV) was calculated from the plasma volume (PV) and hematocrit (Hct), which was corrected for trapped plasma (0.96) and whole body Hct (0.91)

$$BV = PV \times \left[\frac{100}{100 - (Hct \times 10 - 2)(0.96)(0.91)}\right]$$

$$\text{red cell volume (RCV)} = BV - PV$$

$$\text{plasma protein content} = PV \times [\text{plasma protein}](g/dl)$$

$$\text{plasma osmotic content} = PV \times \text{plasma osmolality (mosmol/kg)}$$

Fluid intake and urine volumes. Fluid intake included all liquid intake but not free water in the food. Twenty-four-hour urine volumes were measured daily beginning with the morning excretion.

Statistical analyses. The University of California, Los Angeles BMDP Program P2V was used for *t* tests on dependent (paired) and independent variables and for analysis of variance. Significant time-related differences were identified with the Newman-Keuls, Tukey, and

TABLE 1. *Mean daily dietary composition*

Energy, kcal	CHO, g	PRO, g	FAT, g	H_2O, ml	Na, g	K, g	Ca, g	P, g
				No exercise (n = 5)				
2,678±75	339±11 (62)	113±2 (21)	97±3 (18)	2,080±104	5.4±0.2	4.9±0.0	1.3±0.0	1.8±0.0
				Isotonic exercise (n = 7)				
2,833±82	365±12 (63)	114±3 (20)	102±3 (18)	2,512±109	5.5±0.2	4.8±0.1	1.3±0.0	1.9±0.0
				Isokinetic exercise (n = 7)				
2,890±75	375±11 (63)	112±3 (19)	104±3 (18)	2,389±100	5.6±0.2	4.8±0.1	1.3±0.0	1.9±0.0
				All subjects (n = 19)				
2,813±47	362±7 (63)	113±2 (20)	101±2 (18)	2,353±70	5.5±0.1	4.8±0.1	1.3±0.0	1.9±0.0

Values are means ± SE. CHO, carbohydrate; PRO, protein. Values in parentheses represent percentage of total intake.

Dunnett tests. The null hypothesis was rejected when $P < 0.05$, and nonsignificant differences were denoted by NS. Values are expressed as means ± SE unless noted.

RESULTS

Vascular volumes. Plasma volume in the ITE group was unchanged during bed rest (−1.5 ± 2.3%), while volumes for the NOE and IKE groups decreased progressively ($P < 0.05$), reaching −14.7 ± 2.8 and −16.8 ± 2.9%, respectively (Fig. 2). Red cell volume also was unchanged in the ITE group during bed rest. On bed rest *day 8* it was unchanged in the NOE group but decreased by 7.0 ± 2.0% ($P < 0.05$) in the IKE group. By *day 30* red cell volume decreased ($P < 0.05$) in the NOE and IKE groups to reach −10.3 ± 2.8 and −17.2 ± 4.1%, respectively. Thus, during bed rest there was a close association among the unchanged plasma, red cell, and total blood volumes in the ITE group. On the other hand, changes in plasma and red cell volumes and plasma and total blood volumes were dissociated only in the NOE group by bed rest *day 8*; i.e., red cell and total blood volume reductions were delayed by exercise training, but they decreased to approximately the plasma volume levels by *day 30*. The IKE regimen tended to accentuate red blood cell loss by *day 30* compared with the corresponding NOE level.

The correlation coefficient of 0.50 ($P < 0.05$) between percent change in peak $\dot{V}O_2$ and percent change in resting plasma volume for the three groups combined indicates that only 25% (r^2) of the variance in peak $\dot{V}O_2$ can be accounted for by the changes in plasma volume; correlation coefficients for each group separately were 0.22 (NS) for NOE, 0.12 (NS) for ITE, and 0.39 (NS) for IKE.

Fluid intake and urinary excretion. There were no significant differences in voluntary fluid intake (Fig. 3, *top*) among the three groups in the ambulatory control period [2,198 ± 96, 2,236 ± 84, and 2,084 ± 113 (SE) ml/24 h for NOE, ITE, and IKE, respectively]. During bed rest, however, compared with the NOE group level of 1,715 ± 23 ml/24 h, fluid intakes were higher ($P < 0.05$) in both IKE and ITE groups (1,944 ± 27 and 2,047 ± 26 ml/24 h, respectively) and were different ($P < 0.05$) from each other. In recovery, mean intakes for all groups were not significantly different (1,825 ± 122, 2,026 ± 91, and 1,997 ± 110 ml/24 h for NOE, ITE, and IKE, respectively).

There were no significant differences in mean levels of urinary volumes among the three groups throughout the study (Fig. 3, *bottom*). Greater fluid intakes with un-

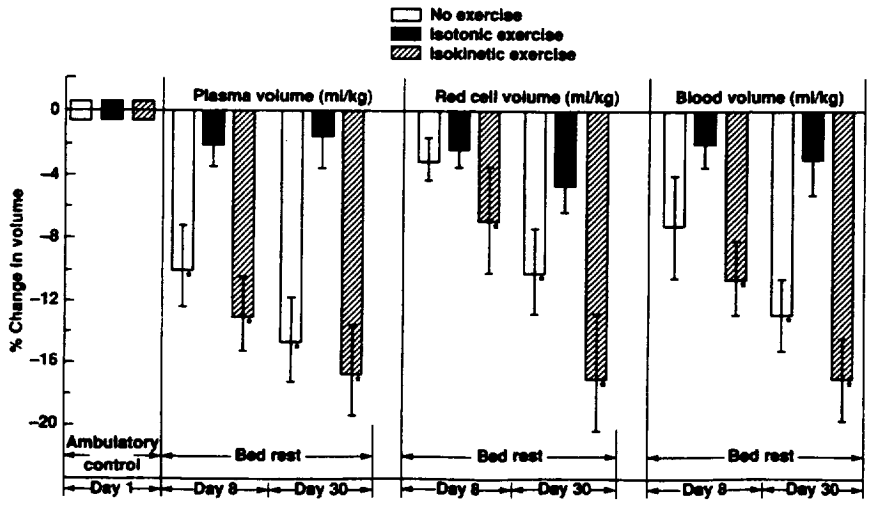

FIG. 2. Percent change in plasma, red cell, and total blood volumes on bed-rest *days 8* and *30*. Values are means ± SE. *$P < 0.05$ compared with corresponding *day −1* ambulatory control value.

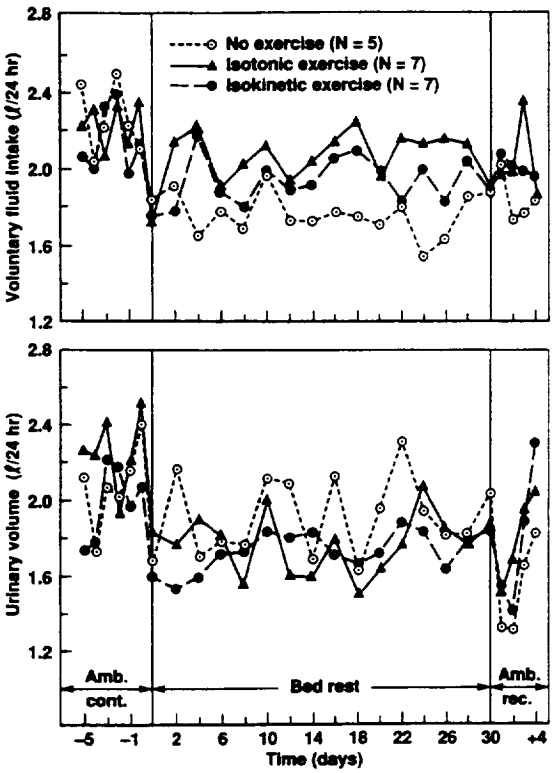

FIG. 3. Daily mean voluntary fluid intakes and urinary volumes during ambulatory control, bed rest, and ambulatory recovery periods.

changed urinary outputs reflected the increased sweating and respiratory water losses during exercise. In recovery, mean urinary volumes for ITE and IKE groups (1,781 and 1,776 ml/24 h, respectively) were higher ($P < 0.05$) than for the NOE group (1,553 ml/24 h). These increased urinary outputs for the ITE and IKE groups reflected the greater fluid intakes.

Fluid balance. There was no significant difference in fluid balance (fluid intake − urinary volume) among the three groups in the ambulatory control period: the mean values were 171 ± 99, 38 ± 77, and 150 ± 44 ml/24 h in the NOE, ITE, and IKE groups, respectively (Fig. 4). There was a significant negative water balance on *day 1* of bed rest in the NOE group, but not in the ITE or IKE groups: NOE, −776 ml/24 h ($P < 0.05$); ITE, −158 ml/24 h (NS); and IKE, −398 ml/24 h (NS); NOE vs. ITE ($P < 0.05$), IKE vs. NOE or ITE (NS). During the full bed-rest period the mean fluid balances were all significantly different ($P < 0.05$) from each other: 295 ± 40, 169 ± 36, and −106 ± 42 ml/24 h in ITE, IKE, and NOE, respectively. Recovery fluid balances were all positive and not different from each other, and they ranged from 182 to 246 ml/24 h.

Blood variables. With significant but essentially unchanged plasma protein concentrations for the three groups, the change in protein content virtually followed the responses of the plasma volumes (Fig. 5). The exception was the change in protein content in the IKE group on *day 30.* Plasma osmolality was unchanged in all groups during the control and bed-rest periods. Also unchanged during the three periods in the three groups were mean resting plasma vasopressin (range 1.12–2.66 pg/ml) and aldosterone (range 11.16–18.16 ng/dl) concentrations and renin activity (range 0.80–3.01 ng angiotensin $I \cdot ml^{-1} \cdot h^{-1}$).

Mean data for plasma protein and osmotic contents for each group at *days 8* and *30* of bed rest were highly correlated ($r = 0.93$, $P < 0.05$; Fig. 6). Points for the IKE and NOE groups were negative, whereas those for the ITE group were positive, indicating retention of osmols or retention of osmotic and protein content.

Diet, body weight, and body composition. The group mean data for daily caloric intake varied between 2,678 ± 75 and 2,890 ± 75 kcal/day (Table 1). The mean daily intake for all 19 subjects was 2,813 ± 47 kcal/day, and the average composition by weight was ~63% carbohydrate, 20% protein, and 18% fat. The mean daily caloric consumption over the 42 days was 2,442 ± 50 kcal/day for the subject with the lowest intake (NOE) and 3,098 ± 37 kcal/day for the subject with the highest intake (ITE). The mean daily volume of free water in the diet followed caloric intake: 2,080 ± 104, 2,512 ± 109, and 2,389 ± 100 ml for NOE, ITE, and IKE, respectively. Electrolyte contents were within the normal range and virtually identical for the three groups (Table 1).

The actual mean daily caloric intakes of 2,678, 2,833, and 2,890 kcal for NOE, ITE, and IKE, respectively, resulted in body weight changes during bed rest (*day 1–day 30*) of −1.01 ± 0.81 (SE) kg (NS), −0.85 ± 0.59 kg (NS), and 0.00 ± 0.52 kg (NS), respectively. ~~(Fig. 6)~~. Compared with ambulatory control *day −1* data, mean body weight ($n = 19$) decreased by 0.75 kg ($P < 0.05$) on bed-rest *day 1* and by 1.32 kg ($P < 0.05$) on bed-rest *day 30.* Mean body weight was unchanged on recovery *day 1* but increased by 0.63 kg ($P < 0.05$) on recovery *day 2* and continued to

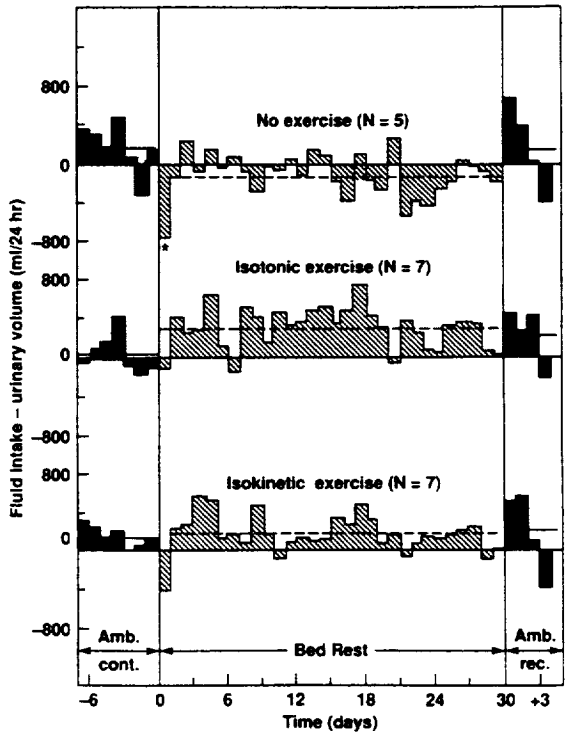

FIG. 4. Daily mean estimated fluid balances (fluid intake − urinary volume) during ambulatory control, bed rest, and ambulatory recovery periods. Solid and dashed lines (other than 0 line) represent mean levels for that period. *$P < 0.05$ compared with zero.

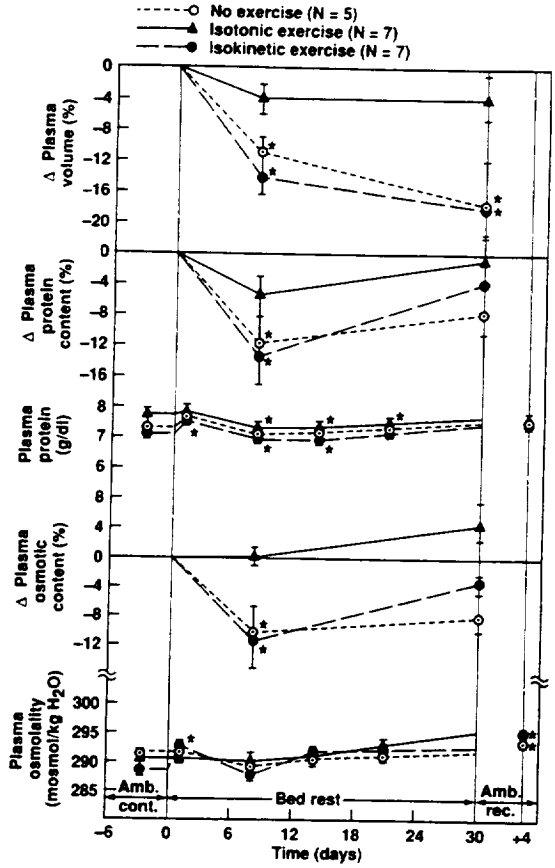

FIG. 5. Percent change in plasma volume, percent change in plasma protein content, plasma protein concentration, change in plasma osmotic content, and plasma osmolality during ambulatory control, bed-rest, and ambulatory recovery periods. Values are means ± SE. Plasma protein content on *day 30* was calculated with *day 21* plasma protein concentration data. *$P < 0.05$ compared with zero or ambulatory control value.

increase thereafter. Body weight on recovery *day 2* had returned to control *day −1* levels. ~~(Fig. 6)~~.

There were no significant changes in body density or fat content in any group during bed rest (control *day −5* vs. recovery *day 2*): ITE, 1.050 vs. 1.051 (21.2 vs. 20.5% fat); NOE, 1.062 vs. 1.062 (16.0 vs. 16.8% fat); and IKE, 1.081 vs. 1.077 (8.7 vs. 7.7% fat). Lower density is reflected in higher fat content. Both density and fat content were lower ($P < 0.05$) in IKE than in ITE and NOE, which were not different from each other.

Peak $\dot{V}O_2$ and strength. Changes in peak $\dot{V}O_2$ from control to bed-rest *day 28* were as follows: NOE, 44 ± 4 to 36 ± 3 ml · min^{-1} · kg^{-1} (−18.2%, $P < 0.05$); ITE, 39 ± 4 to 40 ± 3 ml · min^{-1} · kg^{-1} (+2.6%, NS); and IKE, 44 ± 3 to 40 ± 2 ml · min^{-1} · kg^{-1} (−9.1%, $P < 0.05$) (13). There were no significant changes in any group in knee peak torque (right knee flexion or extension), knee flexion average total work, or shoulder mean total work, measured at weekly intervals. There were significant ($P < 0.05$) changes in knee extension average total work (decrease in NOE and increase in IKE) and in shoulder total peak torque (increases in ITE and IKE) at the end of bed rest.

Mean energy costs for the NOE (resting), IKE, and ITE regimens were 83 (3.6 ± 0.2 ml O_2 · min^{-1} · kg^{-1}), 214 (8.9 ± 0.5 ml · min^{-1} · kg^{-1}), and 446 kcal/h (18.8 ± 1.6 ml · min^{-1} · kg^{-1}), respectively. Mean daily resting metabolism was 0.27 ± 0.1 l/min during the control period and 0.26 ± 0.1 l/min (NS) during *week 4* of bed rest (80 kcal/h). Active exercise time was 6.7 and 60.0 min/day for IKE and ITE, respectively.

Summary 1) During bed rest, there were no significant changes in body weight, body density, or body fat content in any group. Overall ($n = 19$) mean body weight decreased by 0.75 kg ($P < 0.05$) on bed-rest *day 1* and remained at this level throughout bed rest. *2*) During bed rest, urinary volumes were similar in the three groups, voluntary fluid intakes were higher in the two exercise groups, and fluid balance was higher ($P < 0.05$) in the two exercise groups. *3*) During bed rest, compared with the NOE group's mean energy utilization of 83 kcal/h, energy cost increased significantly to 214 (2.5-fold) and 446 kcal/h (5.2-fold) with IKE and ITE regimens, respectively. *4*) Active exercise time was 6.7 and 60.0 min/day for ISE and ITE groups, respectively, with corresponding plasma volume changes of −16.8 and −1.5% at the end of bed rest. *5*) During bed rest the significant decreases in resting plasma volume in the IKE and NOE groups and its maintenance in the ITE group could not be accounted for by resting responses of plasma osmotic, protein, vasopressin, or aldosterone concentrations or renin activity. *6*) At the end of bed rest only 25% of the variance in percent change in peak $\dot{V}O_2$ could be accounted for by the percent change in plasma volume.

DISCUSSION

Plasma volume was maintained at the ambulatory control level during bed rest in the ITE group: the IKE regimen had no effect on plasma volume because the IKE level of hypovolemia was similar to that of the NOE group. Hematocrit and hemoglobin concentrations were unchanged during bed rest in the ITE group and were

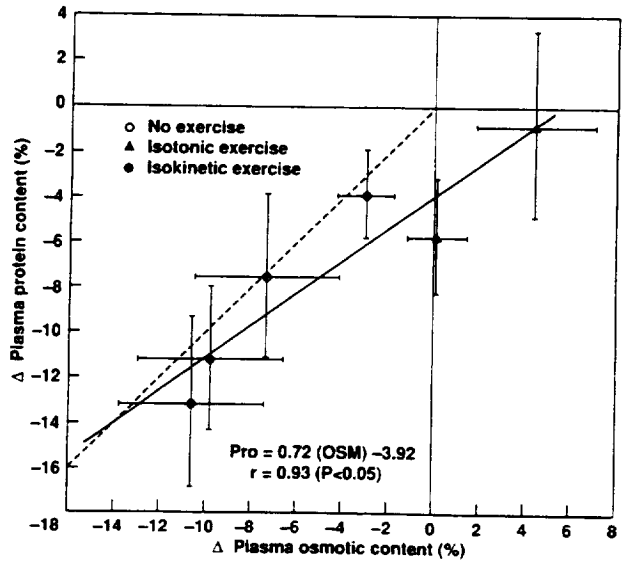

FIG. 6. Regression of change in plasma protein content on change in plasma osmotic content from ambulatory control levels on *days 8* and *30* in resting subjects. Data points are means ± SE for each group. Dashed line, line of identity. Solid line is fitted to data by method of least squares.

elevated (or tended to be) in the IKE and NOE groups, reflecting the respective changes in plasma volume. This chronic hemoconcentration during bed rest was similar to that observed during a 14-day horizontal bed rest study with isotonic and isometric exercise training (14). In that study, two 30-min bouts of continuous isotonic cycle ergometer leg exercise per day at an average relative $\dot{V}O_2$ of 68% resulted in 7.8% hypovolemia, compared with 12.6% hypovolemia with no exercise training. In the present study the average relative $\dot{V}O_2$ with the ITE regimen was only 50% for two 30-min bouts/day (with peak level to 90%), but plasma volume was maintained. Compared with intermittent high-intensity isokinetic exercise and higher average intensity continuous isotonic exercise, it seems that near-maximal variable-intensity isotonic exercise is more effective for maintaining plasma volume and probably extracellular fluid volume during prolonged bed rest. Thus, exercise intensity appears to be more important than duration for maintenance of plasma volume. However, with peak exercise, whether it was basically isotonic or isokinetic, the upper limb, shoulder girdle, and trunk muscles were used for support, so there was no clear distinction between the two types of contractions. Thus it was the summation of various types of muscular contractions in the ITE and IKE regimens that was responsible for the different fluid responses. Exercise duration may also have had an effect: the ITE regimen was 60.0 min/day and the IKE regimen was only 6.7 min/day. Perhaps performance of isokinetic exercise for >10 s/min would have had a greater effect on reducing the hypovolemia, but undue fatigue and injury may result. Of the three subjects who required alterations in their training regimens, two were in the IKE group: one had problems with muscle pain and the other had gastrointestinal distress (13). Thus the stimuli for maintaining plasma volume are related more to the type (isotonic), nature (variable high-intensity continuous), and, perhaps to a lesser extent, duration of exercise.

The mean decrease in plasma volume of the NOE group of 14.7% was similar to that in the study of Taylor et al. (27), where plasma volume decreased 15.5% in men who were exercise-trained before their horizontal bed rest period of 21 days. (Taylor et al. also measured plasma volume with Evans blue dye.) Our men exercised for 30 min/day at ~50% of their peak $\dot{V}O_2$ in the ambulatory control period. Any exercise-induced hypervolemia before bed rest may result in a greater hypovolemia after bed rest. In a study by Smirnova et al. (26), four no-exercise control men lost only 4.0% of their plasma volume after 120 days of 5° head-down bed rest.

Because body densities of the three groups in our study were similar, it appears that the differential changes in plasma volume during bed rest with the three exercise regimens could not be attributed to or be a reflection of body composition changes. Smirnova et al. (26) reported similar decreases in extracellular (−12.0 to −15.0%), interstitial (−14.3 to −17.0%), and plasma (3.0 to −7.8%) volumes in four groups of subjects after 120 days of head-down bed rest where they underwent widely different exercise and pharmacological protocols during bed rest. Their exercise training groups tended to have less severe hypovolemia. Also, in the present study, the nonsignificant group correlations between change in peak $\dot{V}O_2$ and change in plasma volume suggest that, at best, only 25% of the variance in the former could be accounted for by changes in the latter. Since plasma volume was unchanged in the ITE group during bed rest, the mechanism controlling this volume was not linearly related to mean exercise $\dot{V}O_2$ or energy expenditure, because the level of hypovolemia was similar: −16.8 and −14.7% in the IKE and NOE regimens, respectively, which had different energy expenditures of 214 and 83 kcal/h, respectively.

There was a partial association between the changes in plasma volumes and body water balances during bed rest. The essentially unchanged plasma volume with the ITE regimen accompanied the highest water balance of +295 ml/24 h, and the 14.7% reduction in plasma volume with the NOE regimen accompanied the lowest (negative) water balance of 106 ml/24 h. With the IKE regimen, however, the hypovolemia was −16.8%, similar to the NOE group, but water balance was positive (+169 ml/24 h), similar to the ITE group. Thus, there does not seem to be a direct association between the level of plasma volume and water balance. It is clear, however, that plasma and extracellular fluid volumes should ultimately decrease if fluid balance remains negative.

Our original hypothesis when designing these exercise training protocols was that intensity was more important than duration for maintaining work capacity and extracellular fluid volume (13). Because of the nature of isotonic and isokinetic exercise and the fact that we emphasized intensity rather than duration, it was not practical to equate work-induced $\dot{V}O_2$; the time for isokinetic exercise and rest periods would have been much longer than 1 h/day. Longer isokinetic exercise time could have had a more positive effect for attenuating the hypovolemia, but risk of injury increases. Similar results were obtained from a previous 14-day horizontal bed-rest study where plasma volume was reduced by 12.6% with no exercise, by 11.3% with isometric leg exercise (30-s exercise-rest periods for 1 h/day), and by 7.8% with 1 h/day of continuous cycle ergometer leg exercise at a relative $\dot{V}O_2$ of 68% (14). Compared with those results, maintenance of plasma volume in the present study, at an average exercise load of only 50%, gives the exercise intensity factor additional importance.

The thoracic hypervolemia-mediated diuresis that occurred during the first 24–48 h of bed rest eliminated the "excess fluid," and plasma volume decreased by 12–15% (extracellular volume by 5–7%) between *days 2* and *8*, when no exercise or mild exercise training was performed (14, present study). Plasma volume continued to decline more slowly (exponentially) thereafter and reached semiequilibrium at about −20 to −25% at 30–100 days of bed rest (14). There are few reliable measurements of plasma and extracellular fluid volumes beyond 30 days of bed rest when subjects were restricted to the horizontal or head-down body position. Because plasma concentrations of essentially all constituents are within the normal ambulatory range (some exceptions are hemoglobin and hematocrit, see Ref. 14) during prolonged bed rest with accompanying hypovolemia, the constituent contents must have been reduced proportionally by an as yet un-

defined mechanism involving some combinations of reduced production, increased filtration, increased sequestration, or increased excretion. Major mechanisms controlling plasma volume would encompass variations in hydrostatic, colloid osmotic, crystalloid osmotic, and systemic blood pressures.

Resting systemic systolic and diastolic blood pressures were unchanged throughout the three periods (14). The similar responses between percent changes in resting plasma volumes and protein contents on bed rest *day 8* with data from all three groups illustrate tight coupling between these two variables. A similar coupling was found between mean resting changes in plasma protein and osmotic contents. So the major question is, How does exercise training maintain plasma volume during bed rest when the control (no-exercise training) response is significant hypovolemia?

Clearly, maintenance of plasma volume during bed rest in the ITE group was accompanied by minimal loss of plasma protein content and no net loss of plasma osmotic content. The greater losses in the IKE group were similar to those in the NOE group. The shorter IKE regimen of 6.7 min/day was insufficient to prevent hypovolemia, but it must have been the more intensive ITE intervals at relative $\dot{V}O_2$ of 70, 80, and 90% that stimulated the plasma volume maintenance mechanism, because a continuous ITE regimen of similar duration during bed rest at 68% of maximum $\dot{V}O_2$ resulted in 7.8% hypovolemia (14).

It has been suggested that isotonic exercise-induced hypovolemia in ambulatory subjects is caused mainly by increased hydrostatic and systemic blood pressures (19), because the level of hypovolemia is proportional to exercise load; the ensuing isocontent shifts of NaCl accompany minor (<2%) shifts of plasma protein content (18, 22). Restitution of plasma volume after exercise ceases probably occurs via capillary absorption of interstitial fluid due to the increased plasma colloid osmotic pressure. Because oncotic pressure is an important mechanism for acute plasma reconstitution and more chronic hypervolemia (1), there would be a requirement for additional protein to enter the vascular system. A small quantity may return through the capillaries and perhaps more may enter via the lymphatic system's thoracic duct (22), but definitive data on these latter two hypotheses during exercise in humans are lacking. Some results suggest that osmotic pressure may play a role via stimulation of vasopressin: the threshold occurs at a relative work intensity >50%, and concomitant exercise induced hypovolemia >4% to increase plasma osmolality sufficiently to stimulate vasopressin (4–6). The unchanged resting plasma vasopressin concentrations do not appear to account for the significantly different water balances in the three groups. Atriopeptide concentrations increase during and immediately after exercise in humans (1, 8). They also facilitate escape of albumin and fluid from the systemic circulation of resting rats in response to infusion of pharmacological doses (29). It has not been firmly established whether increases in plasma vasopressin or atriopeptins play a role in the control of plasma volume during exercise training, but influx of proteins into the vascular space appears to be the most important mechanism for the acute and probably chronic hypervolemia after exercise and exercise training.

The findings indicate that the most important factors for stimulating the maintenance of plasma volume during bed-rest acclimation (deconditioning) are type (isotonic cycle ergometer), nature (continuous, variable, high intensity), and, to some extent, time of exercise. These factors are not necessarily independent.

We are grateful to the 125 people who had significant roles in this study. We are especially grateful to Dee O'Hara (Human Research Facility) and Edith Crofoot and the nursing and aides staff; Andrew Ertl and the exercise testing group (University of California Davis), including Todd Trowbridge, Gene Myers, and Dave McKenzie; Margorie Hunt (Letterman Army Institute of Research), Robin Williams and Victoria Major and the food preparation staff; Ralph Pelligra; Gail Bennet-Hiley and Ranita Dalton (Bionetics Corp.). We also thank Atticus Tysen for statistical analyses; Debra Fegan Meyer and Bridget Eller for manuscript preparation; the coinvestigators and their staffs; and the Laboratory for Human Environmental Physiology support and technical staff, including Jeff Ball, Victor D'Aloia, Sally Greenawalt, Teresa Hutchinson, Linda Kirby, Sandra Lewis, Joann Meredith, Andrea Ertl, and Joan Silver. We especially thank the members of American Institute of Biological Sciences review panel who shared their thoughts, comments, and recommendations with us: Reggie Edgerton, Philip Gollnick, William Haskell, Michael Pollock, William Stauber, and Charles Tipton (Chair).

This work was supported by National Aeronautics and Space Administration Tasks 199-21-12, 199-22-12, 199-22-22, 199-22-32, 199-22-44, and NAG2-410 and US Army Task MRDC-3A161101A-91C.

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Received 12 July 1990; accepted in final form 21 November 1991.

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Lower Extremity Muscle Thickness and Volume during 30-day 6° Head-Down Bed Rest with Isotonic and Isokinetic Exercise Training

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Abstract

Ellis S, Lee PL, Ortendahl DA, Selzer RH, Kirby LC, Greenleaf JE. Lower extremity muscle thickness and volume during 30-day 6° head-down bed rest with isotonic and isokinetic exercise training. Aviat. Space Environ. Med. 1992; 63: XXXX-XXXX.

Muscle thickness and volume were measured in 19 bedrested (BR) men (32–42 yr) subjected to isotonic (ITE, cycle ergometer) and isokinetic (IKE, torque ergometer) lower extremity exercise training, and no exercise (NOE) training. Thickness was measured with ultrasonography in anterior thigh—rectus femoris (RF) and vastus intermedius (VI), and combined posterior leg—soleus, flexor hallucis longus, and tibialis posterior (S + FHL + TP)—muscles. Volume was measured with magnetic resonance imaging (MRI) in the combined posterior leg group (PLG) containing the (S + FHL + TP), lateral and medial gastrocnemius, and flexor digitorum longus muscles. Correlation coefficients between percent changes in (S + FHL + TP) and (PLG) muscle groups were: ITE 0.79 ($P < 0.05$), IKE 0.27 (NS), and NOE 0.63 (NS). Compared with ambulatory control values, thickness of the (S + FHL + TP) decreased by 9%–12% ($P < 0.05$) in all three test groups. The (RF) thickness was unchanged in the two exercise groups, but decreased by 10% ($P < 0.05$) in the NOE. The (VI) thickness was unchanged in the ITE group, but decreased by 12%–16% ($P < 0.05$) in the IKE and NOE groups. Total vol of the (PLG) muscles decreased similarly ($P < 0.05$) by 4.3%–7.7% in all test groups. Thus, intensive, alternating, isotonic cycle ergometer exercise training is as effective as intensive, intermittent, isokinetic exercise training for maintaining thicknesses of some (RF, VI) anterior thigh muscles but not posterior leg muscles during prolonged BR deconditioning.

Introduction

Skeletal muscle wasting (atrophy) is a major response to removal of weight-bearing loads and occurs with disuse during limb casting (ref. 22), during prolonged bed rest (BR) without additional exercise training (ref. 7), in joint-casted bed-rested patients (ref. 19), and in some astronauts during flight (ref. 25). Skeletal muscles "unloaded" for a few weeks in ambulatory subjects undergo reductions in mass and strength generally in proportion to the duration of unloading. After several weeks of joint immobilization, removal of a cast in ambulatory patients reveals a striking reduction in limb girth and strength, particularly in lean individuals; atrophic changes can be ameliorated after several weeks of normal activity (ref. 22). However, in limb casted patients who had undergone prolonged (4–38 wk) BR without remedial exercise training, there was no direct relationship between the duration of joint immobilization and magnitude of atrophy of casted muscle fibers, or between the latter and girth of the casted limb (ref. 19).

Confounding factors contributing to the poor relationship between limb girth and muscle mass during shorter-term (<4 wk) joint immobilization and BR could be preferential loss of contractile protein (ref. 17), replacement of muscle with fibrous tissue, change of muscle fiber pennation angle or capillarization, differential changes in intracellular and extracellular fluid-electrolyte shifts (ref. 10) in and around muscle cells, and shifts in neural stimuli to motor units and their firing frequency during contractions (ref. 21). Another factor could be the different methods used for measuring muscle atrophy: computer assisted tomography (refs. 1 and 12), magnetic resonance imaging (ref. 15), and ultrasonography (refs. 2, 13, and 14) have been used with some degree of success for measuring muscle volume and cross-sectional area. In this study magnetic resonance imaging (MRI) and ultrasonography were used to estimate changes in lower extremity skeletal muscle volume and thickness, respectively.

Thus, the purpose of the present study was to investigate the effects of isotonic and isokinetic lower extremity exercise training on volume and thickness of anterior thigh and posterior leg muscle groups during bed-rest deconditioning.

Methods

Subjects– Nineteen men; 36 ± SE 1 yr, 178 ± 2 cm, 76.5 ± 1.8 kg, 1.94 ± 0.03 m^2, 44.2 $mlO_2.min^{-1}.kg^{-1}$ (3.36 ± 1.8 $l.min^{-1}$) peak oxygen uptake, and 690 ± 23 N-m knee peak isometric extension strength, who passed a comprehensive medical examination and

gave informed consent, were selected as subjects. They were divided into three groups that were comparable on the basis of age, peak $\dot{V}O_2$, and leg strength: no exercise (NOE) training (N = 5), isotonic (dynamic) exercise (ITE) training (N = 7), and isokinetic exercise (IKE) training (N = 7); see reference 8.

Protocol– The protocol consisted of a 7-d ambulatory control period, 30 d of 6° head-down bed rest, and a 4.5-d ambulatory recovery period (ref. 8). After an intensive 3-mo familiarization period before BR, 12 subjects (section 1: 4 NOE, 4 ITE, and 4 IKE) entered the Human Research Facility at Ames Research Center and were tested in July and August 1986. One week later the remaining seven subjects (section 2: 1 NOE, 3 ITE, and 3 IKE) were tested in August and September 1986. All testing, showering, and excretory functions were performed with the subjects in the head-down and the exercise testing in the horizontal postition. Mean (N = 19) daily caloric intake was 2,813 ± 47 kcal/day and fluids were consumed ad libitum (ref. 10).

Exercise training– The exercise-training groups worked for two 30-min periods/d (a.m. and p.m.) for 5 d/wk during BR. Peak $\dot{V}O_2$ was measured weekly in all groups with lower extremity cycle ergometer exercise (Quinton Imaging/Ergometer Table, model 846T, Seattle, WA 98121). The force was applied at the instep of the foot; heels were supported so the subjects could relax the anterior thigh muscles between the active, alternating muscular contractions. ITE training was 2-min work bouts at 40% of peak $\dot{V}O_2$ alternating with 2-min bouts at 60%, 70%, 80%, and 90% peak $\dot{V}O_2$ (ref. 8). IKE training was performed on a LIDO computer-controlled ergometer (Loredan Biomedical Inc., Davis, CA 95617). It consisted of 10 bouts of 5 repetitions/10 s of peak knee flexion and extension force (from 90° to 100° range of motion) at a speed of 100°/s followed by 50 sec rest, for a total time of 15 min with each leg and thigh (including 2.5 min warm-up and 2.5 min cool-down periods). Resting energy utilization in the NOE group was 3.6 ± 0.2 $mlO_2.min^{-1}.kg^{-1}$ (83 kcal/hr); resting plus exercise energy cost in the IKE group was 8.9 ± 0.5 $mlO_2.min^{-1}.kg^{-1}$ (214 kcal/hr), and 18.8 ± 1.6 $mlO_2.min^{-1}.kg^{-1}$ (446 kcal/hr) for the ITE training regimen. Leg total strength (peak torque) was 645 ± 38 N-m (NOE), 714 ± 42 N-m (ITE), and 704 ± 38 N-m (IKE). Calculated peak torque for the isotonic exercise was 112 ± 9 N-m.

Ultrasonography– Muscle thicknesses from the posterior leg group (medial soleus, flexor hallucis longus, tibialis posterior) and the anterior thigh group (rectus femoris, vastus intermedius) were measured as described previously (refs. 23, 26, and 27) on control day minus 5 (C – 5), on BR d2, 9, 16, 23, and 29, and on recovery day +4 (R + 4) with an imaging system (model DS-1, Diasonics, Inc., Milpitas, CA 95035) equipped with electronic calipers and a 7.5 MHz duplex probe for linear measurement of muscle thickness. All images and data were recorded on magnetic tape. The subjects were tested 6° head-down in standardized positions: supine for measurement of anterior thigh muscles and prone with the feet extending unsupported beyond the end of the guerney, for measurement of the posterior leg muscles. Measurement (probe) locations were marked with indelible pen at two skin sites: 1/3 of the distance from the superior margin of the patella to the anterior-superior iliac spine (about 15 cm above the patella) for measurement of the rectus femoris and vastus intermedius muscles separately; and about 1/3 the distance between the lateral maleolus and the head of the fibula, corresponding to cross-sections E/S 98 to E/S 99 (ref. 5) for measurement of the soleus + flexor hallucis longus muscles combined because their individual fascial boundaries often were poorly defined. Their thickness was measured by triangulation, as the perpendicular distance from the medial surface of the soleus (fig. 1-upper cross) to the midpoint of a line (approximated by the interosseous membrane) between the sharp echos from the tibia and fibula at a site just inferior to the distal edge of the gastrocnemius (fig. 1-lower cross). Ultrasonic gel was applied generously to locate the probe at least 1 mm above the skin surface to avoid compression, which would modify the measurement.

Muscle thickness data were the mean of 3–4 echos taken at precisely the same site by aligning reference lines on the probe, held perpendicular to the long axis of the muscle, with two crossed reference lines centered on the measurement site. Repeated measurements were reproducible to ±2%. Axial displacement of the probe by 1–2 cm could increase the error to ±10% or more depending on the contour of the muscle.

Muscle thickness measurements excluded skin and subcutaneous tissues. The fascial planes separating muscle from subcutaneous tissues could be easily discerned, except with the (S + FHL + TP) group.

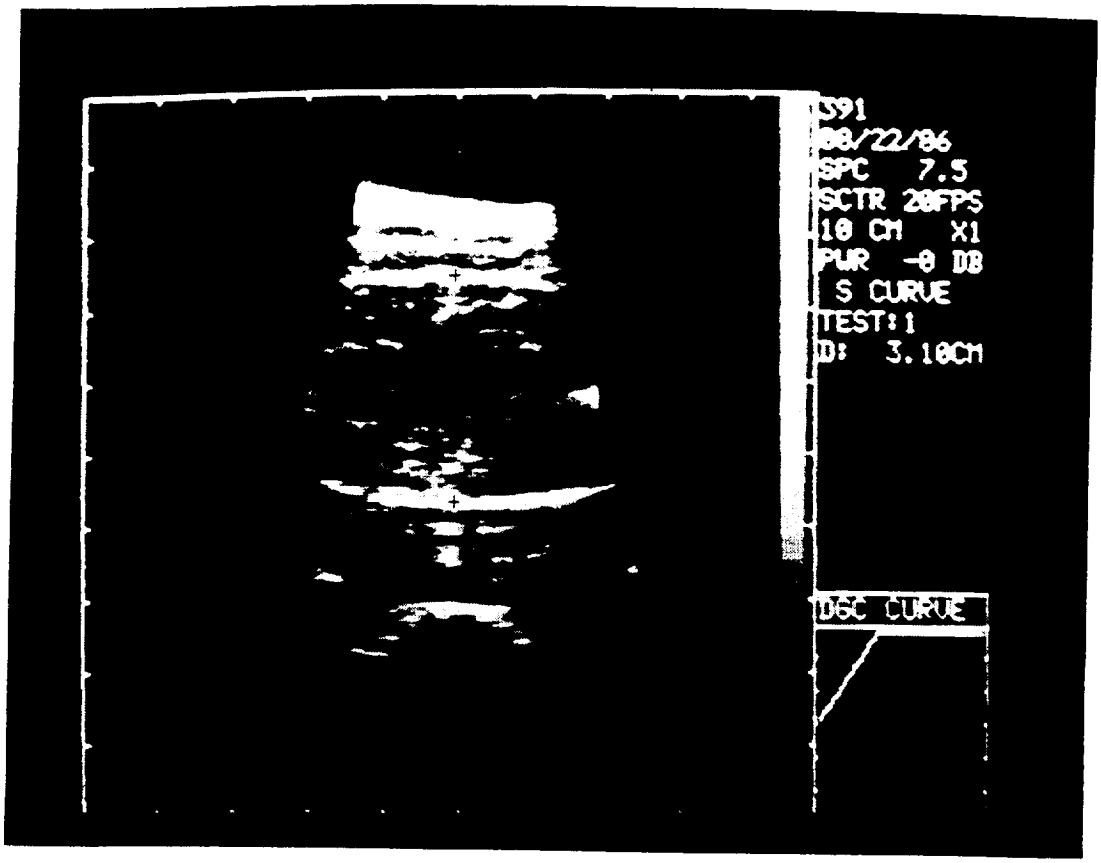


Figure 1. Ultrasound image of the (S + FHL + TP) posterior leg muscle group from subject BEL illustrating points for thickness measurement: upper cross is the medial surface of the soleus; lower cross is the midpoint of a line between the sharp echos from the tibia (lower right) and fibula (lower left). The distance between crosses (thickness) is 4.35 cm.

Magnetic resonance imaging (MRI)– These images were taken at the University of California-San Francisco Radiology Imaging Laboratory on control day –3 (C – 3) and on recovery d +3 (R + 3). The subjects were transported by limousine and tested in a reclining position. The legs of the 19 men were scanned in a Diasonics MT/S (Toshiba America MRI, Inc., South San Francisco, CA 94080) imager with a field strength of 0.35 Tesla. The imaging was performed in a quadrature detection head coil that gave an in-plane resolution of 0.95 X 0.95 mm and a 1.0 cm slice thickness. Since the imager had a field of view of only 20 cm the leg it was imaged sequentially in three 20-cm segments; i.e., 60 cross-sectional image slices at 1-cm intervals were taken on one leg starting from the ankle. The leg was translated 18 cm for each segment of images. The foot of the subject was taped to a lucite leg rest (that facilitated the 18-cm translations) marked to provide reproducible positioning. Separations between the centers of four oil-filled lucite tubes, built into the base of the leg-foot rest, indicated any geometrical changes in imaging conditions. The distances between centers of each of the four tubes for the 20 sections in both segments 1 and 2 are presented in table 1; range of distance errors was +3.74% to –3.17%. The standard testing mode was a spin echo image with a time to recovery (TR) of 1.0 s and a time to echo (TE) of 30 ms. Each of the 2,280 cross-sectional slices was enlarged and filtered to provide a modified image for computer analysis of its area (fig-2, left column); then the areas were combined to form a three-dimensional shaded surface display where locations of the light source and observer can be varied (fig-2, right column).

Table 1. Mean (±SE) distances in pixel units between centers of the four oil-filled calibration tubes in leg segments 1 and 2: pre (C – 5) and post (R + 4) bed rest data for subject BEL.

	Tubes 1–2	Tubes 2–3	Tubes 3–4	Tubes 4–1
		Pre bed rest (C – 5)		
Segment 1	93.49 ± 1.57	63.62 ± 1.08	52.92 ± 0.15	209.80 ± 0.52
Segment 2	74.94 ± 1.15	79.78 ± 1.10	52.62 ± 0.21	207.14 ± 0.30
		Post bed rest (R + 4)		
Segment 1	90.52 ± 1.24	66.00 ± 1.02	53.04 ± 0.21	209.42 ± 0.29
Segment 2	76.89 ± 1.29	78.53 ± 1.08	52.63 ± 0.19	207.94 ± 0.35
% 1	–3.17	3.74	0.23	–0.18
% 2	2.60	–1.57	0.02	0.37

The first step in the computer analysis was to use an edge-detection program to outline the total area that contained all structures except subcutaneous fat. Then areas of the tibia and fibula were outlined and subtracted from the total area. Image quality was not sufficient to delineate the boundaries for the soleus and gastrocnemius muscles in the second section of most subjects legs, so the posterior leg muscles (lateral and medial gastrocnemius, soleus, flexor digitorum longus, tibialis posterior, and flexor hallucis longus) and their connecting interosseous membranes were used instead. The computer edge-detection program was employed, with manual intervention at obscure points, to outline the border and measure the area of this muscle group for each of the 60 sections. For example, the areas for each section (no. 7 to 34) and cumulative areas for subject BEL's posterior muscle group pre- and post-BR are presented in figure 3.

To illustrate a typical analysis, the soleus and gastrocnemius muscles from subject BEL were traced manually. The image quality of his cross-sectional slices was sufficient to allow delineation of the soleus pre-BR in segment 1 at about 11 cm above the ankle (fig. 2, lower left), the soleus plus the distal heads of the gastrocnemius pre-BR in segment 2 at about 22 cm above the ankle (fig. 2, middle left), and only the proximal two heads of the gastrocnemius pre-BR in segment 3 at about 42 cm above the ankle (fig. 2, upper left). The image processing method utilized the determination of muscle edges, which is a more accurate procedure than using relaxation time and pixel intensity to characterize muscle (ref. 15). But, it has the drawback of being labor intensive.

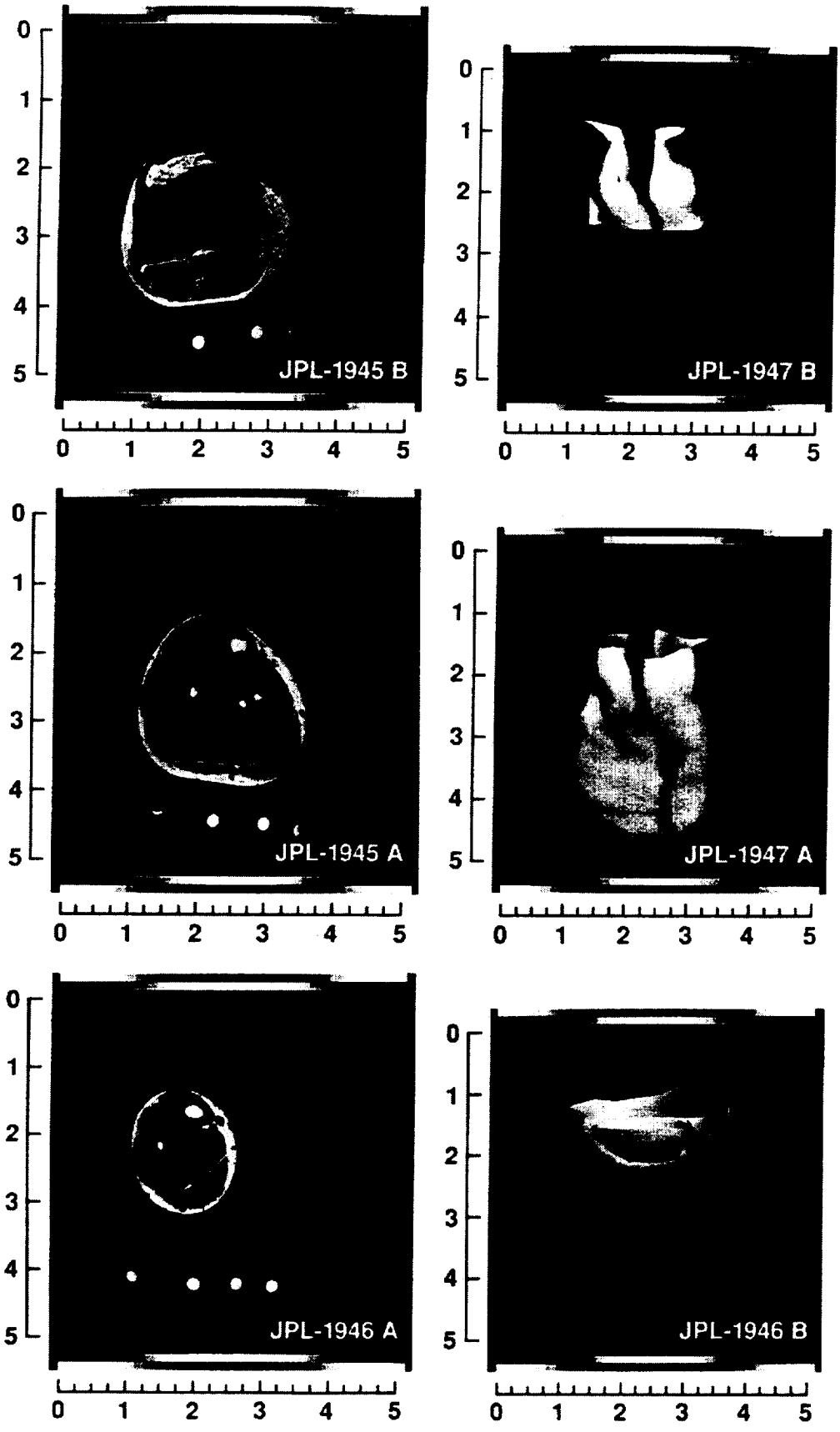
The data were analyzed with the appropriate paired or unpaired t-tests (Hewlett-Packard HP-65 Stat-Pac), and linear regression (ref. 6). The null hypothesis was rejected when $P < 0.05$ for the t-tests and $P < 0.02$ for linear regressions. Non-significant differences were NS.

Figure 2. Cross-sectional MR images (left column) and posterior surface reconstruction views (right column) of the left leg of subject BEL.

Lower panel - left image: pre-BR soleus in segment 1 at 11 cm above the ankle; right view: post-BR tendon of insertion of the triceps surae.

Middle panel - left image: pre-BR soleus and the medial and lateral heads of the gastrocnemius in segment 2 (22 cm); right view: pre-BR medial and lateral heads of the gastrocnemius. The soleus is hidden.

Upper panel - left image: pre-BR proximal medial and lateral heads of the gastrocnemius in segment 3 (42 cm); right view: post-BR heads of the gastrocnemius only at this level behind the knee. The four circles are the oil-filled tubes.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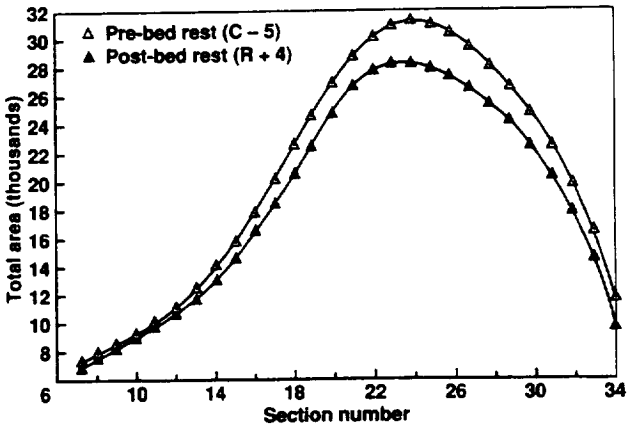

Figure 3. Total area of the posterior leg muscle group pre- and post-BR for subject BEL.

Results

Ultrasound– Mean (±SE) muscle thicknesses for (S + FHL + TP), rectus femoris (RF), and vastus intermedius (VI) in the ambulatory control period (C – 5), weekly during BR (BR 2 to BR 29), and during recovery (R + 4) are presented in figure 4, and percent changes from C – 5 in figure 5. The absolute and changes in (S + FHL + TP) thicknesses (figs. 4 and 5, upper panels) decreased ($P < 0.05$) in the NOE (by 4.2%) and ITE (by 5.0%) groups by BR 2 and continued to decline thereafter in all groups. The slopes of these posterior leg muscle groups from BR 2 to BR 29 were significantly different ($P < 0.05$) from zero, but not from each other. The C – 5 to BR 29 decreases were: NOE from 4.49 ± 0.11 cm to 3.98 ± 0.10 cm, respectively (= –11.4%, $P < 0.05$); ITE from 4.14 ± 0.18 cm to 3.61 ± 0.11 cm (= –12.4%, $P < 0.05$), and IKE from 4.13 ± 0.12 cm to 3.75 ± 0.10 cm, respectively (= –9.0%, $P < 0.05$). Percent changes in muscle thicknesses in all exercise groups did not return to control levels by R + 4 (fig. 5). Thus, neither ITE nor IKE training influenced the rate or magnitude of the decrease in (S + FHL + TP) muscle thicknesses.

Rectus femoris thickness (figs. 4 and 5, middle panels) was unchanged in the three groups from C – 5 to BR 2 and continued unchanged in the two exercise groups throughout BR and recovery. Rectus femoris thickness decreased significantly from C – 5 to BR 29 only in the NOE group from 2.06 ± 0.18 cm to 1.86 ± 0.19 cm (= –9.8%, $P < 0.05$). Percent changes in (RF) thicknesses were unchanged in all groups on R + 4; those for the ITE and IKE groups were unchanged from the C – 5 level, and that for the NOE group did not even show a tendency to return (fig. 5).

The (VI) thickness (figs. 4 and 5, lower panels) responded differently than the (S + FHL + TP) and (RF) muscles; it was unchanged in the two exercise groups from C – 5 to BR 2, and decreased significantly by 6.2% in the NOE. VI thickness was unchanged during BR from C – 5 only in the ITE group; and it decreased significantly in the other groups: NOE from 1.71 ± 0.18 cm to 1.41 ± 0.10 cm at BR 23 (= –16.1%, $P < 0.05$); and IKE from 1.96 ± 0.25 cm to 1.71 ± 0.21 cm at BR 29 (= –12.2%, $P < 0.05$). Neither NOE nor IKE groups' (VI) thicknesses returned to control levels during recovery. Only ITE training maintained (VI) thickness at the control level during BR and recovery.

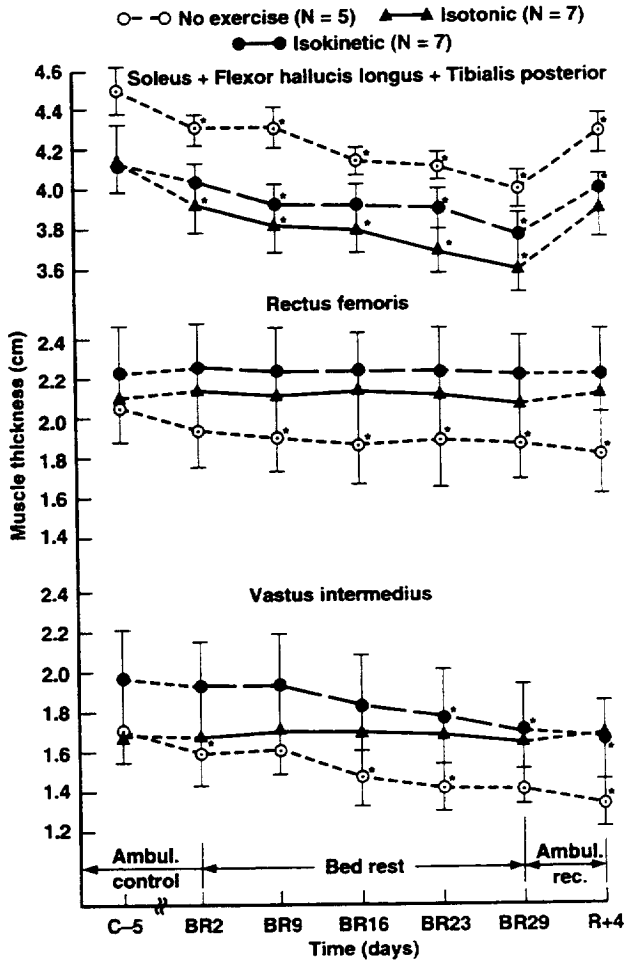

*Figure 4. Mean (±SE) ultrasonic thickness of the (soleus + flexor hallucis longus + tibialis posterior), rectus femoris, and vastus intermedius muscles during control, BR, and recovery periods for the three test groups. *P < 0.05 from corresponding C – 5 value.*

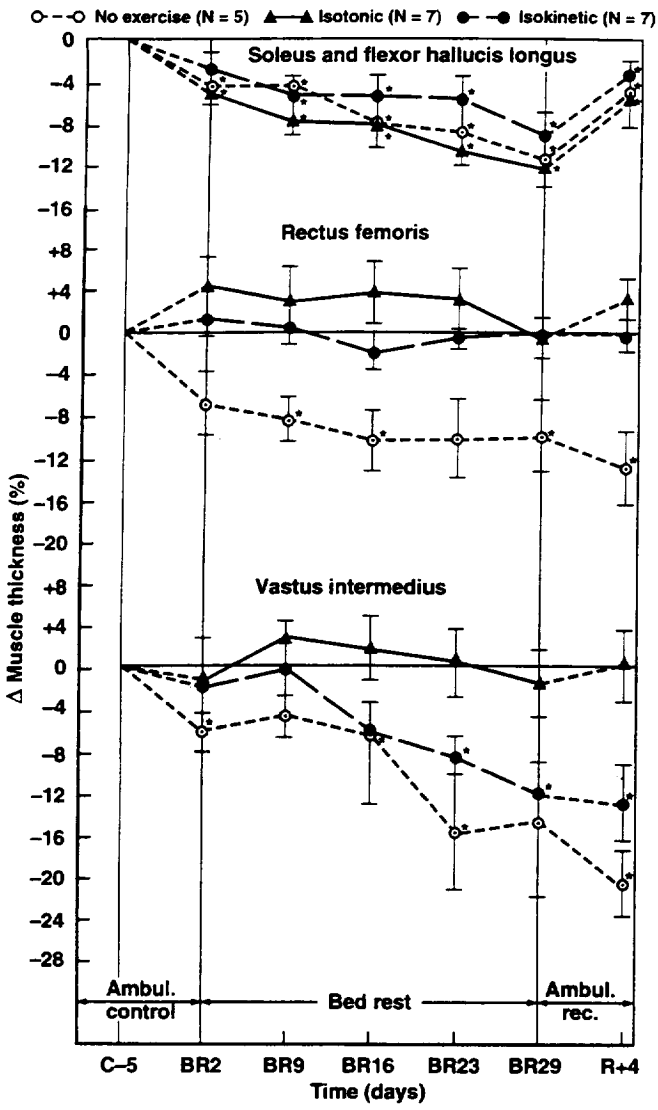

*Figure 5. Mean (±SE) percent changes in ultrasonic thicknesses of the (soleus + flexor hallucis longus + tibialis posterior), rectus femoris, and vastus intermedius muscles during control, BR, and recovery periods for the three test groups. *P < 0.05 from corresponding C – 5 value.*

Imaging– Mean (±SE) total muscle volumes decreased significantly in all groups after BR: NOE –6.3 ± 0.8% ($P < 0.05$); ITE –4.3 ± 1.6% ($P < 0.05$); and IKE –7.7 ± 1.6% ($P < 0.05$) (table 2). Only one ITE subject had an apparent increase (NS) in his muscle volume. There were no significant differences in the decreased volumes between groups; i.e., neither ITE nor IKE training influenced the decreased volumes of this posterior leg muscle group.

Linear regression of percent changes in posterior leg muscle group thicknesses, measured by ultrasonography (C – 6 to R + 3), and volume measured by MRI (C – 3 to R + 3) indicated an overall correlation coefficient of 0.35 (NS) (fig. 6); group coefficients were: NOE $r = 0.63$ (NS), ITE $r = 0.79$ ($P < 0.05$), and IKE $r = 0.27$ (NS).

Summary of Results

Ultrasound– 1. The posterior leg muscle group thicknesses decreased significantly by 9%–12% during BR in all three test groups. 2. Rectus femoris (anterior thigh) muscle thicknesses were unchanged during BR in the two exercise groups, but decreased significantly by 10% in the NOE group. 3. Vastus intermedius (anterior thigh) muscle thickness was unchanged during BR in the ITE group, but decreased significantly by 12%–16% in the NOE and IKE groups.

Magnetic resonance imaging– 4. Total volumes of the posterior leg muscle group decreased similarly and significantly by 4% to 8% in all three test groups. 5. Correlation coefficients between ultrasonic thickness and MRI volume of their respective posterior leg muscle groups were: NOE $r = 0.63$ (NS), ITE $r = 0.79$ ($P < 0.05$), and IKE $r = 0.27$ (NS).

Table 2. Volumes (pixel units) of the posterior leg muscle group in the ambulatory control (C – 3) and recovery (R + 3) periods.

	C – 3	R + 3	%
	No exercise (N = 5)		
X	536478	502190	–6.3*
±SE	40156	35834	0.8
	Isotonic exercise (N = 7)		
X	538541	516688	–4.3*
±SE	36942	40456	1.6
	Isokinetic exercise (N = 7)		
X	574858	530892	–7.7*
±SE	15335	17336	1.6
	All Subjects (N = 19)		
X			–6.1*
±SE			0.9

*P < 0.05 from zero.

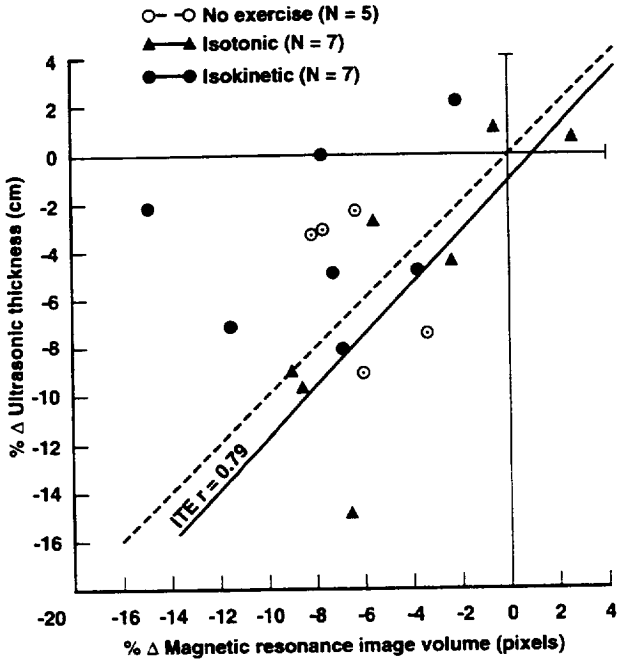

Figure 6. Regression of percent changes (C – 6 to R + 4) in posterior leg muscle groups thicknesses (ultrasonography) on percent changes (C – 3 to R + 3) in posterior leg muscle group volumes (MRI) for the three test groups. Dash line is line of identity; solid line is regression line for ITE group (r = 0.79, P < 0.05).

Discussion

Ultrasound– Thicknesses of the antigravity posterior leg muscle group (S + FHL + TP) was not affected by either exercise training regimen. Atrophy of this muscle group would be expected without leg exercise training because maintenance of upright posture was no longer required. Also, the knee flexion and extension exercise protocols did not require intensive use of those three muscles which act generally to plantarflex the great toe and foot (ref. 20). On the other hand (RF) thickness in the two exercise groups was maintained at control levels throughout BR while that for the NOE group atrophied similarly in time and magnitude to that of the (S + FHL + TP) muscle group. Maintenance of (RF) thickness with both leg exercise regimens would be expected since its action is to extend the leg and flex the thigh. The ITE training (RF) thickness tended to be greater than that for IKE training suggesting a more positive training effect with the former. But the thickness differences between the NOE regimen and the two exercise regimen's levels could also be considered as a positive training response.

The (VI) thickness responses are even more interesting. Why were they maintained at control levels throughout BR in the ITE group, while IKE group thicknesses decreased much like those in the NOE? Unlike the (RF), the (VI) does not originate on the pelvis so it would not act to flex the thigh. Its only action (with the RF) would be to extend the leg, which occurs with the push (downward) phase of the leg during cycling. Apparently performance of maximal isokinetic knee extension did not stimulate the (VI) sufficiently. Conversely, the period of maximal muscular tension during cycling at the higher

loads would tend to be intermittent and alternating between the lower extremities, assuming there would be no accompanying isometric tension during the supposedly alternating isotonic contractions. But results from surface electromyography, on thigh and leg muscles during lower extremity cycling in the sitting position, indicate significant (50% of maximal) EMG activity in the vastus medialis and vastus lateralis muscles (which have origins, insertions, and action similar to the VI) during the push-phase of the cycling motion (ref. 4). At the same time the (RF) was stimulated to only 10% of its maximal activity. These EMG results, while suggestive, may not be directly applicable to lower extremity muscular activity where the heels are supported and the limb motion is lateral rather than vertical. Thus, the ITE regimen appeared to stress the (VI) more than the IKE regimen resulting in better maintenance of muscle thickness. Part of the increased stress may have come from the tendency to hold the legs in the horizontal position, although the subjects were trained to exercise with the legs relaxed. Performance of so-called dynamic (isotonic) exercise at 80% and 90% of peak $\dot{V}O_2$ seems to require (induce) maximal isometric contraction force of nearly every muscle in the body, similar with that required during the maximal IKE regimen. Perhaps the postulated isometric component during ITE could explain some of the difference in (VI) thickness responses.

The similar significant decreases of 4.3% to 7.7% in the MRI volumes of the posterior leg group muscles coincided with the similar significant decreases of 9.0% to 12.4% in thickness. The site selected for the latter measurement would not necessarily be representative of the muscle's total volume, hence one possible reason for the discrepancy in the absolute percent changes. Responses of those magnitudes have been observed following limb casting in normal, ambulatory subjects. Leg casting for about 19 wk resulted in a 12% reduction in total leg volume relative to the non-casted control leg (ref. 22). However, the reduction in muscle cross-sectional area was much greater as indicated by decreases in areas of type I (slow twitch) fibers by 46% and type II (fast twitch) fibers by 37%. Häggmark and Eriksson (ref. 11) measured cross-sectional areas of leg muscles after six wk of casting following Achilles tendon rupture: calf muscle area was reduced by 11%, but soleus and gastrocnemius area was reduced by only 23%, and mean soleus fiber area was decreased by 25%.

In addition to probable loss of muscle contractile protein and fiber area (ref. 16), part of BR induced lower extremity muscular atrophy (including thickness and volume) can be attributed to muscle dehydration from general body water loss (hypohydration) which begins with a diuresis during the first 24 hr after assumption of the recumbent body position (refs. 9, 10, and 18). There is depletion of both cellular volume (CV) and extracellular volume (ECV), but intensive ITE training can maintain plasma volume (refs. 10 and 24) at control levels while interstitial and ECV decreases by 14% (ref. 24).

The significant decreases in muscle thicknesses during the first 2 d of BR, i.e., (S + FHL + TP) with NOE and ITE, and the (VI) in the NOE group, would seem to reflect mainly fluid loss rather than loss of contractile protein. The continued decline of thicknesses from BR 2 to BR 29, particularly in the NOE group and in all groups for (S + FHL + TP), appears to be due to increasing loss of contractile protein (ref. 17) since the negative fluid balance virtually ceases after 48 hr (ref. 10) while the negative nitrogen balance continues.

Dudley et al. (ref. 3) reported decreases in cross-sectional areas of vastus lateralis fast-twitch (by 17%) and of slow-twitch (by 11%) muscle fibers after 30 d of 6° head-down BR which were similar to our NOE decreases of 12% (RF) and 20% (VI). These fiber area decreases were associated with an 8% decrement of the total cross-sectional area of unspecified thigh muscle, determined by computed tomographic analysis, which generally agrees with our 4.3–7.7% decrease in MRI volumes of the posterior leg muscle group where reduction in thickness and volume appears to accompany general body hypohydration. The rapid restoration of (S + FHL + TP) muscle thicknesses in all groups during recovery period supports this hypohydration hypothesis.

There were some deviations in the recovery process. While the NOE group's (RF) thickness continued to decline slowly throughout BR there was no restoration by R + 4. Similarly, the (VI) thicknesses in the NOE and IKE groups remained depressed during recovery. Apparently the mechanism of actively trained (thigh) muscle recovery is different than non-actively trained (leg) muscle recovery, but it does not appear to be solely a function of fluid replacement. Perhaps when contractile protein content is lost during deconditioning, restoration is not apparent by the fourth recovery day.

The rate of thickness decreases of the (S + FHL + TP) muscle group (–9.0% to –12.4%) was about twice to that occurring with calf girth decreases in the three Skylab IV crewmen who exercise-trained for 90 min/d during flight. Two crewmen lost about 2% of their calf girths on the first day (probably water), followed by progressive declines of 3.6% for the three crewmen by flight d25–27 and of 6.3% by d82–83. There was a steep increase in girth during post-flight recovery: to 2.6% below preflight levels on d 4 and only 1.0% below by recovery d8–11.

We conclude that intensive isotonic (dynamic) exercise training is as effective as intensive isokinetic exercise training for maintaining thickness of some anterior thigh muscles but not posterior leg muscles, during prolonged bed rest.

Acknowledgments

The authors express their warm gratitude to the 125 people who had a significant role in this study: especially to C.W. Asling for providing guidance on cross-sectional anatomy, the 19 test subjects, Dee O'Hara, manager of the Human Research Facility, and Edith Crofoot and the nursing and aides staff; the exercise testing group from the University of California Davis; Andrew Ertl, Todd Trowbridge, Dave McKenzie, and Gene Myers; the dietitions, Robin Williams and Victoria Major, and the food preparation staff; the medical monitor Ralph Pelligra; the Bionetics Corp. personnel managers Gail Bennet-Hiley and Ranita Dalton; the co-investigators and their staffs; the Laboratory for Human Gravitational Physiology support and technical staff; Bridget Eller and Angela Hardesty for manuscript preparation; and members of the AIBS review panel.

This work was supported by NASA Tasks 199-21-12, 199-22-12, 199-22-22, 199-22-32, 199-22-44, NAG2-410, and Army Task MRDC-3A161101A-91C.

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Bone Density and Calcium Metabolism

S. B. Arnaud

Decreased os calcis bone density has been measured in healthy subjects (ref. 28) after 6 wk of BR, and decreased lumbar vertebral density of patients treated for prolapsed intervertebral discs was found after 4 wk of BR (ref. 15). Recently LeBlanc et al. reported no change in density (dual photon absorptiometry) of the lumbar spine of healthy subjects at bed rest in the horizontal position for 5 wk (ref. 17). There are few data on alterations in bone density from the effects of bed rest in the –6° head-down position, a more appropriate model for spaceflight with more rapid onset of fluid shifts than those occurring in the horizontal position (ref. 9).

The early metabolic changes in calcium and skeletal metabolism, which precede reduced bone mineralization, in tissue obtained from the iliac crest after 2 wk of horizontal bed rest (ref. 14) have yet to be identified. Calcium exchange increases during bed rest (ref. 19) and increases in calcium and hydroxyproline excretion in the urine become significant after 4 wk of bed rest (ref. 7). Calcium loss, presumed to result from increased bone resorption, increases to 150–200 mg/d and results in a negative calcium balance that does not seem to be counteracted by enhanced intestinal calcium absorption (ref. 1). Direct estimates of soft tissue calcium content, part of the exchangeable pool of total body calcium, have not been made.

Until the discovery of a non-collagenous protein in bone (ref. 13) and its identity with a peptide in the circulation (ref. 25), there was no practical means of evaluating bone cell activity without a bone biopsy. Changes in bone alkaline phosphatase, an enzyme synthesized by the osteoblast, are difficult to interpret because this circulating enzyme can originate in the liver and intestine, as well as in bone (ref. 24). Bone Gla protein (osteocalcin) is a unique product of the osteoblast (ref. 2); circulating levels reflect synthesis of new protein (ref. 26), correlate well with morphologic measurements of bone formation (ref. 19), and can reflect responses to treatment in patients with metabolic bone disease as early as 2 wk after initiation of therapy (ref. 30). The effect of bed rest and inactivity on serum osteocalcin, an indirect measure of osteoblastic activity, has not been determined.

The role of the calcium-regulating hormones in the loss of calcium and the demineralizing effect of acute disuse osteoporosis remains controversial. Parathyroid hormone seems to play a role in the local resorption that occurs following immobilization by plaster casts (ref. 5). Decreased serum parathyroid hormone and urinary cyclic AMP (an index of its end-organ responses) in patients with paraplegia (ref. 29), suggest appropriate responsiveness of the hormone to demineralization. Although data from balance studies indicate reduced intestinal calcium absorption in subjects after 5 wk of bed rest, these findings have not been related to changes in the circulating 1,25-dihydroxyvitamin D, the vitamin D hormone responsible for intestinal calcium absorption (ref. 13).

Methods

Density of the lumbar spine (L1-L4), determined by dual photon absorptiometry (Lunar instrument), and density of the mid-radius of the non-dominant arm (Norland Cameron densitometer), were measured on control day – 1 and R + 2. Twenty-four-hour urine specimens were collected on control day – 5 and on BR days 4 and 26. Blood samples were obtained after completion of the three 24-hour urine collections, and sublingual cells were collected the mornings of blood sampling.

Total serum and urine calcium concentrations were measured either by atomic absorption spectrometry or by a fluorescent calcium binding protein and EGTA titration method (Precision Instruments, Inc.). Ionized calcium and pH were determined on fresh serum injected into microfuge tubes, capped, allowed to clot for 2 hr at 25°C, centrifuged, removed with tuberculin syringes anaerobically, and injected into the ionized calcium analyzer (Radiometer, model ICA-1). Phosphorus was measured by a modified Fiske and Subbarow method (Technicon Autoanalyzer), creatinine by a colorimetric method (Beckman Creatanalyzer), and total protein with the Bradford assay (ref. 4). Osteocalcin was determined with two radioimmunoassays, both of which use an antibody to bovine protein: a commercially available kit (Immunonuclear, Inc.) which uses bovine standard and tracer, and an assay developed at Ames Research Center using standard and tracer from non-human primates which are more similar in structure to human than bovine peptide (refs. 11 and 23). Parathyroid hormone was measured in the laboratory of Dr. R. Marcus (at Stanford University) with a mid-region assay (ref. 1) and 1,25-dihydroxyvitamin D (at Ames Research Center) with the radioreceptor assay (ref. 27). Analyses for a stone risk profile were carried out by Mission Pharmacal, Dallas, TX, and the laboratory of Dr. Pak (ref. 22). Urinary hydroxyproline was measured by Bioscience Laboratories (ref. 10), and urinary cyclic AMP by radioimmunoassay (Immunonuclear, Inc.). Measurements of the concentrations of calcium, phosphorus, magnesium,

sodium, potassium, and chloride in sublingual cells were determined with a method developed by Dr. B. Silver (Spectroscan, Inc.). The cells, scraped from the sublingual region of the mouth after a distilled water rinse, were smeared directly onto a low background carbon slide with an applicator stick and fixed immediately by flooding with a standard cytology fixative (carbowax and alcohol). The intracellular ion concentrations of individual cells were measured by X-ray dispersive analysis selected by electron microscopy. Results are expressed in EXA units:

$$\text{EXA} = \frac{\text{(peak)/(background ratio of X-ray intensity)}}{\text{unit cell volume (800 microns)}}$$

The minimum number of cells (3–10) required for three reproducible values in each subject were analyzed.

Statistical analyses of variance were used to compare data from each group on BR days 4 and 26. The paired t-test was used to evaluate the effects of exercise in the same individuals. Relationships between variables measured were determined primarily by regression analysis of the changes in the variables in the entire group of 19 subjects. Neuman-Keuls and Bonferroni multiple comparison t-tests were used to compare group differences and the changes during bed rest, respectively, of stone risk profile and vitamin D hormone data (SPSS software).

Results

Bone density– There were no statistically significant changes in mean bone densities in the lumbar (L 2-4) vertebrae or in the mid-radius of the three test groups immediately after bed rest (table 1). There was a tendency for lumbar densities to increase and for radial densities to decrease. The change in bone density for the entire group was not related to changes in osteocalcin, parathyroid hormone, 1,25-dihydroxyvitamin D, total blood volume, testosterone, cortisol, urinary calcium, or hydroxyproline. Nine subjects weighing more than 78 kg showed a mean (change in bone density of -0.56 ± 4.1, the same change as 10 subjects weighing less than 78 kg (1.66 ± 4.3); weight changes for these two groups were -2.16 ± 2.3 and -1.52 ± 1.9 kg, respectively.

Individual subject lumbar densities (fig. 1) ranged from –7% (subject 405, isokinetic) to +10% (subject 412, isokinetic). Both subjects had changes in lumbar densities beyond the 50th percentile for age-matched normal men. Lumbar bone density was unrelated to the two subjects' height, weight, age, surface area, percent body fat, or serum osteocalcin; but was inversely related to urine calcium, urine hydroxyproline, serum parathyroid hormone, and serum cortisol (fig. 1).

Table 1. (Mean ± SD) density of lumbar and radius bones before and after bed rest for the three groups

Exercise group	Ambulatory Day – 1	Recovery Day + 2	%Δ
	Lumbar vertebrae (gm/cm^2)		
No exercise	1.130 ± 0.079	1.131 ± 0.107	+0.1
Isotonic	1.144 ± 0.118	1.141 ± 0.115	–0.3
Isokinetic	1.289 ± 0.303	1.295 ± 0.242	+0.5
	Mid-radius (gm/cm)		
No exercise	1.249 ± 0.260	1.243 ± 0.229	–0.5
Isotonic	1.191 ± 0.138	1.184 ± 0.114	–0.6
Isokinetic	1.232 ± 0.104	1.222 ± 0.132	–0.8

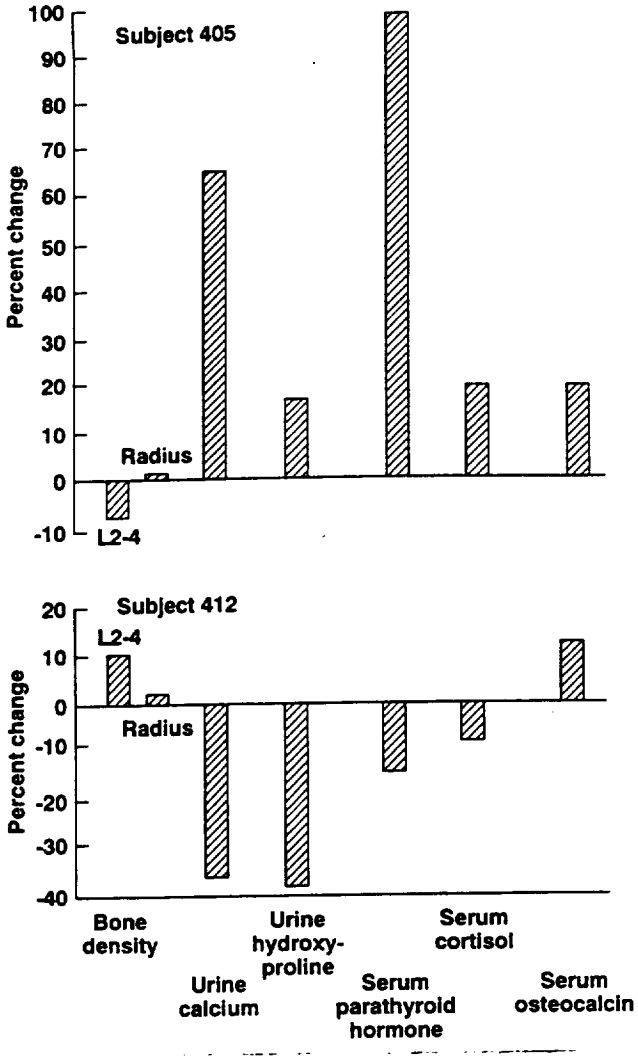

Figure 1. Individual percent changes in lumbar (L 2–4) and radius densities, and indices of bone resorption and formation in urine and blood of two isokinetic group subjects with the greatest increase (412) and decrease (405) in lumbar density on BR day 27.

Calcium homeostasis– Factors involved in the control of serum calcium concentration on BR day 4 and BR day 27 are presented in table 2. Total serum calcium and total protein concentrations were unchanged in all test groups; while serum ionized calcium was increased ($P < 0.01$) only on BR day 27 in the isokinetic and no exercise groups, and unchanged in the isotonic exercise group. There were no significant changes in any test groups in venous pH, serum phosphorus, parathyroid hormone, or in 1,25-dihydroxyvitamin D (table 2). Serum total calcium was correlated significantly with total protein ($r = 0.34$, $P < 0.01$, $N = 56$), but not with parathyroid hormone or 1,25-dihydroxyvitamin D. However, serum ionized calcium was correlated negatively ($r = -0.69$, $P < 0.05$) with venous pH (fig. 2).

Mean serum osteocalcin concentrations, measured with the two procedures, indicated no statistically significant changes in any test group by BR day 27 (table 3). A majority of the subjects (13/19 with the IMN assay, and 14/19 with the monkey assay) exhibited an increase (NS) in osteocalcin on BR day 4. Values from the two assays were not significantly correlated ($r = 0.18$, NS, $N = 57$).

There were no statistically significant changes in urinary variables (volume, creatinine, calcium, phosphorus, hydroxyproline, 3,5 cyclic AMP, prostaglandin E_2, creatinine clearance, percent tubular reabsorption of P, or the calcium/creatinine ratio) on BR day 4 or day 27 (table 4). Urinary hydroxyproline was not correlated significantly with urinary calcium ($r = 0.34$, NS).

Cellular electrolytes– There were significant increases in sublingual cell calcium ($P < 0.05$), phosphorus ($P < 0.05$), and potassium ($P < 0.01$) only on BR day 28, and only in the NOE group (table 5). There were no differences in cellular magnesium, sodium, or chloride in any group during BR.

Urinary stone risk– Urinary stone risk factors were measured on 24 hr urine samples on ambulatory day C – 5, and BR days 8 and 28 (tables 6 and 7).

Ammonium ion production was decreased ($P < 0.05$) in the two exercise groups in the ambulatory and BR 28 samples (table 6). In the ambulatory period the ITE group had the lowest level ($P < 0.05$) of citrate excretion (499 ± 249 mg) compared with 769 ± 155 mg with the NOE and 615 ± 57 mg with the IKE group: BR day 28 IKE citrate was increased ($P < 0.05$). All were well above the lower limit of the normal range of 320 mg/d. Potassium excretion increased ($P < 0.05$) in all three groups on BR day 8 and returned to ambulatory control levels by BR day 28. On BR day 8 oxalate excretion decreased ($P < 0.05$) in the ITE groups, and sulfate excretion increased ($P < 0.01$) in the IKE group. Uric acid excretion decreased ($P < 0.05$) in the ITE group on BR days 8 and 28. Sodium excretion decreased ($P < 0.001$) only in the ITE group on BR day 28. Only urinary volumes, pH, calcium, phosphorus, magnesium, and creatinine were not different from control levels or between groups during BR (table 6).

C-2

Table 2. Mean (±SD) serum variables associated with serum calcium status for the three groups

Exercise group	Ambulatory	Bed rest	
	Day – 1	Day 4	Day 27
Total calcium (mg/dl)			
No exercise	9.0 ± 0.34	9.1 ± 0.18	9.3 ± 0.16
Isotonic	9.5 ± 0.28	9.4 ± 0.30	9.6 ± 0.41
Isokinetic	9.4 ± 0.43	9.2 ± 0.35	9.2 ± 0.32
Total protein (g/dl)			
No exercise	6.2 ± 0.22	6.3 ± 0.69	6.9 ± 0.59
Isotonic	6.8 ± 1.10	6.8 ± 0.71	6.6 ± 0.57
Isokinetic	7.0 ± 0.53	6.9 ± 0.69	7.0 ± 0.45
Ionized calcium (mg/dl)			
No exercise	4.49 ± 0.11	4.78 ± 0.22	4.95 ± 0.14*
Isotonic	4.66 ± 0.36	4.82 ± 0.15	4.98 ± 0.10
Isokinetic	4.58 ± 0.26	4.71 ± 0.17	4.88 ± 0.14*
Venus pH (units)			
No exercise	7.48 ± 0.03	7.45 ± 0.06	7.45 ± 0.07
Isotonic	7.47 ± 0.05	7.45 ± 0.06	7.43 ± 0.06
Isokinetic	7.46 ± 0.03	7.46 ± 0.04	7.44 ± 0.06
Phosphorus (mg/dl)			
No exercise	2.9 ± 0.26	2.9 ± 0.16	2.9 ± 0.16
Isotonic	2.9 ± 0.34	3.2 ± 0.54	3.1 ± 0.63
Isokinetic	2.6 ± 0.45	2.7 ± 0.41	2.8 ± 0.40
Parathyroid hormone (pg/ml)			
No exercise	33 ± 9	31 ± 13	27 ± 8
Isotonic	26 ± 12	27 ± 16	22 ± 11
Isokinetic	27 ± 8	27 ± 15	25 ± 12
1,25-Dihydroxyvitamin D (pg/ml)			
No exercise	50 ± 16	34 ± 6	34 ± 11
Isotonic	44 ± 12	38 ± 20	31 ± 11
Isokinetic	36 ± 13	33 ± 11	33 ± 10

*$P < 0.01$ from ambulatory.

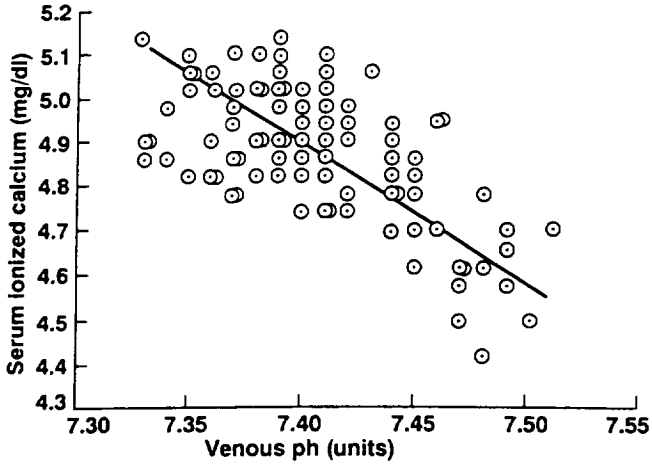

Figure 2. Regression of serum ionized calcium on venous pH with data from the three groups on BR days 4 and 27 ($r = -0.69$, $P < 0.05$).

Relative supersaturation or urinary variables and three supersaturation ratios are presented in table 7. The ITE group exhibited significant ($P < 0.05$) increases in brushite (the stable phase of calcium phosphate in normal acid urine) on BR days 8 and 28, and a decrease ($P < 0.01$) in undissociated uric acid on BR day 8. Similar responses occurred in the IKE group on BR day 8: increased brushite ($P < 0.05$) and decreased ($P < 0.05$) normal and undissociated uric acid. Calcium oxalate, monosodium urate, and struvite were not different from control levels or between groups during BR (table 7).

Table 3. Mean (±SD) serum osteocalcin concentrations for the three groups

Exercise group	Ambulatory	Bed rest	
	Day – 1	Day 4	Day 27
Osteocalcin (ng/ml) (IMN – bovine standard)			
No exercise	2.84 ± 0.82	3.38 ± 0.60	2.97 ± 1.0
Isotonic	3.58 ± 0.77	3.45 ± 0.68	3.34 ± 1.2
Isokinetic	3.28 ± 1.20	3.34 ± 0.70	3.10 ± 1.4
Osteocalcin (ng/ml) (NASA – monkey standard)			
No exercise	7.12 ± 1.13	8.52 ± 2.71	9.20 ± 1.29
Isotonic	7.12 ± 1.20	7.21 ± 1.57	8.32 ± 1.73
Isokinetic	8.57 ± 3.89	9.21 ± 3.97	8.73 ± 4.00

Table 4. Mean (±SD) 24-hour urinary variables for the three groups

Exercise group	Ambulatory	Bed rest	
	Day – 1	Day 4	Day 27
Volume (ml/24 h)			
No exercise	2,071 ± 521	1,704 ± 488	1,801 ± 726
Isotonic	2,420 ± 535	1,750 ± 911	1,861 ± 591
Isokinetic	2,214 ± 669	1,590 ± 586	1,621 ± 723
Creatinine (mg/24 h)			
No exercise	1,761 ± 379	1,805 ± 244	1,835 ± 322
Isotonic	1,753 ± 213	1,817 ± 219	1,785 ± 303
Isokinetic	1,776 ± 118	2,008 ± 339	1,787 ± 183
Calcium (mg/24 h)			
No exercise	217 ± 63	239 ± 76	252 ± 88
Isotonic	239 ± 49	300 ± 36	290 ± 17
Isokinetic	223 ± 81	293 ± 92	227 ± 77
Phosphorus (mg/24 h)			
No exercise	877 ± 127*	1,011 ± 268**	911 ± 101
Isotonic	1,048 ± 254	1,430 ± 425	815 ± 127
Isokinetic	942 ± 233*	1,223 ± 399	906 ± 291
Hydroxyproline (mg/24 h)			
No exercise	27.6 ± 15.7	20.0 ± 8.2	32.4 ± 11.2
Isotonic	26.7 ± 9.2	27.6 ± 10.8	23.6 ± 7.7
Isokinetic	30.4 ± 9.7	32.7 ± 15.8	34.0 ± 10.1
3'5'-Cyclic adenosine monophosphate (μg/24 h)			
No exercise	2.07 ± 0.50	2.06 ± 1.21	1.80 ± 0.80
Isotonic	2.26 ± 1.50	1.35 ± 0.83	1.66 ± 0.63
Isokinetic	2.84 ± 1.07	1.63 ± 0.64	2.26 ± 0.93
Prostaglandin E_2 (μg/24 h)			
No exercise	6.41 ± 4	5.90 ± 6	3.83 ± 3
Isotonic	2.20 ± 1	5.44 ± 5	4.64 ± 5
Isokinetic	1.81 ± 2	4.46 ± 6	3.38 ± 3
Creatinine clearance (ml/min/1.73 m^2)			
No exercise	140 ± 25	132 ± 34	120 ± 31
Isotonic	120 ± 16	131 ± 19	121 ± 10
Isokinetic	129 ± 38	120 ± 20	121 ± 19
Phosphorus (% tubular reabsorption)			
No exercise	85 ± 4	83 ± 5	85 ± 5
Isotonic	77 ± 11	77 ± 9	82 ± 7
Isokinetic	80 ± 5	79 ± 11	84 ± 2
Calcium/creatinine ratio			
No exercise	0.123	0.132	0.137
Isotonic	0.136	0.165	0.162
Isokinetic	0.126	0.146	0.127

*N = 4, **N = 6

Table 5. Mean (±SD) sublingual intracellular electrolyte concentrations (EXA units/800 μ^3) for the three groups

Exercise group	Ambulatory	Bed rest	
	Day – 1	Day 4	Day 28
Calcium			
No exercise	81 ± 14	96 ± 22	109 ± 15*
Isotonic	69 ± 11	75 ± 15	81 ± 10†
Isokinetic	77 ± 16	75 ± 14	69 ± 11
Phosphorus			
No exercise	1,180 ± 109	1,231 ± 97	1,577 ± 209*
Isotonic	1,123 ± 46	1,154 ± 66	1,220 ± 130
Isokinetic	1,153 ± 84	1,140 ± 110	1,170 ± 108
Magnesium			
No exercise	775 ± 18	790 ± 20	811 ± 16
Isotonic	766 ± 25	780 ± 33	785 ± 34
Isokinetic	788 ± 38	776 ± 33	796 ± 26
Potassium			
No exercise	92 ± 29	141 ± 98	206 ± 60**
Isotonic	95 ± 25	90 ± 11	117 ± 31
Isokinetic	93 ± 26	90 ± 40	101 ± 24
Sodium			
No exercise	13 ± 1	14 ± 1	14 ± 1
Isotonic	13 ± 1	14 ± 1	13 ± 1
Isokinetic	13 ± 1	14 ± 1	15 ± 2
Chloride			
No exercise	26 ± 4	28 ± 3	24 ± 4
Isotonic	24 ± 5	27 ± 6	22 ± 4
Isokinetic	27 ± 6	31 ± 7	26 ± 7

*$P < 0.05$, **$P < 0.01$ from ambulatory, †$N = 6$

Table 6. Mean (±SD) general urinary stone risk factors for the three groups

	Vol (liters)	pH	Calcium (mg)	Phos-phorus (mg)	Oxalate (mg)	Sodium (meq)	Potas-sium (meq)	Magne-sium (mg)	Ammo-nium (meq)	Citrate (mg)	Sulfate (mmol)	Uric acid (mg)	Creatin-ine (mg)
No exercise													
Ambulatory	1.73	6.11	224	1049	45.7	215	67	171	41	769	24.9	886	1881
	0.40	0.35	89	144	4.0	55	9	24	4	155	3.2	219	255
BR day 8	1.75	7.22	213	1160	39.1	261	107*	159	34	848	28.4	670	1568
	0.57	1.02	75	258	8.6	39	22	42	13	261	7.4	78	147
BR day 28	1.81	7.16	184	1315	46.6	156	78	128	41	697	24.5	728	1833
	0.61	1.43	83	277	15.3	74	21	64	7	279	6.2	120	184
Isotonic exercise													
Ambulatory	2.24	6.15	269	1340	58	254	82	157	35†	499†	29.2	928	1964
	0.60	0.29	64	361	14	25	21	23	5	249	3.7	107	178
BR day 8	1.55	6.55	301	1207	40.9*	222	104*	156	27	563	29.1	648*	1638
	0.40	0.45	127	240	9.6	49	16	43	9	166	5.3	104	262
BR day 28	1.76	6.82	289	1336	43.6	177#	79	167	31†	562	24.5	620*	1818
	0.66	1.05	73	295	10.6	35	18	61	7	146	4.9	213	201
Isokinetic exercise													
Ambulatory	1.77	6.51	213	1350	52.0	220	75	144	33†	615	27.0	742	1912
	0.64	0.99	89	408	18.8	69	16	41	6	57	5.6	140	202
BR day 8	1.73	7.22	263	1324	40.9	230	112*	156	30	732	33.2**	620	1908
	0.62	1.00	73	175	13.4	47	20	20	5	239	6.5	111	258
BR day 28	1.76	6.60	275	1379	44.9	193	88	134	30†	749*	24.6	608	1947
	0.58	0.73	112	255	7.8	39	14	42	66	168	3.5	254	188

*$P < 0.05$, **$P < 0.01$, †$P < 0.05$ versus comparable no-exercise value, #$P < 0.001$ from ambulatory

Table 7. Mean (±SD) specific urinary stone risk factors for the three groups

	Relative supersaturation ratio			Relative supersaturation					
	Brushite	Calcium oxalate (mg)	Monosodium urate	Brushite	Calcium oxalate	Monosodium urate	Struvite	Uric acid	Undissociated uric acid concentration
No exercise									
Ambulatory	2.10	8.82	6.37	1.67	2.10	4.68	1.84	2.01	5.47-04
	0.46	3.16	3.16	0.37	0.75	2.32	1.22	1.19	3.25-04
Bedrest day 8	4.51	6.11	7.58	3.58	1.45	5.56	172	0.36	9.85-05
	2.63	2.87	5.26	2.09	0.68	3.84	360	0.44	1.20-05
Bedrest day 28	3.23	6.24	4.66	2.57	1.49	3.42	326	1.05	2.86-04
	1.99	2.43	3.79	1.58	0.58	2.78	533	1.30	3.54-04
Isotonic exercise									
Ambulatory	2.74	10.4	5.22	2.18	2.48	3.83	1.38	1.45	3.96-04
	1.50	4.3	3.32	1.19	1.02	2.44	1.14	0.83	2.27-04
Bedrest day 8	6.38**	11.1	7.02	5.07**	2.65	5.15	9	0.87	2.27-04**
	1.41	4.5	3.48	1.12	1.07	2.55	10	0.81	2.21-04
Bedrest day 28	5.82*	10.9	3.97	4.63*	2.62	2.91	140	0.76	2.07-04
	1.78	4.1	3.43	1.42	0.98	2.51	344	0.88	3.39-04
Isokinetic exercise									
Ambulatory	3.21	8.85	6.10	2.55	2.11	4.48	52	1.45	3.95-04
	1.67	4.1	3.05	1.33	0.99	2.24	132	1.10	2.98-04
Bedrest day 8	6.16	7.68	5.82	4.90*	1.83	4.27	190	0.43*	1.18-04*
	2.53	3.56	2.24	2.10	0.85	1.65	372	0.53	1.44-04
Bedrest day 28	5.40	10.4	3.80	4.29	2.48	2.79	79	0.82	2.22-04
	3.49	4.6	1.73	2.77	1.09	1.27	203	0.69	1.88-04

* $P < 0.05$, ** $P < 0.01$ from ambulatory

Summary of Results

Bone density– Mean lumbar and radial densities were unchanged in the three groups during BR. Change in lumbar vertebrae density in two isokinetic group subjects of +7% and –10%, respectively, were associated with appropriate metabolic and hormonal responses.

Calcium homeostasis– The increase in serum ionized calcium at the end of BR, accompanied by mild metabolic acidosis, was not associated with the unchanged serum total calcium. The decreasing trends (NS) in serum 1,25-dihydroxyvitamin D during BR were most marked in the NOE group, and least marked in the IKE group.

Cellular electrolytes– There were significant increases in sublingual cell calcium, phosphorus, and potassium at the end of BR only in the NOE group; i.e., the cellular concentrations of these three electrolytes were suppressed by the two exercise regimens.

Urinary stone risk– Significant increases in the relative supersaturation of brushite (the stable form of urinary calcium phosphate) only in the two exercise groups during BR, were not associated with concomitant increases in urinary excretion of calcium or phosphorus.

Discussion

Exercise effects– The only variables that exhibited clear differences between the no-exercise group and the two exercise groups were significant increases in some cellular ion concentrations (calcium, phosphorus, potassium), suggesting they were suppressed (remained within ambulatory levels) by the exercise regimens. Since there were no serum variables that responded differently in the two exercise groups, the selective maintenance of plasma volume ($\Delta = -1.5\%$, NS) in the ITE group, and not in the IKE group ($\Delta = -14.7\%$, $P < 0.05$), eliminates hypovolemia as a factor. While it is generally acknowledged that weight-bearing activity (exercise) has a great effect on bone metabolism and density (ref. 16), there are no studies that have compared the effects of isotonic and isokinetic exercise regimens. And data on the effects of long-term exercise training on calcium metabolism are sparse.

Bone density– The lack of significant change in mean lumbar and radius densities after 27 d of BR agrees with the findings of others. LeBlanc et al. (ref. 17) also found no significant change in mean vertebral (L 2–4) density in six men after 35 d of absolute, horizontal BR; and Vico et al. (ref. 31) reported no significant change in bone mass in the iliac crest in 20 men after horizontal BR for 28 d. No change in os calcis densities have been reported up to 28 d of BR, but mineral losses of 27% to 54% were reported in the left os calcis of the three men after 30 to 36 wk of BR (ref. 32). Bone mineral content, measured with dual-photon (153 Gd) absorptiometry, lumbar (L 2–4) vertebrae in 34 patients (18–60 yr) hospitalized for lumbar disc protrusion, decreased by 3.4% after 11–61 d ($\bar{X} = 27$ d) of bed rest (ref. 15). Bone mineral content decreased by 0.9%/wk and recovery was nearly complete after 4 mo of reambulation. Dual photon measurements are reproducible to ±2% (ref. 33). Seven subjects had lumbar density increases above 2%, and six had density decreases below 2%. Except for the two isokinetic group subjects, the lumbar densities of the remaining subjects were within the 95% confidence limits for this measurement. These variable results raise questions of the variability of lumbar vertebral mineral content in normal ambulatory people.

Respective decreased lumbar vertebrae density of 7%, and increased density of 10%, were associated with appropriate and opposite changes in urine calcium, urine hydroxyproline, serum parathyroid hormone, and serum cortisol. Serum osteocalcin increased in both subjects. Increased production of parathyroid hormone (a potent activator of osteoclastic bone resorption) to the upper limit of normal in subject 405, may have accounted for his loss of lumbar bone density. But stimuli for production of parathyroid hormone—hypocalcemia induced by diet or acidosis, increased catecholamine secretion (ref. 8), or hypercortisalemia—were not present for this subject when compared with the other five isokinetic group subjects (except 412). A more likely explanation is that these two subjects' levels were at the tails of the normal distribution curve—the subject with decreased density manifested mainly deconditioning effects, and the subjects with the increased density manifested mainly the exercise-training effects. Lack of change in radius densities could be attributed to extensive use of the arms during isokinetic exercise for moving the body in bed and for performance of daily activities. There was no significant relationship between change in bone density and body weight, change in body weight, or diet. Caloric and calcium intakes were well within recommended allowances for these men, and additional calories were provided for the additional exercise energy expenditure. However, there was a tendency for the subjects weighing more than 78 kg to lose more weight during BR (2.16 kg) than those weighing less than 78 kg (1.52 kg): mean change in bone density was –0.56 for the heavier, and +1.66 for the lighter subjects. Reduced caloric intake was one factor in the development of osteoporosis in young women runners (ref. 20), but it has not been identified as a factor in the etiology of bed-rest bone demineralization.

Calcium homeostasis– The major alteration in calcium homeostasis was the increase in serum ionized calcium

for all subjects (N = 19), from an ambulatory control level of 4.58 ± 0.27 mg/dl to the BR day 27 level of 4.93 ± 0.13 mg/dl ($P < 0.01$), which would not have been caused by either exercise regimen. This hypercalcemia was associated with mild metabolic acidosis ($\Delta pH = -0.06$ units, $p < 0.05$) due perhaps to residual effects of the exercise cardiac output test, coupled with a mild disturbance in pulmonary ventilation from the head-down tilt position.

Cellular electrolytes– The most significant finding was the increase in cellular total calcium, phosphorus, and potassium only in the no-exercise group implying that the exercise training regimens depressed these electrolytes. Most cellular calcium is sequestered inside organelles (e.g., mitochondria), with relatively smaller amounts bound to membranes and as the free ion in cytoplasm (ref. 6). Most cellular calcium emanates from metabolic process which facilitates cellular exchange. There is more rapid movement of the exchangeable calcium pool in bed-rested subjects compared with ambulatory individuals (refs. 13 and 18). The increased cellular calcium and phosphorus concentrations are not the result of cell damage since there was no loss of potassium (ref. 6). In fact, potassium actually increased to a greater degree than calcium or phosphorus. Since sublingual cells are renewed every 3 days, these increased ion concentrations, while perhaps induced by cephalic fluid shifts at the beginning of bed rest, persisted thereafter when fluid shifts were approaching equilibrium. Also, these increased ion concentrations were not related to the differential changes in plasma volume in the three groups.

Urinary stone risk– The variety of elements in the urine that can influence stone formation in this study showed a different profile from that found in subjects bed-rested in the horizontal position; primarily with respect to the amount of calcium excreted. Only five of the 19 subjects, some from each group, had increased urinary calcium excretion that approximated that formed in horizontal bed-rested subjects (ref. 1). It was not possible to identify factors which could predict this calcium loss.

In spite of the finding of no significant change in urinary calcium for all subjects, the increased brushite excretion in the two exercise groups, along with the trend toward higher pH and lower urine volumes, would tend to favor stone formation.

The reason for the lack of calciuria and phosphaturia is unclear. Dietary calcium averaged about 300 mg/d, more than that consumed by subjects in most horizontal bed rest studies. Protein intake exceeding 125 gm/d can amplify calcium loss; protein intake in the present study averaged 114 gm/d, slightly more than the amount consumed by horizontally bed-rested subjects. The intentional lack of rigid dietary control in the present study was to simulate the dietary regimen of astronauts prior to and during flight. We were unable to demonstrate any significant relationship between the various dietary substances and the amount of calcium in the urine. Perhaps there is a degree of self-regulation that helps to maintain calcium homeostasis during prolonged bed rest.

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Performance and Mood-State Parameters during 30-Day 6° Head-Down Bed Rest with Exercise Training

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Abstract

DeRoshia CW, Greenleaf JE. Performance and mood-state parameters during 30-day 6° head-down bed rest with exercise training. Aviat. Space Environ. Med. 1993; 64:0000-0000. In press.

The study was designed to determine if performance and mood impairments occur in bed-rested subjects, and if different exercise-training regimens modify of prevent them. Eighteen normal, healthy men were divided on the basis of age, peak oxygen uptake, and maximal isometric knee extension strength into three similar groups: no exercise (NOE), isotonic exercise (ITE), and isokinetic exercise (IKE). A 15-min battery of 10 performance tests and eight mood and two sleep scales were administered daily during ambulatory control, 30 days of absolute bed rest (BR), and four days of ambulatory recovery. Performance test proficiency increased ($P < 0.05$) for all three groups during BR in 7 of 10 tests and there were no consistent significant differences between the three groups. However, during BR, the ITE group was distinguished from the other groups by a decline ($P < 0.05$) in the activation mood dimension and in two of its constituent scales (motivation and concentration), and by improvement ($P < 0.05$) in the trouble-falling-asleep and psychological-tension scales. Since few deleterious changes in performance and mood occurred in the three groups and did not exceed baseine ambulatory levels, we conclude that mood and performance did not deteriorate in response to prolonged BR and were not altered by exercise training. However, the decline in activation mood scales in the ITE group may reflect overtraining or excess total workload in this group.

Introduction

Bed-rested individuals are subjected to restricted mobility, moderate confinement, and isolation, all of which probably result in reduced proprioceptor and kinesthetic input (refs. 19 and 28), particularly in response to the change from an upright to a horizontal posture (ref. 28). Moderate confinement or restriction of body movement, in combination with perceptual deprivation, can result in altered mood states and in decrements in intellectual and perceptual-motor task performance in otherwise normal, healthy people (ref. 28). Moreover, performance of acute physical exercise can ameliorate psychological stress (ref. 18), and more extensive physical exercise during 7 days of perceptual deprivation significantly ameliorated perceptual impairments (ref. 27).

Subjects bed rested for up to 120 d suffer from asthenia defined as a loss of strength, energy, motivation and concentration, with increased fatigability, sleep impairment, and sensitivity to physical or emotional stressors (refs. 1, 14, 17, 22, and 23). Performance decrements in controlled scanning (refs. 25 and 26) and productive thinking (ref. 2) have been reported after the initial adaptation to BR, but others have found no consistent performance changes during BR (refs. 19, 20, 23, and 24).

Physical exercise training during BR attenuated, but did not eliminate, decrements in controlled scanning (ref. 26). Exercise training during BR has a much greater remedial effect for counteracting mood and sleep impairment, relative to non-exercised bed-rested subjects (refs. 1, 19, 22, and 27). Therefore, impairments in performance, sleep, and mood states observed during BR without exercise training may be a direct consequence of reduced hydrostatic pressure, a diminution of the psychologically beneficial effects of exercise, or the attenuation of exercise associated stimuli such as proprioceptor feedback and mechanical forces on muscles and bones.

The overall purpose of this project was to devise lower-extremity isotonic and isokinetic exercise training regimens that would maintain maximal oxygen uptake and muscular strength and endurance, respectively, during 30 days of BR deconditioning. As part of the project, we wanted to determine if performance and mood

impairments occur in bed-rested subjects, and if different exercise-training regimens modify or prevent them.

Methods

Subjects– Informed consent was obtained from 18 men (age 36 ± 1 yr, ht. 178 ± 2 cm, wt. 76.8 ± 1.8 kg) selected from a pool of over 2,000 applicants by means of an initial telephone interview; a personal interview; a comprehensive medical examination, including blood and urine analysis and a treadmill stress test; and observation during a preliminary orientation test phase. Members of the final group were selected on the basis of their motivation, friendliness, compatibility, and their assessed ability to adapt to moderate isolation and confinement. The interview procedure was used in place of standard personality tests because such tests are generally designed to select out those with psychopathological traits rather than to select in those with more optimal personality traits (ref. 10).

Procedure– This study was conducted in the Human Research Facility (HRF) at Ames Research Center in the summer of 1986. Details of the protocol have been published (ref. 8). The 18 men who particpated were divided, on the basis of age, peak oxygen uptake, and maximal isometric knee extension strength, into three similar groups: no exercise (NOE, N = 5), isotonic exercise (ITE, N = 7), and isokinetic exercise (IKE, N = 6) training groups.

The men lived for 41 days in the HRF and ate a controlled, nutritionally adequate normal diet containing 2,678 ± 75 kcal/day (NOE), 2,833 ± 82 kcal/day (ITE), and 2,890 ± 75 kcal/day (IKE) composed of 20% protein, 62% carbohydrate, and 18% fat (ref. 9). From 3 to 11 weeks (wk) after the orientation test training the subjects were admitted to the HRF for the pre-BR ambulatory control period (7 d), the –6° head-down BR period (30 d),and the ambulatory recovery period (4 d). The men were housed in two-to-four-man rooms with moveable partitions so they could be isolated at night or during testing. The photoperiod was 16 hr light:8 hr dark (lights on at 0700h). During the ambulatory control period, the men exercised for 30 min/day sitting on a cycle ergometer to retard confinement deconditioning. During BR, the subjects were restricted to absolute head-down recumbency, except during meals when they were permitted to prop their heads up on an elbow; as time permitted, they were allowed to nap during the day, to freely interact with the staff, investigators, and other subjects, to engage in personal hobbies, to listen to personal stereo systems, to read, and to view television and videocassette movies. No visitors were permitted in the facility but the men had unlimited outside communication by means of a single pay telephone, to which they were transported by gurney.

Exercise training procedure: Lower-extremity IKE training and peak testing were conducted with the subjects in the supine body position on an electronic cycle ergometer (Quinton Imaging/Ergometer Table, model 846T, Seattle, WA 98121). Isotonic exercise training was performed for 30 min in the a.m. and 30 min in the p.m. for 6 d/wk. Peak oxygen uptake testing was performed weekly during BR on all subjects.

Lower-extremity IKE training was also performed for 30 min in the a.m. and 30 min in the p.m. for 6 d/wk on a LIDO computer-controlled ergometer (Loredan Biomedical, Inc., Davis, CA 95617). Peak IKE testing was performed weekly during BR by all subjects (ref. 9). The design of the two exercise training regimens was to maximize intensity to have sufficient duration to maintain peak oxygen uptake in the ITE group and strength and endurance in the IKE group, while minimizing risk of overtraining and injury (ref. 8). Only three subjects had symptoms that required alteration of their training regimens. One ITE subject had the load reduced from 90% to 40% in three consecutive exercise periods because of calf-muscle strain. Left lower-extremity training was cancelled for one ITE subject on consecutive training periods because of muscle pain. One a.m. training session was cancelled for another ITE subject and the p.m. session was performed at a lower level than expected because of gastrointestinal distress.

Performance tests– Performance testing was done with the microcomputer-based Automated Portable Testing System (APTS, Essex Corp., Orlando, FL 32803), which consisted of a portable NEC 8201A personal computer, test software, and an eight-line liquid crystal display and was selected for portability, reliability, test automation capability, and utility for short-duration testing (refs. 4 and 13). Ten performance tests (ref. 13) (table 1) from the 30 recommended PETER program tests (4) were selected to evaluate verbal cognitive reasoning (REASON), encoding (CODSUB), visuo-spatial ability (MANKIN), pattern comparison (PATRNC), pursuit tracking (ACM), and short term memory (STERNB), as well as the motor function abilities: preferred hand tappping (PHTAP), two-finger tapping (TFTAP), nonpreferred hand tapping (NPTAP), and simple reaction time (SREACT).

Table 1. Performance proficiency and mood-state tests

Performance Tests	Duration (sec)	Output Metric
Simple Reaction Time (SREACT)	60 or 15 trials	Latency (msec)
Code Substitution (CODSUB)	75	#Right - #Wrong
Pattern Comparison (PATRNC)	75	#Right - #Wrong
Sternberg Short Term Memory (STERNB)	75	#Right - #Wrong
Air Combat Maneuver Pursuit Tracking (ACM)	120	Score (# of hits)
Two Finger Tapping (TFTAP)	10 (two runs)	Speed (# alternate key presses)
Preferred Hand Tapping (PHTAP)	10 (two runs)	Speed (# alternate key presses)
Non-preferred Hand Tapping (NPTAP)	10 (two runs)	Speed (# alternate key presses)
Manikin Spatial Transformation (MANKIN)	60	#Right - #Wrong Log Latency (msec)
Grammatical Reasoning (REASON)	90	#Right-#Wrong

Mood state Tests	Test Adjectives
Activation Mood Dimension	Mean of Four Scales Below
Motivation to Perform (MOTIV)	Bored (0)/Interested (10)
Arousal State (AROUS)	Sleepy (0)/Alert (10)
Fatigue Level (FATIG)	Weary (0)/Energetic (10)
Ease of Concentration (CONCN)	Very low (0)/Very High (10)
Affective Mood Dimension	
Psychological Tension (TENSE)	Tense (0)/Relaxed (10)
Elation (HAPPY)	Sad (0)/Happy(10)
Physical Discomfort (PDISC)	Very high (0)/Very low (10)
Contentedness (PLEAS)	Unpleasant (0)/Pleasant (10)
Sleep Quality	
Trouble Falling Asleep (SLEEP)	Much worse (0)/Much better (10)
Number of Waking Episodes (WAKE)	Total episodes (Range 0-6)
Self-Rated Performance	
Relative to that on the previous test battery	Much worse (0)/Much better (10)

The number of trials required for performance test means, variances, and correlation matrices to stabilize during training was determined by the methods of Bittner (ref. 3). The five performance tests with error scores (REASON, CODSUB, MANKIN, PATRNC, STERNB) were analyzed as net accuracy (table 1). The MANKIN test responses were also evaluated as log-latency since this transformation is more reliable than accuracy scores (ref. 6). However, since no ceiling effects were detected in accuracy scores (Cochran's homogeneity of variance test), and no important differences between analyses done on accuracy or log-latency scores were detected, MANKIN accuracy scores were used as a measure of spatial ability.

Mood-state tests– A visual analog scale (VAS) mood test was developed independently and incorporated into the APTS performance software. Visual analog scale mood tests provide fast and reliable mood assessment (refs. 5 and 15) with a high degree of mood-state resolution and less chance of subject noncompliance, response stereotyping, or remembered responses (ref. 15). It provided 21 levels of mood-state resolution on a 10-cm scale between the two mood-state adjectives (table 1). The test included eight mood scales, two sleep questions extracted from the St. Mary's sleep questionnaire (ref. 7) to document sleep latency and disturbance, and a measure of self-rated performance (table 1).

Using the validation procedure of Monk (ref. 15), the eight mood scales were allocated four each into two composite major mood dimensions (table 1). The global "Affective Mood Dimension" which included measures of feelings or affective states incorporated physical discomfort (PDISC), elation (HAPPY), psychological tension (TENSE), and contentedness (PLEAS) indices. The global vigor, or "Activation Mood Dimension" which incorporated measures of activation states included energy level (FATIG), arousal state (AROUS), motivation to perform (MOTIV), and ease of concentration (CONCN). Except for the physical discomfort scale, the other seven mood-state scales have been validated

(ref. 5). The PDISC indicated the degree of physical uneasiness or the extent of mild aches and pains which are common at the onset of bed rest (refs. 2, 14, and 17). These two global dimensions were statistically distinct and differentially sensitive to such factors as sleep loss, diurnal rhythms and seclusion (ref. 15). Since the mood-state parameters comprising the Affective and Activation Mood Dimensions used were not identical with those used by Monk (ref. 15), paired mood-scale correlation coefficients within and between these two dimensions were ranked and compared with the Mann-Whitney U-test. Correlation coefficients were higher ($P < 0.05$) for paired scales within the two global scales (mean $r = 0.43$ and 0.41, respectively) than between them (mean $r = 0.31$), thereby validating the separate clustering of the mood scales into two global mood dimensions. The PDISC scale had a significantly higher correlation with the mood scales within the Affective Mood Dimension (mean $r = 0.42$, $P < 0.05$), than with the mood scales within the Activation Mood Dimension (mean $r = 0.22$, NS), thereby justifying its placement in the Affective Mood Dimension.

The mood test initiated the APTS test battery to avoid possible modulation of mood responses by the performance tests. After an 8 to 10 trial training period during orientation and one training test at the onset of the ambulatory control period, this 15-min test battery was given to all subjects daily during the ambulatory control, BR, and ambulatory recovery periods in the late afternoon at least 1–2 hr after exercise, showers or naps. The computer was located directly below the heads of prone subjects on gurneys. The Sleep Quality scales were trouble-falling-asleep (SLEEP), scored on a much worse (0) to much better (10) scale, and number of waking episodes (WAKE) scored on a total episode (0–6) scale (table 1). For the Self-Rated performance test the men rated their overall performance on all performance tests with respect to their overall performance on the previous test battery (table 1).

Composite performance– The measures of performance proficiency (i.e., accuracy, number of alternate key-presses, reaction time latency) had widely differing magnitudes and ranges. Also, reaction time latency differed in direction of improvement from the other tests. Therefore, to obtain a composite measure of overall performance, daily values for each test were converted to integer ranks with the "worst" (minimum = 1) and "best" (maximum = 50). The daily ranks for each test were then averaged across tests for each subject and then averaged across subjects by exercise group (fig. 1). The mean of the three tapping tests was computed prior to data ranking to avoid providing excessive weight to the tapping data in the composite performance means.

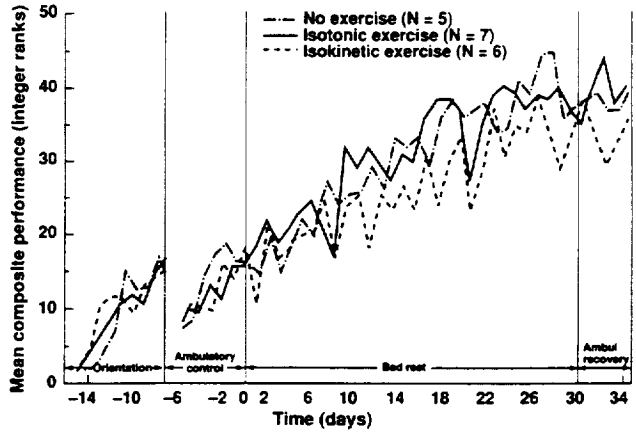

Figure 1. Mean daily composite performance levels expressed as integer ranks (1 = minimum and 50 = maximum). Values are group means for each of eight performance tests (including mean of the three tapping tests) during training (10 trials), ambulatory-control, bed rest, and ambulatory-recovery for the three groups.

Questionnaire composition– On the last day of BR (day 30), the subjects were asked to respond to the following two questions to assess their impressions of the study and performance tests: What aspects of the bed rest study environment were pleasant or rewarding or unpleasant and irritating? Did you look forward to the daily performance test as an activity to relieve the boredom of the study environment or did you perceive the test as an unwelcome interruption of your daily routine and activities?

Statistical analyses– The three exercise groups were evaluated for study treatment-period (orientation, ambulatory control, BR, and ambulatory recovery) effects, and BR-day treatment effects upon the performance and mood test means, by two-way repeated-measures analysis of variance (ANOVA). Statistically significant differences in treatment means were compared with the Newman-Keuls test. Bed-rest-day-dependent mean trends were also evaluated by linear regression (LR) with slope comparison by analysis of covariance (ANCOVA). The resultant percentage changes for the performance tests are presented in figure 2 and the corresponding absolute changes for the mood-state and sleep-quality scales are presented in figure 3. The null hypothesis for ANOVA, ANCOVA and LR was rejected when $P < 0.05$; nonsignificant differences were indicated by NS.

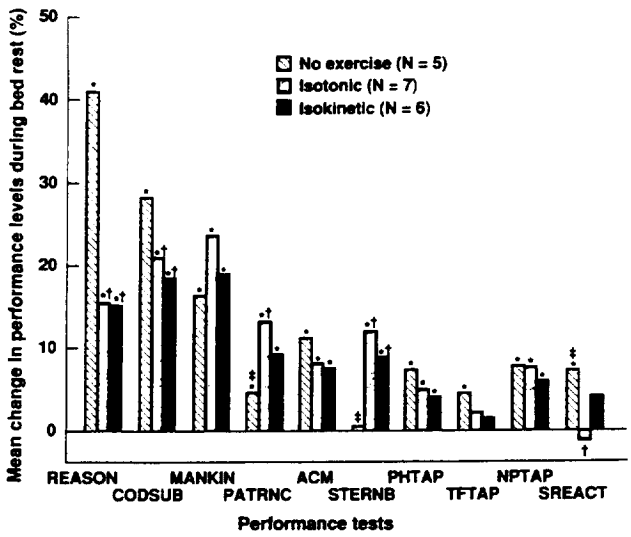

*Figure 2. Mean percent change in performance proficiency test scores during bed rest in the three groups, as determined by linear regression. Test abbreviations are defined in table 1. *P < 0.05 from zero slope, †P < 0.05 from NOE group, ‡P < 0.05 from ITE group.*

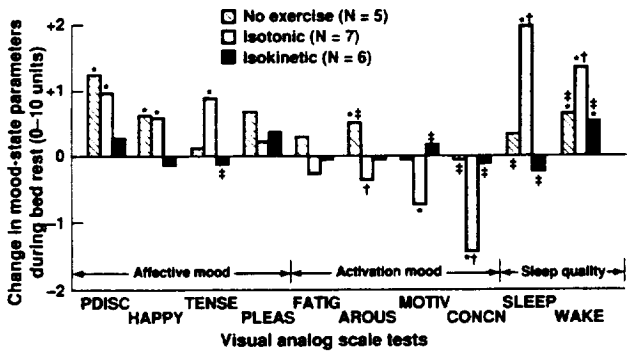

*Figure 3. Mean change in activation and affective mood state parameters and sleep quality scales during bed rest in the three groups, as determined by linear regression. Test abbreviations are defined in table 1. Zero on the y-axis indicates no change during bed rest, a positive change indicates relative improvement, and a negative change indicates relative deterioration. *P < 0.05 from zero slope, †P < 0.05 from NOE group, ‡P < 0.05 from ITE group.*

Results

The assignment of the subjects to the three groups was appropriate since no initial differences in performance levels or mood states were detected. As a reference, changes in peak oxygen uptake after BR were +2.6% (NS) with ITE, –9.1% ($P < 0.05$) with IKE, and –18.2% ($P < 0.05$) with NOE (ref. 8).

Performance tests– During BR all performance scores improved in the three subject groups (fig. 1), except for the unchanged reaction time (+1.2%, NS) in the ITE group (fig. 2). Otherwise, improvement ranged from 7.7% (NOE: NPTAP, $P < 0.05$) in the motor tasks to 40.9% (NOE: REASON, $P < 0.05$) in the cognitive tasks (fig. 2) and was significant ($P < 0.05$, LR) in all three groups in 7 (except TFTAP, SREACT, and STERNB) of the 10 tests.

There was no significant difference between exercise groups in any performance test by treatment regimen. The significant differences occurred only between the two exercise groups and the NOE group during BR (ANCOVA, fig. 2). These differences were inconsistent as the exercise groups improved in STERNB (ITE + 12%, $P < 0.05$; IKE + 9%, $P < 0.05$) relative to the NOE (+0.3%, NS) group, but the NOE group improved in the cognitive tests (REASON: NOE + 41%; ITE and IKE + 15%, $P < 0.05$; CODSUB: NOE + 28%, ITE + 21%, IKE + 18%, $P < 0.05$), relative to the exercise groups.

Mood and sleep quality– The Activation Mood Dimension showed no treatment-regimen or BR day by exercise group effects. However, the mean Activation Dimension score declined during BR by 0.2 units ($P < 0.05$, LR). CONCN was the only Activation Dimension parameter that changed during BR (–0.6 units, $P < 0.05$). A marked deterioration in the Affective Mood Dimension of 2–7 d duration occurred at the onset of BR and was most pronounced in the PDISC mood scale. This deterioration was significant for BR d1 relative to pre-BR d4 and BR d8 ($P < 0.05$). Subsequent improvement (ANOVA by BR day) in the Affective Mood Dimension was evident in ITE and NOE, $P < 0.05$, fig. 3). The means of daily Affective Mood Dimension during BR were better fitted by second-degree polynomials ($r^2 = 0.77$, $P < 0.05$) than by linear regression ($r^2 = 0.2$, $P < 0.05$). These curvilinear trends peaked from BR d17 (IKE) to d18 (ITE, NOE), then declined to the end of BR.

No treatment regimen by exercise group effects were detected by ANOVA for the Affective Mood Dimension. However, BR-day effects were found for the Affective Mood Dimension, where improvement occurred in ITE from BR d1 to d11 ($P < 0.05$), and in NOE from BR d1 to d3 ($P < 0.05$).

The ITE group exhibited the only significant ($P < 0.05$) trend during BR in the Activation Mood Dimension; this decline was significant relative to NOE (ANCOVA, $P < 0.05$). All four activation mood parameters (table 1) exhibited a declining trend (FATIG and AROUS, NS, MOTIV and CONCN, $P < 0.05$) during BR in ITE (fig. 3), with significant progressive deterioration in MOTIV relative to IKE ($P < 0.05$), AROUS relative to

NOE ($P < 0.05$), and CONCN (relative to IKE and NOE, $P < 0.05$).

In contrast, during BR, ITE showed improvement in TENSE relative to IKE ($P < 0.05$), in SLEEP relative to IKE and NOE ($P < 0.05$), and in WAKE relative to IKE and NOE, ($P < 0.05$). A regimen by variable interaction ($P < 0.05$) was found only for the SLEEP scale, in which sleep quality improved significantly from BR to ambulatory recovery in ITE (5.5 to 7.3, $P < 0.05$), but not in the IKE (6.0 to 6.1, NS) or NOE (6.9 to 6.8, NS) groups.

Treatment by study day effects were found for SLEEP ($P < 0.05$) and WAKE ($P < 0.05$) indices. This resulted from a significant decline in these indices at the onset of the ambulatory control period. For example, the number of awakenings increased by 1.4 –2.2 per night ($P < 0.05$) during the first 3 days of ambulatory ($P < 0.05$), relative to orientation d1, d2, and d8.

Self-rated performance means within the three subject groups during ambulatory control and BR periods ranged from 5.2–5.6 units; the subjects rated their performance as improved relative to no change, which was 5.0 units. No significant changes were detected in self-rated performance by treatment regimen or BR day. A simultaneous decreasing trend (NS) in both composite test (fig. 1) and self-rated performance was evident at the onset of the ambulatory control period and was attributed to the lack of practice during the 3–11 week interval between the orientation and ambulatory control. No statistically significant improvement occurred after 17 d BR or between BR and ambulatory recovery periods.

During BR, IKE exhibited the most stable mood and performance. Of the 21 combined mood, sleep and performance scales, significant parameter by BR effects were found in eight mood or performance parameters for NOE, in nine for ITE, but only in two for the IKE group.

Composite performance– The orientation training was sufficient to achieve stable asymptotic levels for the 10 tests (fig. 1). All means and variances stabilized by seven trials, and differential stability was achieved in 8 of 10 tests by five trials. Composite performance, expressed as mean integer ranks, improved continuously by treatment regimen ($P < 0.05$) throughout the study.

Questionnaire responses– These were obtained from all ITE subjects, from four of six IKE subjects, and from three of five NOE subjects. Thus, 14 of 18 subjects responded and the remaining four declined to respond. The quality of social interaction between subjects, staff and investigators was rated as positive by all 14 subjects. Daily performance testing was negatively rated by 3 of 7 ITE subjects but in none of the three NOE respondents.

Discussion

The pattern of performance and mood changes during BR is an initial deterioration during the first wk, followed by improvement for about 2 wk, then progressive deterioration throughout the remainder of the BR period (refs. 1, 14, and 22). This deterioration is manifested by asthenia, emotional lability, sleep disturbances, and inconsistent performance. In the present study a similar sleep and mood deterioration pattern from the onset of BR was observed, followed by sleep and mood recovery, then mood deterioration beyond 20 d of BR. In contrast to the previous results (refs. 1, 14, and 22), most (13 of 24) mood scales in the present study showed overall improvement from the onset to the end of BR, and performance tests consistently improved from the onset of ambulatory control to the end of BR. The effectiveness of daily exercise training during BR to counteract deterioration in performance, mood, or sleep quality (refs. 1, 19, 22, and 26) was probably diminished in our study by the lack of detrimental changes in these functions during BR in the NOE group.

The high degree of subject adaptability to the conditions in our study, in contrast to previously cited studies, is attributed to several factors. First, our selection process was effective in identifying candidates with optimal characteristics (e.g., motivation, friendliness, and compatibility) for adaptation to isolation, confinement, restricted mobility, and exercise training. Second, several factors contributed to mood and performance deterioration in previous BR studies, i.e., conflicts between subjects and support staff (refs. 14 and 17), immobilization or greatly restricted movement (refs. 22 and 25), restriction of communication among and between subjects and their friends and relatives (ref. 25), and restriction of naps (ref. 20). Therefore, our more favorable habitability factors probably contributed to maintenance of stable affective mood, arousal, and the positive desire to perform during BR, which may have been the key to the unexpectedly consistent improvements in performance accuracy.

Several interesting differences emerged between the three exercise groups during BR. Progressive improvement in sleep quality and reduction in psychological tension occurred in the ITE group, relative to those in the other groups. Since the IKE training regimen was of comparable intensity but of shorter duration (6.7 min/d) than the ITE regimen (60 min/d), perhaps the daily duration of exercise is important for inducing positive mood and sleep-quality effects. This positive influence of strenuous exercise upon sleep (ref. 16) and anxiety (refs. 16 and 18) has been demonstrated in some exercise studies, but not in others (refs. 11 and 21).

The generally positive effects of chronic exercise training on the state of well-being (ref. 16) and have been attributed to three major hypotheses: distraction, where exercise provides a diversion from other stress; monoamine, where exercise stimulates action of norepinephrine and serotonin which counteract depression; and endorphin, where exercise stimulates release of endorphins which reduce pain and produce euphoria (ref. 16). Only the ITE group exhibited significant post-BR improvements in mood and sleep quality which suggests that strenous exercise training enhanced the adaptation to the physical demands of ambulatory recovery. However, the ITE group also showed impaired concentration after transition to ambulatory recovery, and two of its Activation Mood Dimension scales (MOTIV, CONCN) decreased significantly during BR.

The NOE group improved in all performance tests during BR, and showed greater improvement in the cognitive performance tests than the two exercise groups. Also, there were no differences between the NOE and IKE groups in any mood-state or sleep-quality parameter. Therefore, the significant improvement in cognitive performance in ambulatory exercised subjects, but not in sedentary control groups reported previously (ref. 12), was not confirmed in our study. The NOE group respondents were the only subjects who did not express a negative attitude toward daily performance testing.

Three major conclusions emerge. First: the degraded mood, sleep, and inconsistent performance reported from previous BR studies are not due solely to inactivity. This deterioration was more likely the consequence of selection of less motivated and adaptable subjects, problems or constraints concerning subject interaction with personnel internal and external to the study, attenuation of environmental stimuli, and restriction of naps. Second: the less favorable trends in cognitive performance and activation mood scales and the negative attitude toward the performance test regimen in the ITE group probably reflected chronic exercise induced overtraining fatigue or excessive total workload resulting from the combination of exercise, other test demands, and subject activities. Third: maintenance of concentration and motivation with improvements in cognitive performance in the NOE group implies that the performance test regimen relieved boredom by providing distraction.

Acknowledgments

The authors express their warm gratitude and appreciation to the 125 people who had significant roles in this study: especially to the test subjects, Dee O'Hara, manager of the Human Research Facility, and Edith Crofoot and the nursing and aides staff; Bonnie Rosenberg and Kristen Lindseth-Gomez for their excellent technical assistance during the study and to Dr. Malcolm Cohen, who provided valuable support; and Bridget Eller and Debra Meyer for manuscript preparation. A special thanks to the members of the AIBS review panel who shared their thoughts, comments, and recommendations with us: Reggie Edgerton, Philip Gollnick, William Haskell, Michael Pollock, William Stauber, and Charles Tipton (Chair).

This work was supported by NASA Tasks 199-21-12, 199-22-12, 199-22-22, 199-22-32, 199-22-44, NAG2-410, and Army Task MRDC-3A161101A-91C.

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The Effect of Habitability and Selection upon Human Performance and Mood during Head Down Bed Rest

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Abstract

DeRoshia CW. The effect of habitability and selection upon human performance and mood during head down bed rest. Performance task proficiency and mood were investigated in a repeated-measures study of two groups (G1, n = 12; G2, n = 6) of healthy men during separate 30 day head down (–6°) bed rest (BR) regimens, with 7 days of pre-BR and 4 days of post-BR ambulatory confinement. The daily battery consisted of 10 performance tests and eight mood and two sleep scales. Mean performance changes during BR ranged from +2.6 to +23.4%; this improvement was significant ($P < 0.05$) in 8 tests. Unexpected significant differences between groups were detected, including higher means in three performance tests in G1 during pre-study training, a confinement onset increase in waking episodes of 0.9–1.3 per night in G1, relative to G2, and an improvement in the Affective Mood Dimension in G2, relative to G1. I attribute these differences and the unexpected absence of performance and mood deterioration during BR to favorable subject selection procedures and differences in group size and environmental habitability.

Introduction

Bed rest (BR) exposes humans to restricted mobility, confinement and isolation which probably produce a subtle form of sensory deprivation with reduced proprioceptor and kinesthetic input (refs. 32 and 46). The associated loss of strength, energy, motivation and concentration, with increased fatigability, sleep impairment, and sensitivity to physical or emotional stressors (asthenia), has been reported in several BR studies (refs. 2, 28, 30, 38, 40, and 42).

Performance deficits in controlled scanning (ref. 44), visual acuity (ref. 16) and productive thinking (ref. 3) occurred after initial BR adaptation, but others found no consistent performance changes (refs. 33, 35, 39, 42, and 43). Previous BR studies have three deficiencies: (a) they used single tests of performance efficiency and lacked statistical verification of test reliability and sensitivity, (b) they provided only anecdotal descriptions of changes in mood and well-being (refs. 2, 3, 28, 38, 40, and 42), and (c) they lacked information on study habitability and subject selection. Therefore, the objective of this study was to provide daily quantitative assessment of the effects of long duration head down BR on validated performance tests and selected mood and sleep quality scales in two separately conducted studies, and to evaluate the impact of subject selection procedures and environmental habitability upon the observed responses.

Methods

Subjects– A pool of over male 2000 respondents to a newspaper ad was reduced to 500–600 men after a telephone interview, reduced to 120 men by a personal interview, and reduced to 27 men after a physical (ref. 15) and detailed briefing. The interview procedure was used instead of standard personality screening tests because such tests select out those with psychopathological traits rather than select in those with optimal personality traits (ref. 24) and have not been as effective as the interview procedure in selecting subjects for biomedical experiments conducted in the Human Research Facility (HRF) at Ames Research Center. After an orientation test phase conducted in the (HRF), informed consent was obtained from 23 selected subjects who had the option to participate in a study starting June 30, 1986 (Group 1, N = 12) or a repeat study starting August 18 (Group 2, N = 11). The choice of study option was necessary to accommodate subjects with fall job commitments. All 12 subjects in Group 1 completed the study. Four Group 2 subjects declined to participate and one subject left the study for personal reasons prior to the BR phase which left six subjects in the second group. Subjects were selected in on the basis of a healthy appearance, friendliness, compatibility, motivation, and their assessed ability to adapt to isolation and confinement in the HRF. Three men had been subjects in prior BR studies.

About one of three nursing staff candidates were selected after an interview with the head nurse. Favorable criteria included prior BR study nursing experience, positive attitude and inclination for cooperative teamwork.

This study was part of a multidisciplinary experiment on the effectiveness of lower-extremity isotonic and isokinetic exercise training regimens upon the maintenance of maximal oxygen uptake and muscular strength and endurance during 30d of BR. Subject selection was restricted to match the average age (36 ± 1 yr) and maximal oxygen uptake (44 $ml \cdot min^{-1} \cdot kg^{-1}$) of the active astronaut corps. The subjects were allocated, on the basis of age, peak oxygen uptake, and maximal isometric knee extension strength, into three groups: no exercise (Group 1: N = 4; Group 2: N = 1), isotonic exercise (Group 1: N = 4; Group 2: N = 3) and isokinetic exercise training (Group 1: N = 4; Group 2: N = 2). Diet, exercise,

and clinical procedures details (ref. 22) and the effects of the exercise regimens upon mood and performance (ref. 15) have been published.

Experimental design– From three to 11 weeks after the orientation test phase in the HRF, subjects were confined in the HRF for an ambulatory control phase (pre-BR, 7d), head down (–6°) BR (30d), and ambulatory recovery phase (post-BR, 4d). The men were confined in two-to-four-person rooms with moveable partitions so they could be isolated at night or during tests. The photoperiod was 16 hr light:8 hr dark (lights on at 0700 hr). During BR, subjects were restricted to head-down recumbency, except during meals when they were permitted to prop their heads up on an elbow. As time permitted, they were permitted to nap during the day, to freely interact with the staff, investigators and other subjects, and to engage in personal hobbies, to listen to personal stereo systems, to read, and to view television and videocassette movies. Subjects participated in other experimental test regimens, which included exercise (refs. 15 and 22) twice daily for 30 minutes in the exercise groups, weekly isokinetic exercise in all subjects, blood sampling, cardiac output and ultrasound. Posture/gait, tilt table, muscle magnetic imaging and bone densitometry tests were performed during the ambulatory periods. No visitors were permitted in the HRF but the men had unlimited outside communication by means of a single pay telephone, to which they were transported by gurney.

Performance tests– Performance testing was done with the Automated Portable Testing System (APTS, Essex Corp., Orlando, FL. 32803) software implemented on a NEC 8201A microcomputer. This system was selected for portability, reliability, test automation capability, and utility for short-duration testing (refs. 7, 26, and 27). Ten performance tests (refs. 26 and 27, table 1) from the 30 recommended PETER program tests (ref. 7) were selected to tap visuo-spatial (MANKIN, PATRNC), encoding (CODSUB), short term memory (STERNB), verbal cognitive reasoning (REASON), pursuit tracking (ACM) and manual dexterity abilities (SREACT, PHTAP, TFTAP, NPTAP).

The number of trials required for performance test means, variances, and correlation matrices (differential stability) to stabilize was determined by Bittner's methods (ref. 6). The five performance tests with error scores (REASON, CODSUB, MANKIN, PATRNC, STERNB, table 1) were analyzed as net accuracy but were also scored for response latency (msec) and number of errors.

Although log-latency is claimed to be the most reliable index for the MANKIN test (ref. 11), MANKIN accuracy scores were used in this study since no ceiling effects were detected in accuracy scores (Cochran's homogeneity of variance test) and no substantial differences between analyses done on accuracy or log-latency scores were detected. The measures of performance (i.e., accuracy, number of alternate keypresses, latency) had different magnitudes and ranges. Therefore, to obtain a composite measure of overall performance, daily values for each test were converted to integer ranks with the "worst" or minimum = 1 and "best" or maximum = 50. The daily ranks for each test were then averaged across tests for each subject and then averaged across subjects by study group (fig. 1). The mean of the three tapping tests was computed prior to the data ranking to avoid providing excessive weight to the tapping data in the composite performance means.

Mood test– A visual analog scale (VAS) mood test was developed and incorporated into the APTS performance software. The VAS mood test was used because it provides fast and reliable (refs. 9 and 29) mood assessment with a high degree of mood state resolution and less chance of subject non-compliance, response stereotyping or remembered responses (ref. 29). The VAS mood test provided 21 levels of mood state resolution on a 10-cm scale between the two mood-state adjectives. The VAS mood test included eight mood scales, two sleep questions from the St. Mary's sleep questionnaire (ref. 18) to document sleep latency and disturbance, and a self-rated estimate of overall change in performance proficiency between tests (table 1).

Using the validation procedure of Monk (ref. 29), the mood scales were allocated four each into two composite mood dimensions (table 1). The global "Affective Mood Dimension" included four measures of feelings or affective states and the global vigor, or "Activation Mood Dimension" incorporated four measures of activation states. These global scales are statistically distinct and differentially sensitive to environmental factors such as sleep loss, diurnal rhythms and seclusion (ref. 29). The physical discomfort (PDISC) scale indicated the state of physical uneasiness or the extent of mild aches and pains which are common at the onset of bedrest (refs. 3, 28, and 30). The other seven mood-state scales (ref. 9) and the configuration of the mood scales within each mood dimension have been validated (ref. 15).

The mood test initiated the test battery to avoid modulation of mood responses by the performance tests. After an 8–10 trial training period during orientation and one training test at the onset of ambulatory confinement, this 15-min test battery was given to all subjects daily in the late afternoon at least 1–2 hr after exercise, showers or naps. Data were recorded only on six of the seven pre-BR days. The computer was located directly below the head of the prone subject on a gurney.

Table 1. Performance and mood-test information

Performance Tests	Duration (sec)	Constructs Tested
Simple Reaction Time (SREACT)	60 or 15 trials	Manual dexterity[1]
Code Substitution (CODSUB)	75	Encoding[2]
Pattern Comparison (PATRNC)	75	Visuo-spatial[2]
Sternberg Short Term Memory (STERNB)	75	Short-term memory scan rate[2]
Air Combat Maneuver (ACM)	120	Pursuit tracking[3]
Preferred Hand Tapping (PHTAP)	10 (two runs)	Manual dexterity[4]
Grammatical Reasoning (REASON)	90	Reasoning, logic[2]
Two Finger Tapping (TFTAP)	10 (two runs)	Manual dexterity[4]
Manikin (MANKIN)	60	Visuo-spatial transformation[2]
Non-preferred Hand Tapping (NPTAP)	10 (two runs)	Manual dexterity[4]

1) Latency in milliseconds
2) Accuracy (number correct minus number of errors)
3) Score (number of hits)
4) Number of alternate key presses, highest of two runs

Mood State Tests	Test Adjectives
Activation Mood Dimension	Mean of Four Scales Below
Motivation to Perform (MOTIV)	Bored (0)/Interested (10)
Arousal State (AROUS)	Sleepy (0)/Alert (10)
Fatigue Level (FATIG)	Weary (0)/Energetic (10)
Ease of Concentration (CONCN)	Very low (0)/Very High (10)
Affective Mood Dimension	Mean of four scales Below
Psychological Tension (TENSE)	Tense (0)/Relaxed (10)
Elation (HAPPY)	Sad (0)/Happy(10)
Physical Discomfort (PDISC)	Very high (0)/Very low (10)
Contentedness (PLEAS)	Unpleasant (0)/Pleasant (10)
Sleep Quality	
Trouble Falling Asleep (SLEEP)	Much worse (0)/Much better (10)
Number of Waking Episodes (WAKE)	Total episodes (Range 0-6)
Self-Rated Performance	
Relative to that on the previous test battery (PERF)	Much worse (0)/Much better (10)

Habitability questionnaire– On BR d30, the subjects were asked to respond to four questions to assess their impressions of the study environment: "What aspects of the bed rest study environment were pleasant or rewarding or unpleasant and irritating? Was the bed rest study environment boring and monotonous or stimulating and interesting? Did you look forward to the daily performance test as an activity to relieve the boredom of the study environment or did you perceive the test as an unwelcome interruption of your daily routine and activities? What were the positive and negative aspects of the performance test?"

Statistical analyses– The two study groups were evaluated for treatment-phase (orientation, pre-BR, BR, post-BR) and BR-day treatment effects by two-way repeated-measures analysis of variance (ANOVA). Statistically significant differences in treatment means were compared with the Newman-Keuls paired comparison test. BR-day-dependent mean trends were also evaluated by linear regression (LR) with slope comparison by analysis of covariance (ANCOVA). The resultant percentage changes obtained for the performance tests are presented in figure 5; the corresponding absolute changes for the mood and sleep quality scales are presented in figure 6. The null hypothesis for ANOVA, ANCOVA and regression was rejected when $P < 0.05$; nonsignificant differences were indicated by NS.

Results

The training regimen achieved stable asymptotic levels of performance since performance means and variances stabilized by seven trials and differential stability was achieved in eight of ten tests by five trials. Composite performance, expressed as mean integer ranks (fig. 1), improved between treatment phases (ANOVA, F3, 21 = 112.0, $P < 0.0005$) although there was a NS decrement between training and HRF confinement (fig. 1) due to lack of practice during the 3–11 wk interval between these phases. No significant change (Newman-Keuls) occurred in composite performance between BR and post-BR phases.

During BR, mean daily performance changed (F29, 464 > 1.6, $P < 0.05$, ANOVA) in eight tests (except SREACT and STERNB), including changes in four tests in Group 1 (F29, 464 > 1.8, $P < 0.01$) and six tests in Group 2 (F29, 464 > 1.6, $P < 0.05$). These changes reflected improvement from 2.6% (TFTAP) to 6.9% (NPTAP) in the psychomotor tasks to a maximum of 22.2% (CODSUB) and 23.4% (REASON) in the cognitive tasks. This improvement was significant ($t > 2.0$, $P < 0.05$, LR) in nine tests in Group 1 (except SREACT) and all tests in Group 2 (fig. 5). No significant changes were detected in self-rated performance by treatment phase or BR day.

The Activation Mood Dimension scale means (fig. 2(a)) showed no treatment-phase effects (ANOVA) but it declined during BR (–0.2 units, $t28 = -2.2$, $P < 0.05$, LR). A marked deterioration in the Affective Mood Dimension (fig. 2(b)) of two to seven days duration occurred at the onset of BR (fig. 2(b)) and was most pronounced in the PDISC scale (fig. 3). This change was significant ($P < 0.05$, Newman-Keuls) for BR d1 relative to orientation d1–3, pre-BR d4, and BR d8. Subsequent improvement trends in this dimension were reflected in BR day effects (F29, 493 = 3.4, $P < 0.0005$, ANOVA) in both groups (1: F29, 464 = 2.0, $P < 0.01$; 2: F29, 464 = 2.4, $P < 0.0005$). The means of daily Affective Mood Dimension during BR were better fit by second-degree polynomials ($t29 > 5.2$, $P < 0.00001$) than by LR (Group 1: $t29 = 1.5$, NS; Group 2: $t29 = 4.5$, $P < 0.0005$). These curvilinear trends peaked at d17 (Group 1) and d20 (Group 2), then declined to the end of BR (Fig. 2(b)).

Sleep quality study day effects were found in the SLEEP (F48, 816 = 2.0, $P < 0.0005$, ANOVA) and WAKE (F48, 816 = 2.8, $P < 0.0005$) indices. At the onset of ambulatory confinement the SLEEP scale decreased 1.8–2.3 units, (Newman-Keuls, $P < 0.05$), relative to orientation d1–4, 8 and 9 and the WAKE scale (fig. 4) increased by 1.4–2.2 awakenings per night, $P < 0.01$ relative to orientation d1–2, 5–9 and BR d10, 23, 26–27, 29–30. No significant BR onset associated changes in sleep quality were detected.

Several unexpected differences were found between the two study groups. Questionnaire responses were obtained from all six subjects in Group 2 but only eight of 12 subjects in Group 1. The negatively rated aspects were complaints about food quality (five of seven respondents in Group 1 but only one of six in Group 2) and telephone access (three subjects, Group 1 only). The study environment was rated as stimulating or interesting by all eight Group 1 respondents but only by two of six from Group 2.

The major difference was an increase in awakenings during confinement of 0.9–1.3 episodes per night (fig. 4) in Group 1, relative to Group 2 (ANOVA by BR day, F1, 16 = 6.0, $P < 0.05$, by treatment phase interaction, F3, 48 = 2.8, $P < 0.05$). Initial differences (a priori sample error ANOVA) during training were detected between Groups 1 and 2 in performance (PATRNC mean accuracy = 52.4, 40.8, respectively, F1, 16 = 18.4, $P < 0.0005$; TFTAP mean accuracy = 53.6, 46.2, respectively, F1, 16 = 6.9, $P < 0.025$). Self-rated performance means were higher in Group 2 (6.0) than in Group 1 (5.1, F1, 16 = 9.8, $P < 0.01$). These initial differences persisted for PATRNC (ANOVA by treatment phase, F1, 16 = 14.4, $P < 0.01$) and self-rated performance (F1, 16 = 25.4, $P < 0.0005$). Self-rated performance and mean performance test change per day were higher during BR in Group 2 (6.4, 0.45%, respectively) than in Group 1 (4.9, 0.32%). The Affective Mood Dimension improved from orientation to post-BR in Group 2 (6.3–6.9 units), but declined in Group 1 (6.2–5.8 units, ANOVA by treatment phase interaction: F3, 48 = 4.6, $P < 0.01$).

During BR, improvement indicated by positive LR slope ($t29 > 2.05$, $P < 0.05$) occurred in 72% of mood scales and 92% of performance tests among Group 2 subjects, but only in 48% of mood scales and 80% of performance tests in Group 1 (figs. 5 and 6). Five performance tests (MANKIN, REASON, PATRNC, ACM, PHTAP) showed more positive trends during BR in Group 2 than in Group 1 (fig. 5, ANCOVA, F1, 56 > 4.3, $P < 0.05$), while only CODSUB showed a more positive trend in Group 1 (F1, 56 = 6.0, $P < 0.05$). The Affective Mood Dimension and the PDISC, PLEAS, and FATIG scale daily means showed more positive trends during BR in Group 2 than in Group 1 (ANCOVA, F1, 56 > 4.5, $P < 0.05$). The MOTIV scale trend was more positive during BR in Group 1 (F1, 56 = 8.7, $P < 0.005$; group by BR day ANOVA interaction, F29, 464 = 2.0). A confinement effect was detected only in PDISC, which was higher in Group 1 in the ambulatory confined state (combined pre-BR and post-BR mean = 5.3) than in the

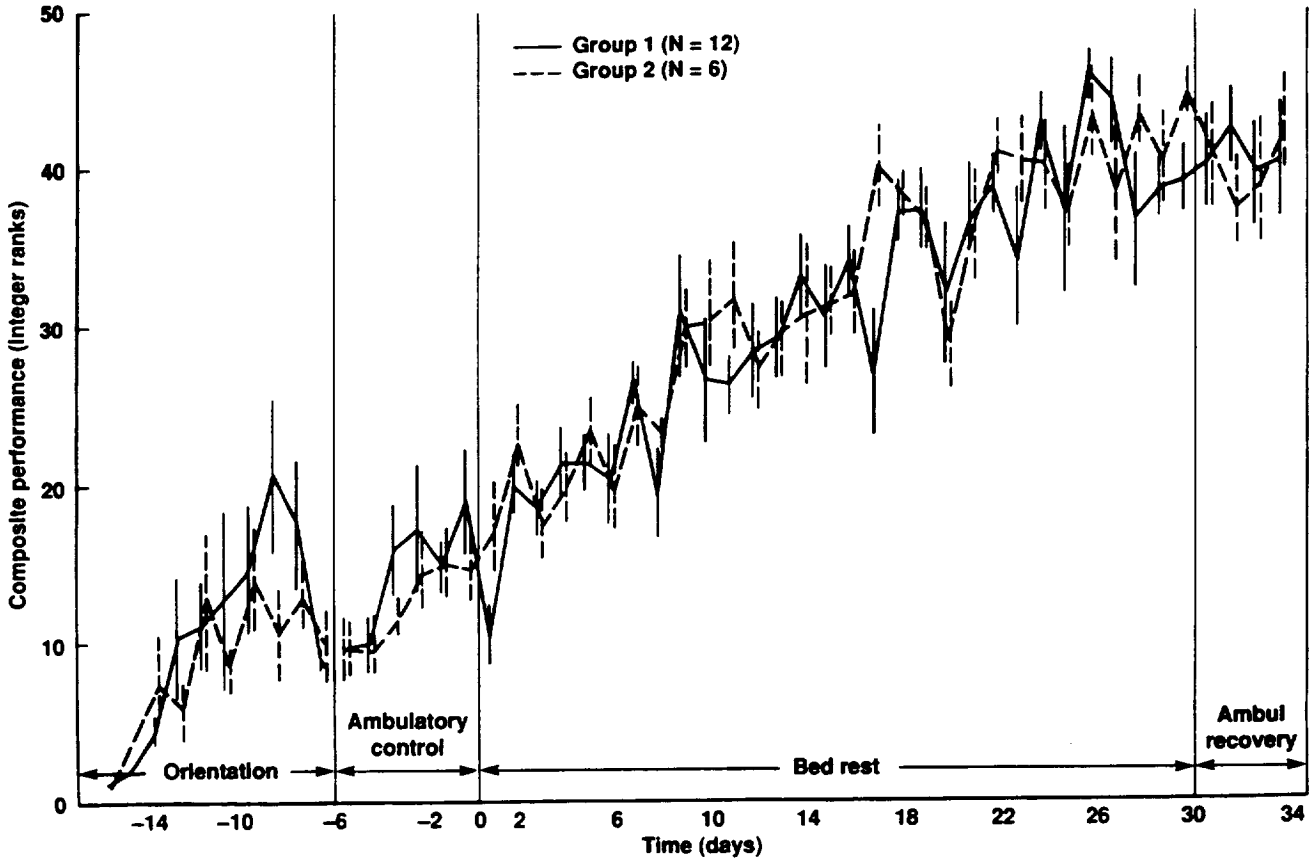

Figure 1. Daily performance levels expressed as integer ranks where 1 = minimum and 50 = maximum. Values are group means ± standard error) for each of eight performance tests (including mean of the three tapping tests) in the two subject groups.

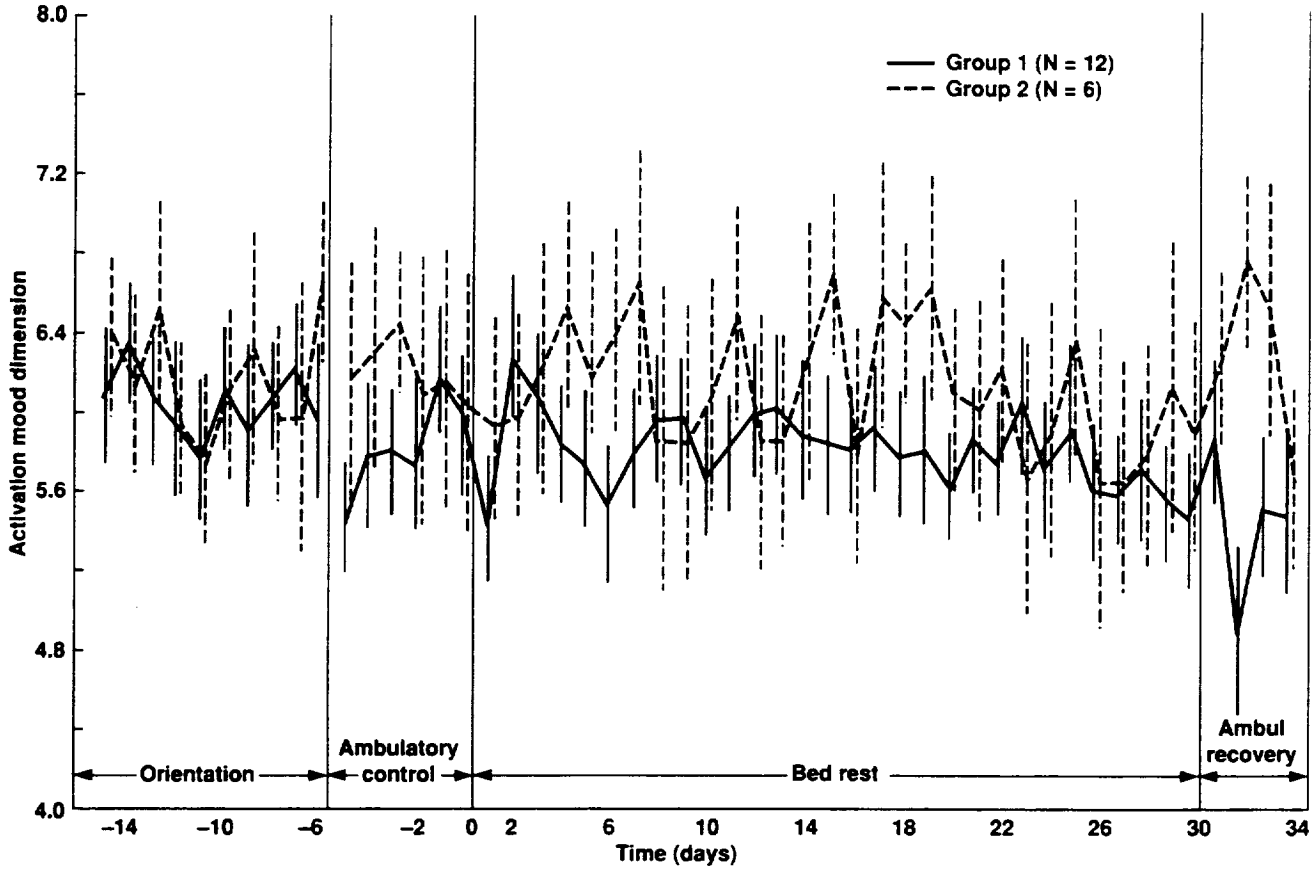

Figure 2.(a) Daily activation mood dimension scores in the two subject groups. Values are group means (± standard error) with a possible range of minimum, or least favorable (0) to maximum, or most favorable (10).

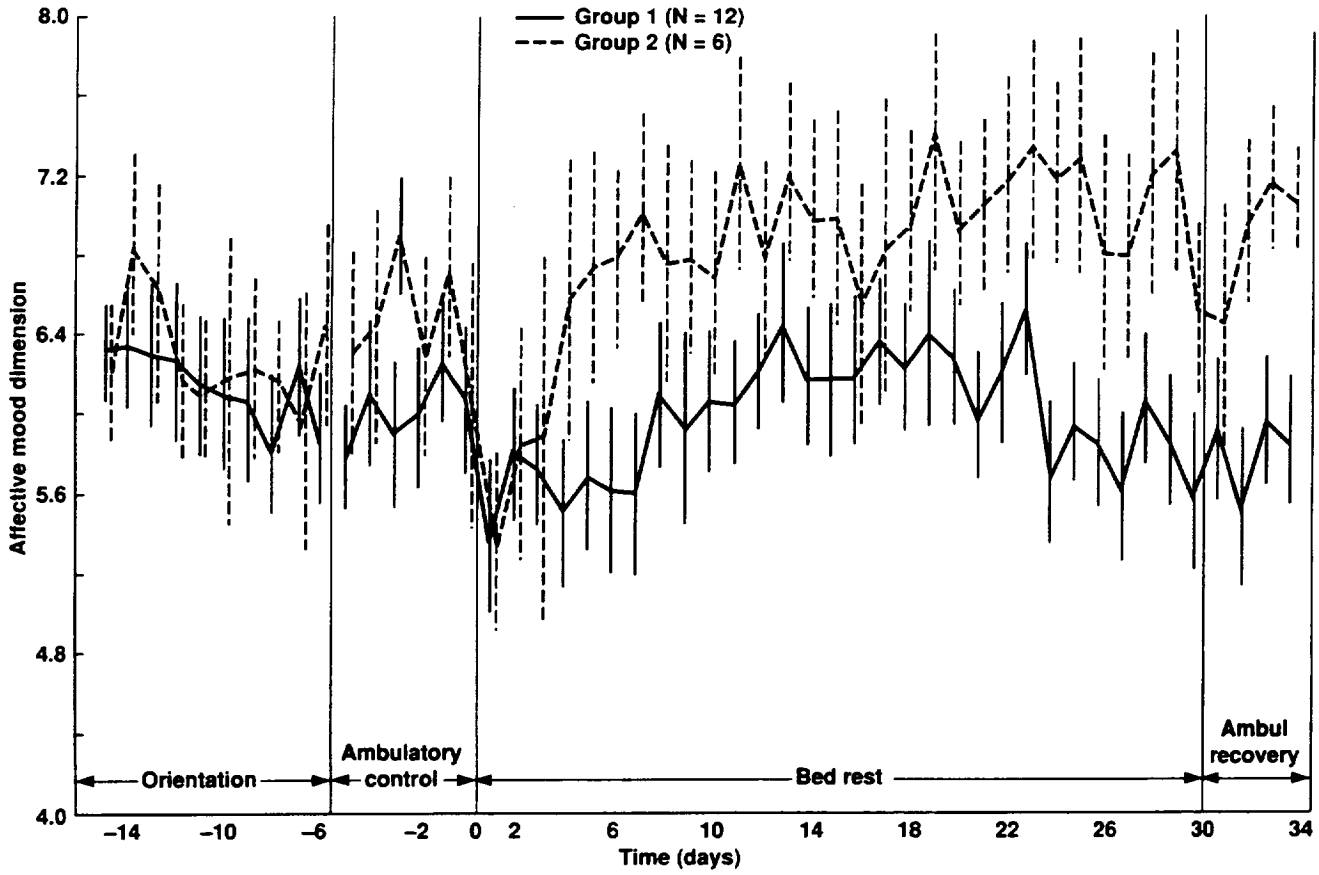

Figure 2(b). Daily affective (2(b)) mood dimension scores in the two subject groups. Values are group means (± standard error) with a possible range of minimum, or least favorable (0) to maximum, or most favorable (10).

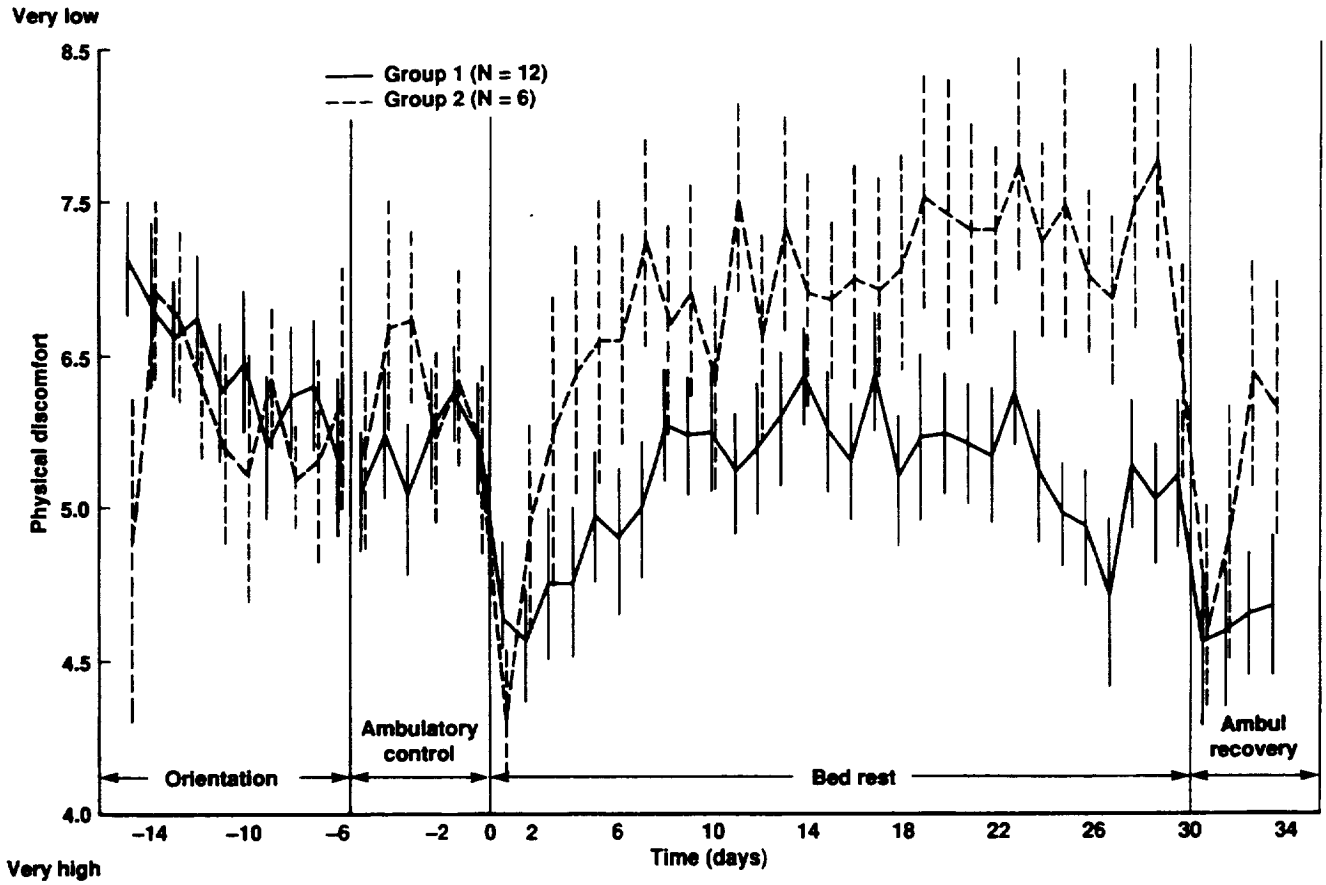

Figure 3. Daily physical discomfort mood rating in the two subject groups. Values are group means (± standard error) with a possible range of maximal (0) to minimal (10) discomfort.

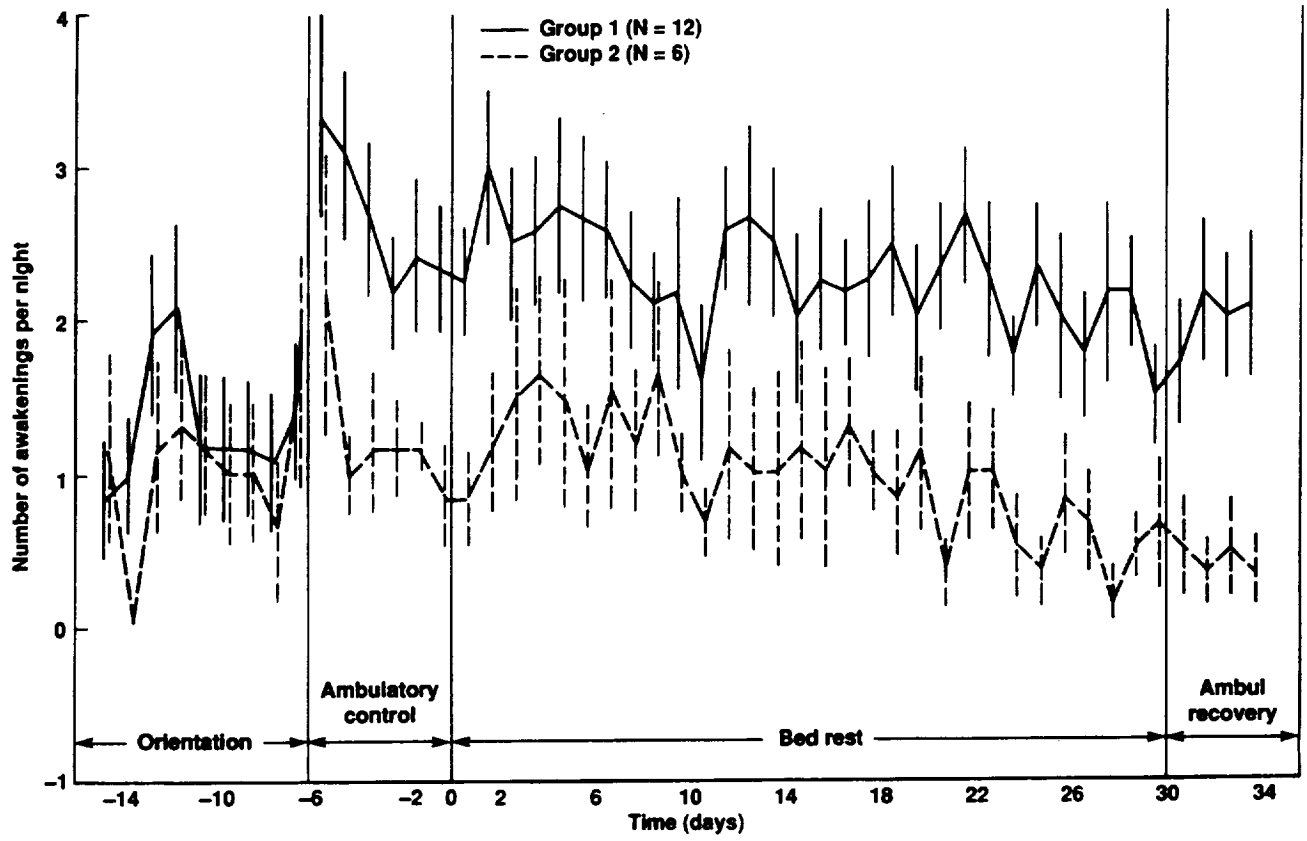

Figure 4. Daily number of waking episodes per night in the two subject groups. Values are group mean (± standard error) with a possible range of 0–6 awakenings per night.

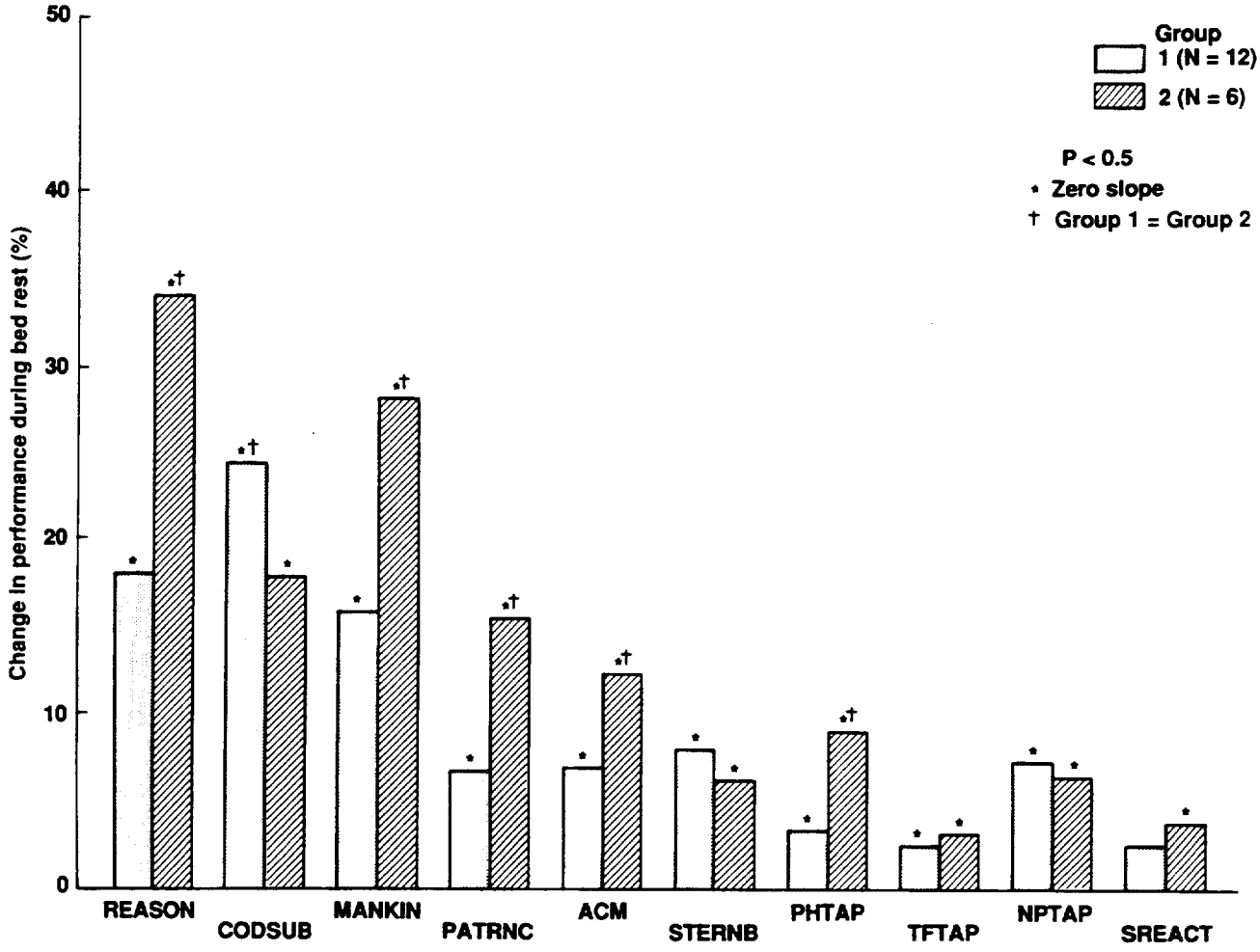

*Figure 5. Mean percent changes in performance test scores during bed rest as determined by linear regression. Test abbreviations are defined in table 1. *P < 0.05 from zero slope, †P < 0.05 from Group 1.*

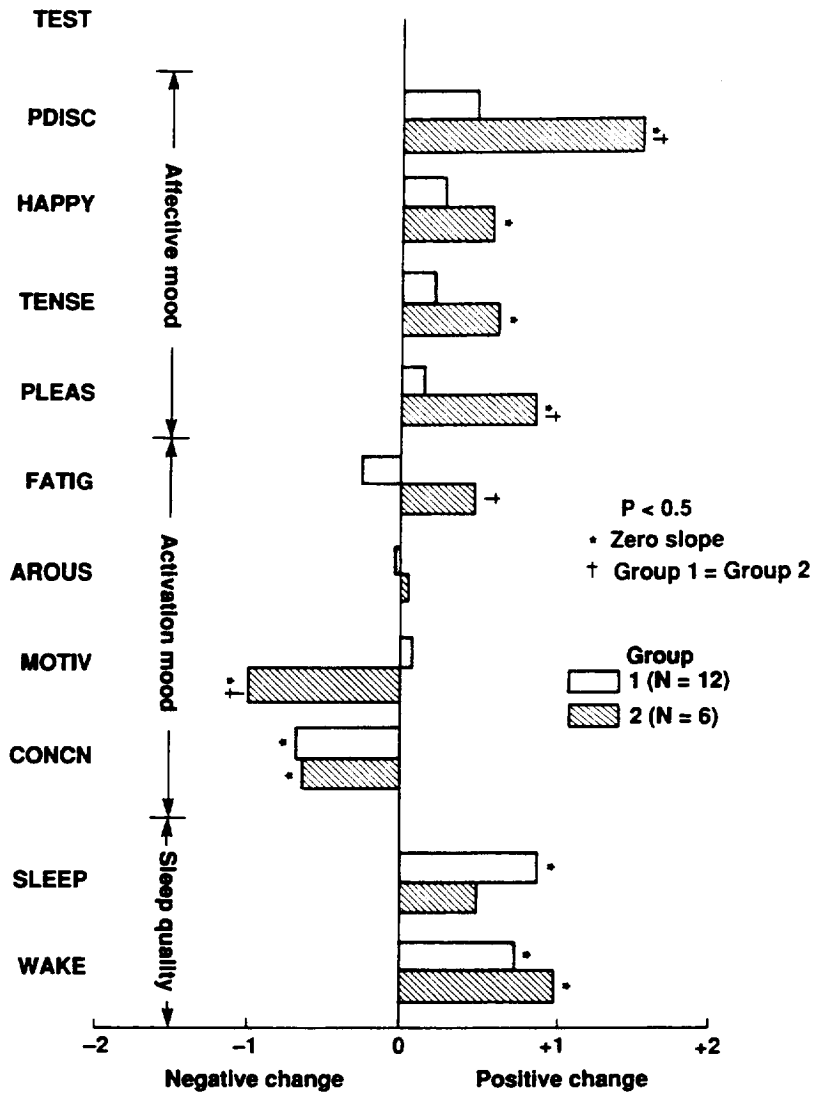

*Figure 6. Mean change in activation and affective mood state parameters and sleep quality scales during bed rest in the two subject groups as determined by linear regression. Test abbreviations are defined in table 1. Zero on the y-axis indicates no change during bed rest, a positive change indicates relative improvment, and a negative change indicates a relative deterioration, *P < 0.05 from zero slope, +P < 0.05 from Group 1.*

unconfined state (orientation mean = 6.4, F1, 44 = 7.1, P < 0.01). Despite the negative trend (t28 = –2.9, P < 0.01, LR) in the MOTIV scale in Group 2 during BR, the MOTIV means remained positive (i.e., >5.8 scale units) in both groups in all treatment phases.

Both groups improved in REASON accuracy from orientation to post-BR (ANOVA by treatment phase, Group 1: F3, 48 = 14.7, P < 0.0005, +38.9%; Group 2: F3, 48 = 17.5, P < 0.0005, +86.4%). REASON was the only performance test with error scores that showed a substantial (3.4 per trial) incidence of errors. Improvement in Group 1 occurred by reduction in latency (F3, 48 = 5.7, P < 0.01, –18.2%) but not errors (F3, 48 = 1.7, NS), while both latency (F3, 48 = 9.8, P < 0.0005, –28.8%) and errors (F3, 48 = 6.8, P < 0.001, -46.0%) were reduced in Group 2. During BR a negative trend in daily errors occurred in Group 2 (t29 = –2.4, P < 0.05, –29.2%, LR), but not in Group 1 (t29 = –0.9, NS, –7.6%).

Discussion

The pattern of mood changes during head down BR was initial deterioration followed by improvement for about two weeks and increasing mood deterioration during the last ten to 13 days of BR. Similar mood patterns were reported in earlier BR studies (e.g., refs. 2, 28, 40, and 42) but these studies reported significant mood deterioration,

manifested by asthenia, emotional lability, sleep disturbances, and inconsistent performance during BR. In the present study, performance improved throughout confinement and most mood scales improved from the onset to the end of BR. The lack of procedural detail on subject selection, habitability, and performance test validation in the earlier, predominantly Soviet BR studies (refs. 2–4, 16, 28, 37, 38, 40, 44, and 45) was a problem in evaluating the discrepancy between the absence of mood and performance deterioration in the present study and its presence in the earlier studies. In these studies subjects were allowed to read and converse with each other and were provided with radio and television (ref. 37). However, mobility was highly restricted (refs. 37, 40, and 44) and outside contact was limited (ref. 44). Dr. Eugene Ilyin (Institute of Biomedical Problems, Moscow, personal communication 1989) indicated that Soviet BR subjects are chosen from institute staff, subject selection is primarily based upon clinical criteria, some subjects have prior BR experience, and there is no direct contact permitted between subjects and people outside the research facility.

I attribute the higher degree of subject adaptability to the environment of the present study to several factors. First, the selection process was effective in selecting in candidates with optimal characteristics (e.g., motivated, friendly, compatible and mature) for adaptation to isolation, confinement and restricted mobility from a large subject pool. Rigid psychiatric assessment may be necessary to obtain normal subjects for clinical studies (refs. 23 and 34) since 16.5% of candidates presenting themselves as normal have been diagnosed with mental disorders (ref. 23) and 50.9% of applicants have been excluded for psychiatric, neurologic, or medical disorders that might affect brain function (ref. 34). Our selection process was not done by quantitative criteria (refs. 23 and 34) but was effective since (1) standard personality assessments are less effective in selection since they are designed to select out individuals with psychopathology rather than select in individuals with optimal personality traits (ref. 24), (2) voluntary refusal to participate (self-selection out) may be more important in excluding psychologically unfit subjects in a long duration confinement study than in short term clinical studies, where the degree and duration of psychological contraints is considerably lower, (3) a NASA-sponsored study may attract more healthy and motivated subjects than clinical studies, and (4) the orientation regimen in our study can detect maladaptive behavior which is only elicited by exposure to study environment and test conditions.

Second, prior experience enables individuals to better overcome the effects of isolation and confinement (ref. 36) and reduces incidences of hostility and anxiety in subsequent BR studies (ref. 41). The inclusion of subjects with prior BR study experience provided subjects of proven adaptability whose experience helped the naive subjects adjust to environmental conditions.

Third, the effective selection of nursing staff likely contributed to the reported high quality of staff-subject social interactions. Conflicts between isolates and support staff are the most important source of adjustment problems during long term isolation (ref. 36) or BR confinement (refs. 14, 28, and 30). Minor daily stress events and physical symptoms have greater effects on daily mood levels than chronic stress or major life events (ref. 17) but chronic stress increases the adverse effects of daily stress events while social supports reduce it (ref. 12). Therefore, the positive social interactions and social support provided to subjects in this study probably minimized daily stressful conflicts and the negative impact of such conflicts upon mood.

Fourth, a large variety of experimental and subject activities provided a stimulating environment which may have prevented the deterioration in sleep and arousal observed in a BR study in which there was an intentional lack of sensory stimuli (ref. 10). Fifth, the low degree of restricted mobility during head down recumbency may have prevented the deterioration in mood observed in studies with cast immobilization of subjects (refs. 14 and 41) or restricted arm and leg movements (refs. 40 and 44) which may constitute a type of sensory deprivation (ref. 33).

Sixth, outside communication with friends and relatives may have prevented the functional impairment and performance deficits observed in bedrested patients who had restricted social contacts (ref. 25). Although outside contact is discouraged in the Soviet BR studies, frequent audio contact with relatives, friends and celebrities is very important for the well being of cosmonauts during long duration Soviet space missions (ref. 31), in which mood impairment is less severe (ref. 8) than in the BR studies.

Seventh, daytime naps may have counteracted sleep difficulties induced by the onset of confinement or BR. When napping was restricted during BR (ref. 33), all subjects were physically tired after 1–2 weeks. Eighth, the maintenance of stable affective mood and positive motivation to perform may have been responsible for the unexpected improvements in performance since high subject motivation prevents performance deterioration in isolation (ref. 21).

The two consecutive BR studies were conducted under identical experimental conditions with identical test procedures. The unexpected differences between the two groups in performance, sleep and mood probably resulted

from a bias in group selection and an improvement in habitability resulting from a reduction in group size between the studies. The selection bias resulted from subject choice of study group participation and from the loss of the five subjects who declined to participate in the second study which resulted in a group of more adaptable subjects. The combination of high subject density and numerous testing procedures in the first group may have created nap disturbances and psychological tensions in response to frequent interruptions, movement of subjects, environmental noise, and limitation of environmental resources. The latter conclusion is supported by information from another 30d head down BR study which was conducted a year after the present study with 11 male subjects, including four subjects with previous BR study experience. These subjects adjusted well to the study environment, expressed fewer complaints, and had fewer daytime naps than the 12 Group 1 subjects in the present study (Dr. Joan Vernikos, personal communication, 1987). The incorporation of one major test protocol (muscle electrical stimulation) and the absence of exercise regimens may have promoted more favorable adjustment in the latter study by eliminating the strain and discomfort of exercise and by reducing the experimental test demand. This may have resulted in lower incidences of subject interruptions, and noise and psychological tensions created by test procedures and the frequent movement of subjects to test sites; thus this study environment may have been more comparable to the Group 2 environment in the present study, in which there were more activities but fewer subjects to create psychological disturbances. Although the study environment was more stressful for Group 1 subjects, these subjects had a more positive trend in motivation to perform and indicated that the study environment was more interesting than the Group 2 subjects. This implies that a certain level of "micro-stressor" stimulation may be necessary to counteract boredom.

The performance daily means changed from an exponential pattern of improvement during training to a linear pattern during BR. Performance failed to improve only during the late BR and post-BR phases perhaps due to the transition from BR to post-BR ambulation, a performance asymptote or ceiling effect, or an end of study anticipation effect. Performance improvement during the confinement phase may represent the transition from a controlled to an automatic mode of performance process, in which performance is less sensitive to environmental influences (ref. 19). Alternatively, the improvement may reflect a progression from a less efficient cognitively loaded performance process to a more efficient perceptual, then perceptual motor loaded performance process (ref. 1).

Self-rated performance levels were significantly higher in Group 2, starting with the orientation phase. The self assessment of performance in Group 2 may have been influenced by the more positive mood levels and adjustment in these subjects. Self-rated performance may be important in evaluating human responses to hypokinesia since subjects undergoing long duration water immersion may underestimate performance capability, which may impact subsequent performance expectations and proficiency (ref. 20).

The physical discomfort scale is highly correlated with the other Affective Mood Dimension scales (ref. 15) and it more clearly differentiated the response of the two study groups to BR than the other mood scales although the two BR groups were subjected to identical experimental conditions and no group differences in discomfort would have been expected. The physical discomfort scale, while not used in standard mood tests, provided the most sensitive index of psychological response to BR. It showed the largest magnitude change at the onset of BR and was the only scale to detect a confinement only effect between the ambulatory training and the confined ambulatory pre-and-post-BR phases. This effect may represent a confinement effect upon mood or may reflect the impact of the exercise training regimen which was conducted only during confinement.

Psychological factors may be an important barrier to long duration space flight (ref. 5). The results of this study suggest that given appropriate personnel selection and favorable habitability, mood and performance changes with potentially adverse operational consequences can be prevented during hypokinesia. These results have several implications for the maintenance of stable mood and performance levels in space mission analog environments which subject individuals to long duration isolation and confinement: (1) personnel selection and prior experience are important factors to ensure more favorable adjustment and prevent interpersonal conflict, (2) habitability factors may have a more important impact on adaptation than exercise regimens, and (3) adaptation is optimized by maintainng a balance between boring or monotonous conditions and excessive workload or stimulation.

Unstable mood, sleep difficulties and decline in performance efficiency may occur in long duration space missions (ref. 13) and BR studies (refs. 28 and 45). In the present study the onset of negative trends in several mood scales after 17 days of BR suggests that adverse changes in mood might have occurred with longer exposure to hypokinesia. There is a need for quantitative evaluation of mood and performance in longer duration hypokinesia studies where the dynamics of long term changes in mood and performance can be documented. There is also a need

for more studies on the effect of group size, composition and structure upon adaptability to confinement and a need for prestudy psychological evaluation of subjects prior to confinement to identify personality traits which are predictive of adverse reactions in susceptible individuals.

Acknowledgment

The author expresses appreciation to the 125 people who had significant roles in this study, the bed rest subjects, to Bonnie Rosenberg and Kristen Lindseth-Gomez for their excellent technical assistance during the study and to Dr. Malcolm Cohen, who provided valuable support.

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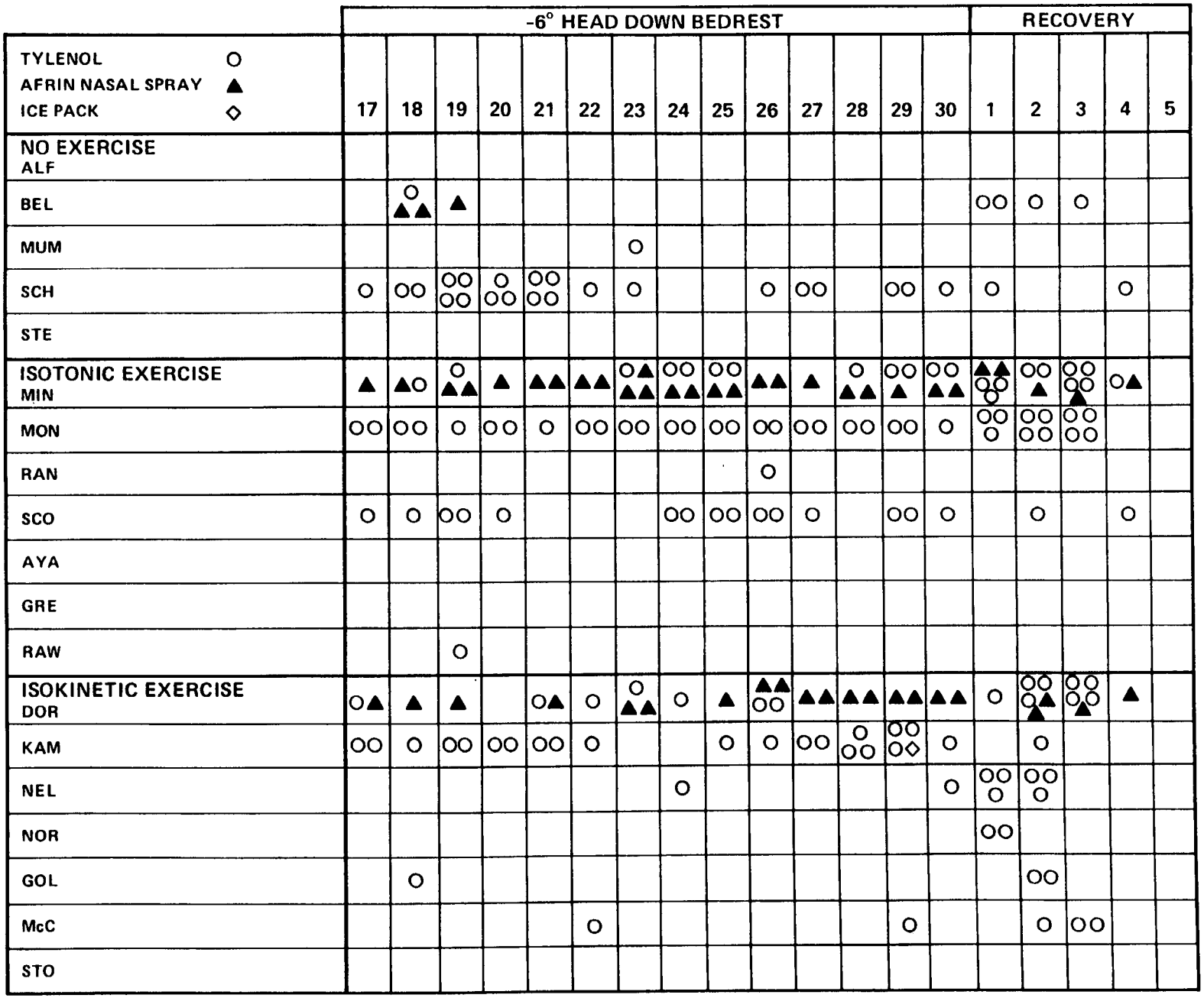
Appendix A

HEADACHE, CONGESTION, GENERAL DISCOMFORT

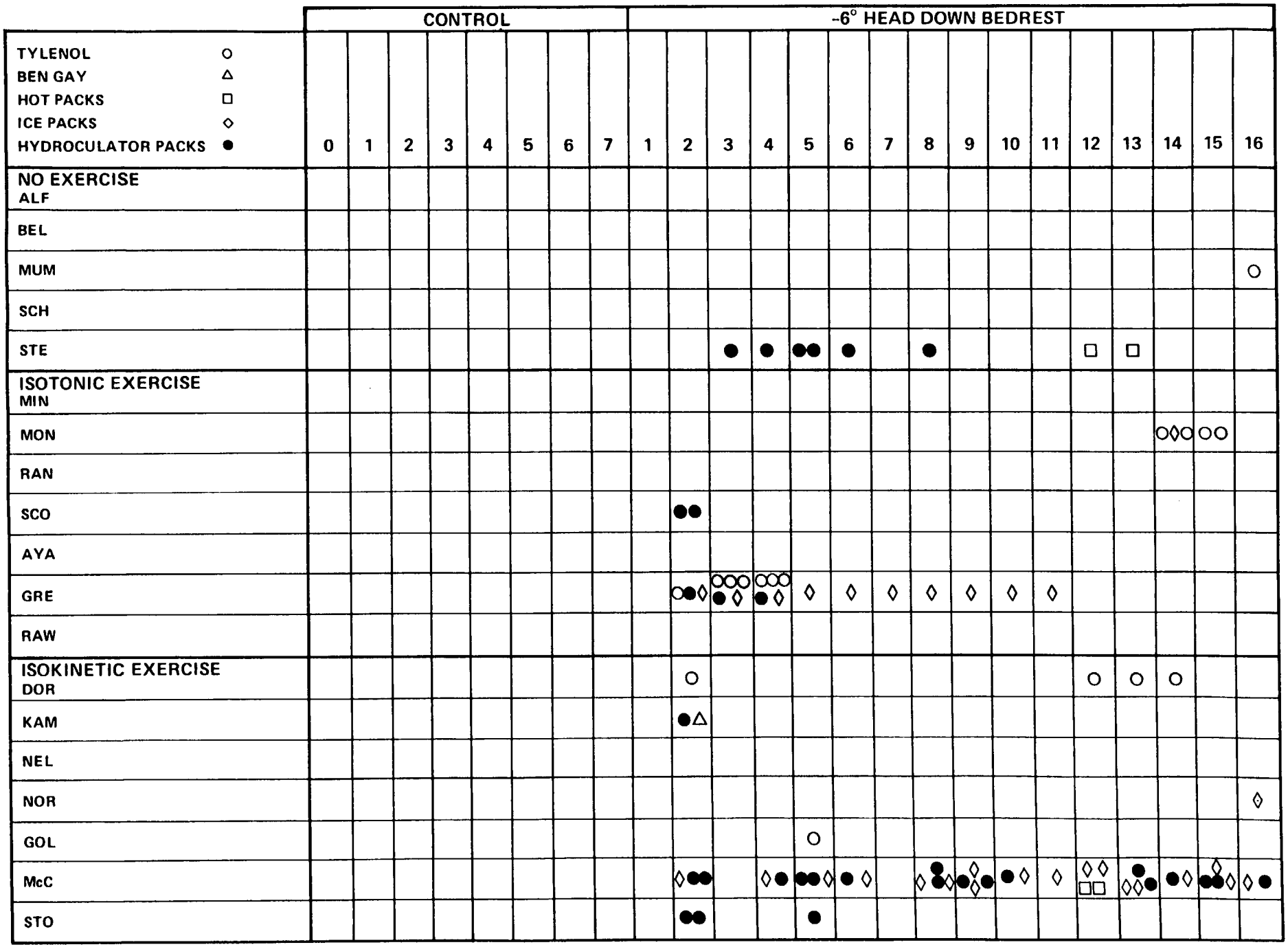
	CONTROL								-6° HEAD DOWN BEDREST															
TYLENOL ○ AFRIN NASAL SPRAY ▲ ICE PACK ◇	0	1	2	3	4	5	6	7	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
NO EXERCISE ALF																								
BEL																								
MUM																								
SCH			○○	○○ ○○	○				○	○	○	○○ ◇▲	○	○	○○		○		○			○ ○○	○○ ○○	○○ ○
STE																								
ISOTONIC EXERCISE MIN														○			○▲	○○ ▲	▲▲	○▲	▲▲	○○	▲	○○ ▲
MON										○	○	○○	○○	○○	○ ○○		○	○○	○○	○	○	○	○○	○○
RAN	○									○		○	○	○		○		○						
SCO									○				○			○							○	
AYA																								
GRE																								
RAW																								
ISOKINETIC EXERCISE DOR		○○							○									○○ ▲	▲	▲	▲	○	▲▲ ○	○
KAM										○	○	○○	○							○○		○	○	○
NEL															○							○		
NOR												○	○	○○ ○				○						
GOL											○						○	○						
McC																				○				
STO																								

HEADACHE, CONGESTION, GENERAL DISCOMFORT

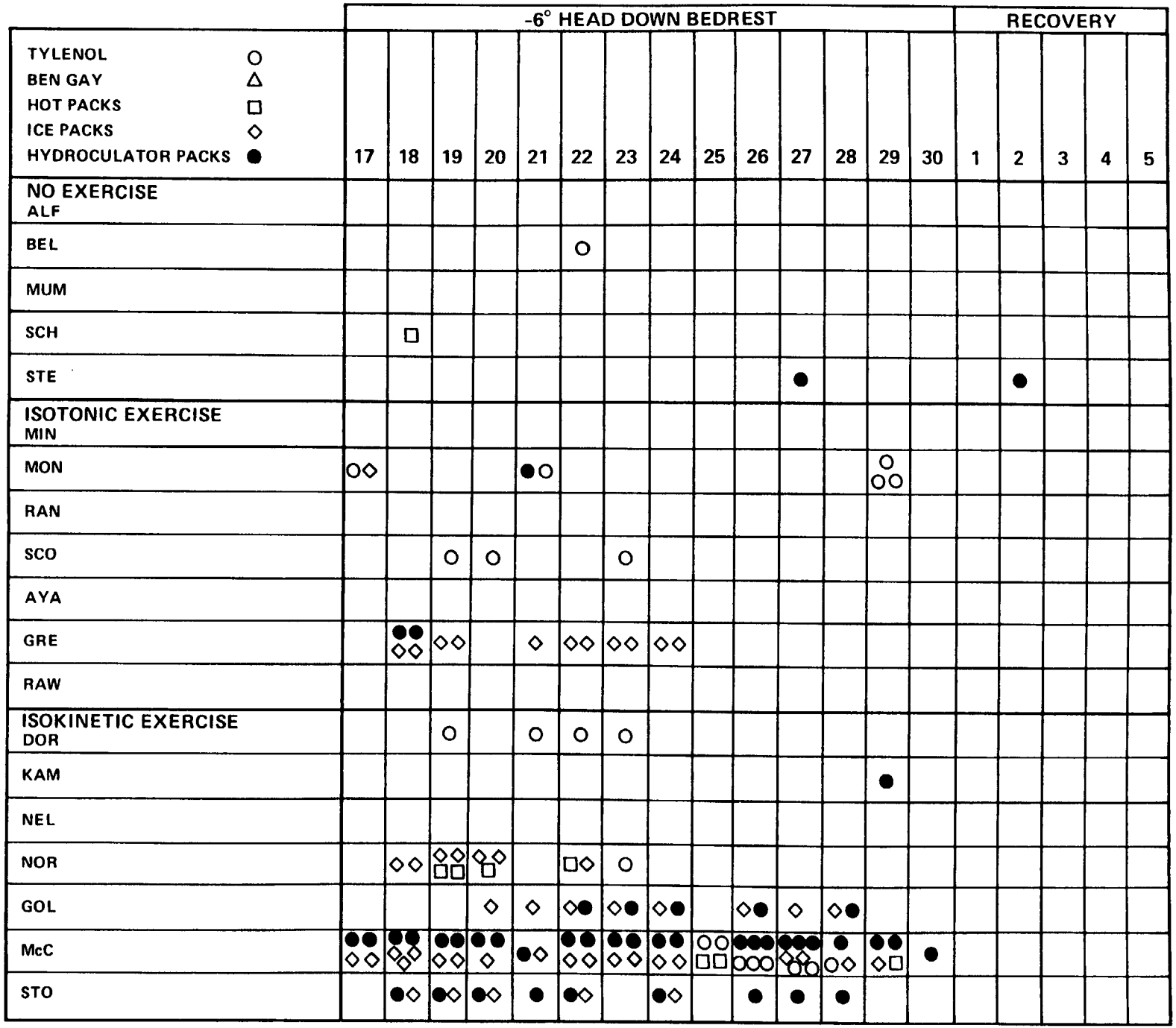


Appendix B

MUSCLE ACHES

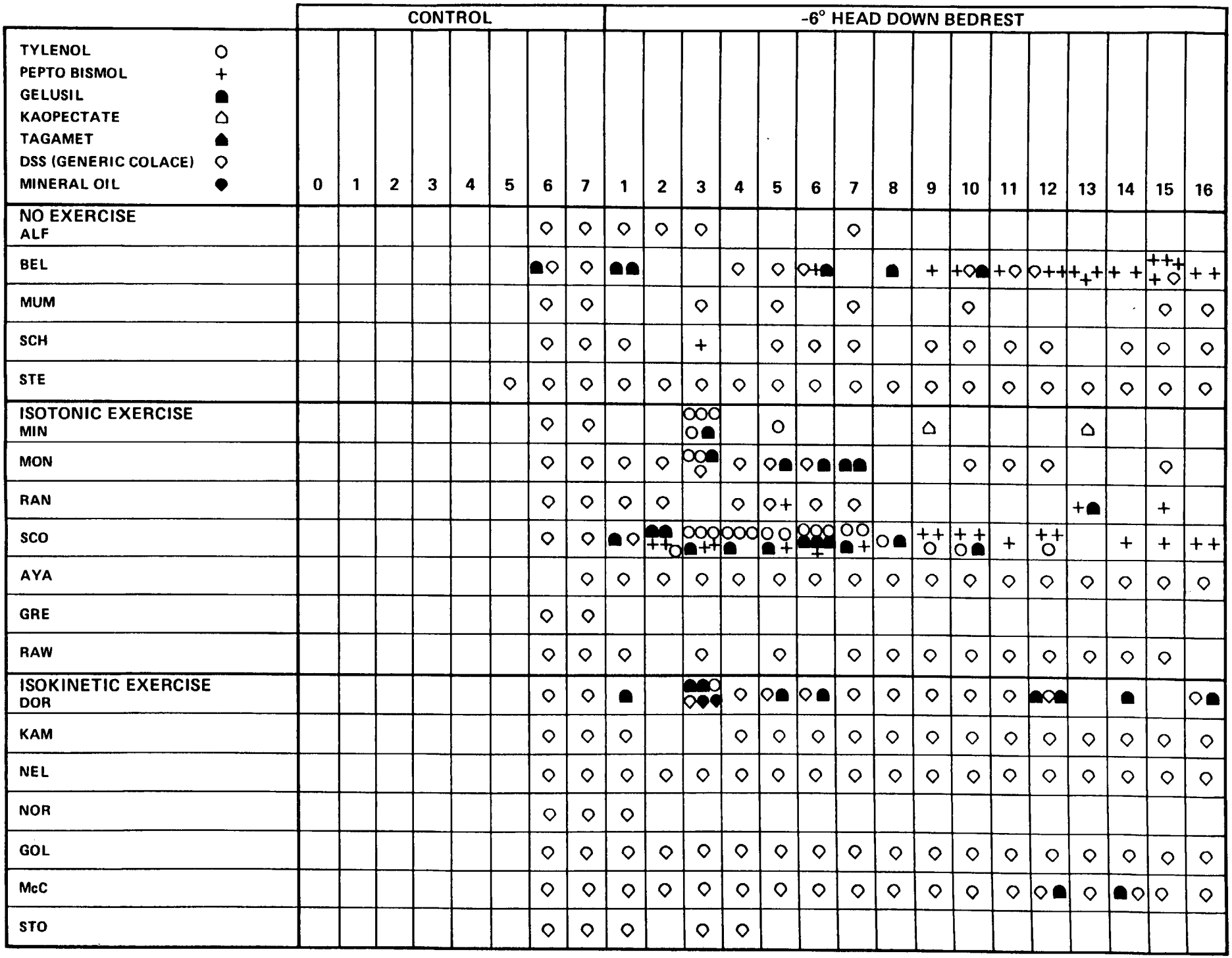


MUSCLE ACHES



Appendix C

STOMACH DISTRESS, STOOL SOFTENER



STOMACH DISTRESS, STOOL SOFTENER

TYLENOL ○
PEPTO BISMOL +
GELUSIL ●
KAOPECTATE △
TAGAMET ▲
DSS (GENERIC COLACE) ◇
MINERAL OIL ◆

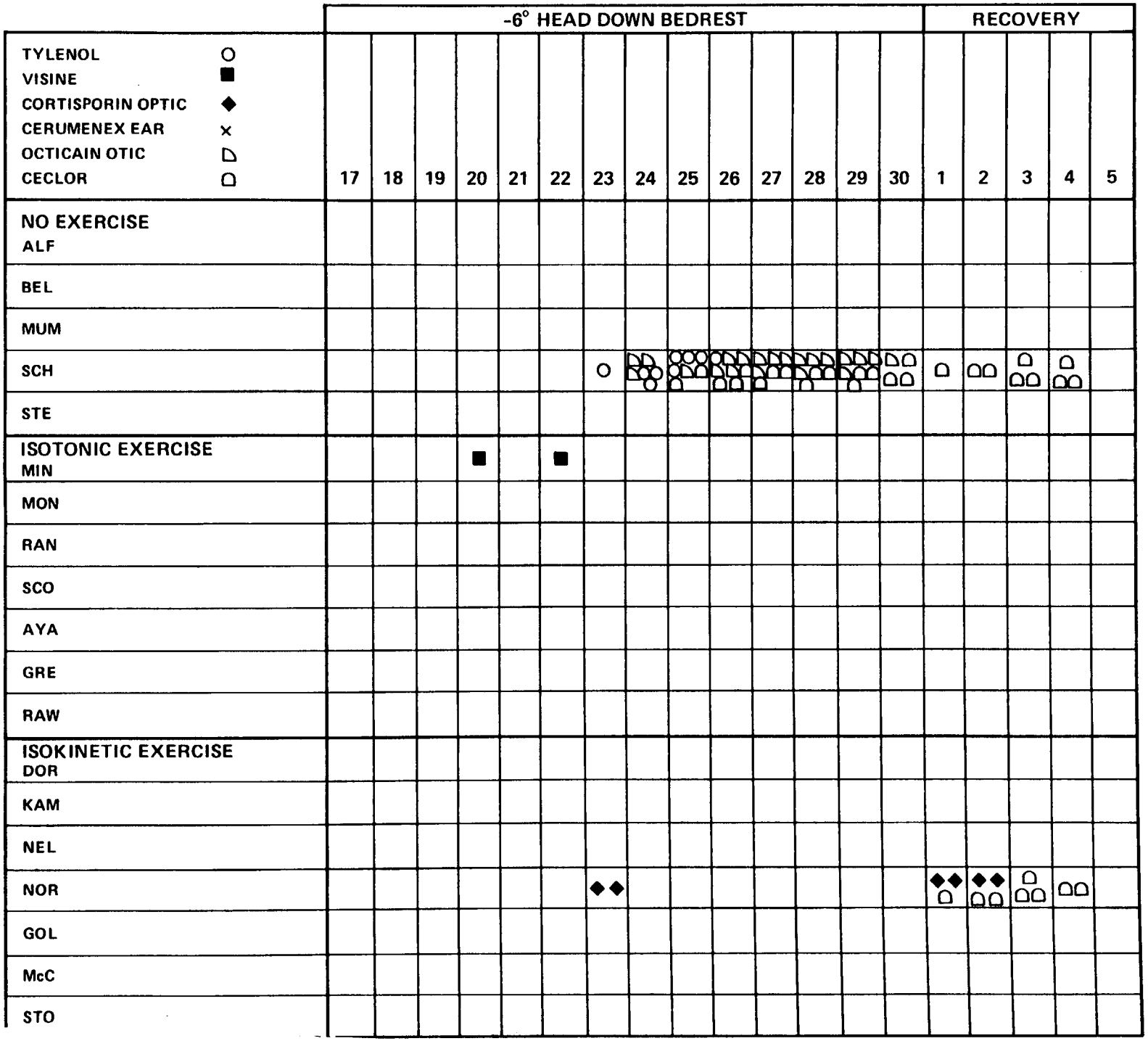
	-6° HEAD DOWN BEDREST														RECOVERY				
	17	18	19	20	21	22	23	24	25	26	27	28	29	30	1	2	3	4	5
NO EXERCISE ALF																			
BEL	+◇	++ ◇	+◇	+◇	++ ◇		++ ◇	+	++ ◇	++	++	++ ◇◇ ●●	++ ◇		+	+	+		
MUM	◇	◇	◇		◇		◇	◇	◇	◇	◇		++ +◇	◇					
SCH	◇	◇		◇	◇	◇	◇	◇		◇	◇								
STE	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇					
ISOTONIC EXERCISE MIN		▲	▲		+▲					▲▲	+▲	+▲	+△	▲					
MON			◇	◇						◇		◇		◇					
RAN	●◆	●◇																	
SCO	+	+	▲	++	+		+		++	++	▲+ ◇	●●	○○ +						
AYA	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇						
GRE																			
RAW				◇			◇												
ISOKINETIC EXERCISE DOR	●◇	○ ●◇		●○	▲	▲	▲		▲	▲	▲▲								
KAM	◇	◇	◇	◇	◇	◇	◇			◇	◇	◇							
NEL	◇	◇	◇	◇	◇	◇	◇		◇	◇	◇	◇	◇						
NOR	◇																		
GOL	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇						
McC	◇	◇	◇●	◇	◇	◇	◇	◇	◇	◇	◇	◇	◇						
STO																			

Appendix D

EYE, EAR, SKIN IRRITATIONS — INFECTIONS

	CONTROL								-6° HEAD DOWN BEDREST																
TYLENOL ○ VISINE ■ CORTISPORIN OPTIC ◆ CERUMENEX EAR × OCTICAIN OTIC ⊃ CECLOR ⊂	0	1	2	3	4	5	6	7	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
NO EXERCISE ALF													××	×××		×								
BEL																								
MUM																								
SCH																								
STE																								
ISOTONIC EXERCISE MIN																								
MON																								
RAN																								
SCO																								
AYA																								
GRE																								
RAW															⊃									
ISOKINETIC EXERCISE DOR																								
KAM																								
NEL																								
NOR																								
GOL																								
McC																								
STO																								

EYE, EAR, SKIN IRRITATIONS — INFECTIONS



Appendix E

BASAL STUDY

SODIUM (mEq/l)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	138.40	138.20	138.30	136.40	137.50	136.30
407	139.50	138.00	138.50	136.10	138.20	137.10
409	136.40	137.50	138.30	136.40	137.70	137.70
397	138.40	139.10	137.80	139.00	138.00	138.30
391	139.70	135.80	138.20	140.60	139.10	138.80
MEAN C	138.48	137.72	138.22	137.70	138.10	137.64
STD. DEV. C	1.31	1.22	0.26	2.00	0.62	0.98
390	138.40	138.70	139.20	136.10	137.70	136.20
420	137.30	139.10	139.60	136.30	138.20	136.60
412	137.70	137.30	137.40	137.00	138.00	138.10
403	140.60		139.00	139.10	138.70	139.40
385	136.60	140.60	141.60	141.60	140.30	141.10
405	135.00	139.40	140.50	141.20	140.00	139.90
394	140.30	134.80	137.10	138.60	138.10	139.50
MEAN L	137.99	138.32	139.20	138.56	138.71	138.69
STD. DEV. L	1.99	2.03	1.60	2.24	1.03	1.80
381	138.10	138.60	137.50	139.70	136.30	135.00
408	139.00	138.30	140.10	138.00	138.40	136.50
422	138.90	137.90	136.90	136.40	137.40	139.20
392	137.40	138.10	135.90	137.10	136.60	138.40
372	134.00	139.00	138.40	140.60	138.10	138.70
399	134.50	140.80	138.40	140.60	138.60	140.70
402	136.60	135.70	138.30	139.50	138.60	139.70
MEAN E	136.93	138.34	137.93	138.84	137.71	138.31
STD. DEV. E	2.01	1.52	1.33	1.69	0.96	1.95
TOTAL MEAN	137.73	138.16	138.47	138.44	138.18	138.27
TOTAL STD. DEV.	1.87	1.56	1.34	1.93	0.97	1.65

POTASSIUM (mEq/l)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	4.36	4.33	4.24	4.24	4.08	3.95
407	4.31	4.31	3.87	3.88	3.86	3.87
409	4.66	4.52	4.50	4.27	4.25	3.94
397	3.72	4.02	3.63	3.88	3.87	4.08
391	4.36	4.12	4.40	4.20	4.21	4.07
MEAN C	4.28	4.26	4.13	4.09	4.05	3.98
STD. DEV. C	0.34	0.20	0.37	0.20	0.18	0.09
390	4.17	4.27	4.08	4.62	4.08	3.91
420	4.45	4.24	4.17	4.27	3.89	3.98
412	4.05	4.41	4.15	4.04	3.70	4.13
403	4.35		4.20	4.25	4.04	3.90
385	4.23	4.25	4.34	4.90	4.29	4.27
405	4.53	4.45	4.04	4.81	4.55	4.52
394	4.86	4.57	4.29	4.23	4.37	4.21
MEAN L	4.38	4.37	4.18	4.45	4.13	4.13
STD. DEV. L	0.27	0.13	0.11	0.33	0.29	0.22
381	4.54	4.29	4.29	4.31	4.22	4.01
408	4.12	4.31	4.22	4.09	3.96	4.12
422	4.76	4.63	4.14	3.80	3.96	3.88
392	4.21	4.81	4.21	4.28	4.17	4.31
372	4.84	4.22	4.00	5.04	3.88	4.19
399	4.18	4.51	4.02	3.96	4.03	3.94
402	4.38	4.13	4.12	4.07	4.19	4.00
MEAN E	4.43	4.41	4.14	4.22	4.06	4.06
STD. DEV. E	0.29	0.24	0.11	0.40	0.13	0.15
TOTAL MEAN	4.37	4.36	4.15	4.27	4.08	4.07
TOTAL STD. DEV.	0.29	0.20	0.20	0.35	0.21	0.17

OSMOLALITY (mosm/kg)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	290.00	287.00	291.00	288.00	287.00	290.00
407	292.00	292.00	291.00	286.00	290.00	291.00
409	292.00	291.00	285.00	291.00	292.00	292.00
397	292.00	293.00	290.00	292.00	290.00	292.00
391	288.00	290.00	290.00	294.00	294.00	294.00
MEAN C	290.80	290.60	289.40	290.20	290.60	291.80
STD. DEV. C	1.79	2.30	2.51	3.19	2.61	1.48
390	287.00	292.00	287.00	286.00	290.00	291.00
420	288.00	294.00	292.00	287.00	288.00	294.00
412	294.00	296.00	289.00	292.00	290.00	291.00
403	286.00		292.00	296.00	294.00	295.00
385	289.00	292.00	288.00	296.00	294.00	302.00
405	288.00	289.00	285.00	292.00	294.00	297.00
394	286.00	287.00	280.00	287.00	289.00	294.00
MEAN L	288.29	291.67	287.57	290.86	291.29	294.86
STD. DEV. L	2.75	3.27	4.20	4.26	2.63	3.80
381	290.00	291.00	294.00	290.00	288.00	294.00
408	290.00	290.00	298.00	294.00	293.00	293.00
422	291.00	295.00	285.00	289.00	291.00	293.00
392	289.00	288.00	288.00	290.00	289.00	290.00
372	292.00	287.00	288.00	290.00	291.00	296.00
399	290.00	295.00	284.00	293.00	293.00	293.00
402	292.00	290.00	289.00	290.00	298.00	295.00
MEAN E	290.57	290.86	289.43	290.86	291.86	293.43
STD. DEV. E	1.13	3.13	4.96	1.86	3.29	1.90
TOTAL MEAN	289.79	291.06	288.74	290.68	291.32	293.53
TOTAL STD. DEV.	2.25	2.84	4.04	3.09	2.77	2.84

CPK (IU/l)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	120.40	122.10	47.40	79.70	48.90	215.90
407	182.50	199.00	82.80	97.20	90.70	195.10
409	158.70	189.40	135.30	108.20	90.30	162.30
397	113.00	96.20	73.20	52.60	48.20	88.60
391	136.30	160.20	57.40	57.90	62.30	415.00
MEAN C	142.18	153.38	79.22	79.12	68.08	215.38
STD. DEV. C	28.54	43.80	34.21	24.12	21.22	121.60
390	142.60	165.30	84.20	68.10	88.70	364.30
420	163.70	191.60	63.30	95.20	115.10	161.10
412	175.60	162.50	72.70	83.40	99.90	261.30
403	168.80		98.60	107.20	97.00	224.60
385	150.40	248.20	99.60	93.20	129.70	124.70
405	232.80	479.60	155.30	144.10	350.70	275.30
394	112.10	120.40	91.80	102.20	107.50	126.90
MEAN L	163.71	227.93	95.07	99.06	141.23	219.74
STD. DEV. L	37.03	130.26	29.72	23.66	93.32	88.34
381	94.0	110.10	50.50	44.70	38.30	103.10
408	189.90	205.70	88.60	86.60	108.20	190.50
422	117.20	132.60	106.50	113.70	119.90	198.60
392	103.70	94.60	63.40	94.40	64.20	100.20
372	114.40	315.30	344.10	78.00	56.70	62.50
399	152.50	109.00	104.10	87.10	96.30	208.10
402	178.80	155.20	76.30	101.80	97.40	133.80
MEAN E	135.87	160.36	119.07	86.61	83.00	142.40
STD. DEV. E	37.83	77.83	101.31	21.82	30.07	57.11
TOTAL MEAN	147.79	180.94	99.74	89.23	100.53	190.10
TOTAL STD. DEV.	35.75	93.58	65.16	23.30	66.04	91.54

LDH (IU/l)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	118.50	166.60	95.60	101.20	89.90	144.00
407	113.10	130.30	92.60	79.00	66.20	110.10
409	140.10	143.40	123.60	81.20	79.00	167.90
397	146.50	110.40	82.20	81.30	59.90	177.50
391	147.90	128.70	112.00	118.80	123.30	176.70
MEAN C	133.22	135.88	101.20	92.30	83.00	155.42
STD. DEV. C	16.28	20.81	16.47	17.34	25.01	28.64
390	167.70	156.70	83.60	92.40	73.70	128.00
420	169.30	148.20	111.30	125.50	118.40	155.90
412	128.10	134.20	99.10	99.60	106.30	144.90
385	117.50	92.00	98.00	90.30	106.80	107.70
405	138.30	193.10	102.20	102.40	106.90	138.40
394	105.20	106.80	116.50	116.10	121.50	144.80
MEAN L	136.61	138.50	101.23	101.96	104.43	135.66
STD. DEV. L	24.16	36.31	10.59	14.14	15.79	15.60
381	184.30	109.70	133.70	125.00	111.20	151.90
408	135.90	166.90	110.90	109.40	99.00	167.60
422	113.10	145.40	121.00	97.40	98.30	142.20
392	89.70	109.10	86.00	85.20	85.30	133.30
372	171.60	159.20	172.40	157.70	125.40	127.00
399	143.00	150.10	119.20	100.80	102.30	135.10
402	156.70	139.80	110.50	111.00	113.90	155.20
MEAN E	142.04	140.03	121.96	112.36	105.06	144.61
STD. DEV. E	32.89	22.72	26.57	23.53	12.97	14.31
TOTAL MEAN	137.72	138.37	108.86	103.25	99.19	144.11
TOTAL STD. DEV.	25.05	25.98	20.94	19.60	19.22	19.85

LACTATE (mg/dl)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	5.00	9.30	6.20	5.40	8.20	5.20
407	7.00	16.30	4.60	5.10	3.40	3.80
409	10.90	11.80	8.20	8.00	8.10	7.30
397	9.70	6.60	6.30	5.00	9.30	2.90
391	7.40	7.00	6.30	5.10	7.70	4.70
MEAN C	8.00	10.20	6.32	5.72	7.34	4.78
STD. DEV. C	2.33	3.99	1.28	1.28	2.28	1.66
390	9.20	10.50	5.80	6.60	5.80	6.40
420	4.60	7.20	7.00	7.60	9.00	6.70
412	9.30	13.30	9.00	6.80	11.10	8.90
403	12.60		6.90	7.00	4.70	9.20
385	11.70	10.30	6.50	4.70	4.80	6.90
405	8.10	10.50	5.10	4.40	5.70	6.40
394	4.30	15.70	6.40	4.40	5.30	6.40
MEAN L	8.54	11.25	6.67	5.93	6.63	7.27
STD. DEV. L	3.19	2.91	1.22	1.37	2.45	1.23
381	9.60	13.30	13.10	11.30	11.00	11.30
408	6.50	10.80	6.50	5.30	8.40	6.30
422	12.20	9.20	4.70	3.90	3.80	5.60
392	8.60	5.90	5.40	7.20	4.80	7.30
372	7.80	12.00	5.70	5.10	4.40	10.00
399	6.00	19.20	6.10	4.60	5.50	4.80
402	7.60	8.60	6.00	6.50	3.40	7.10
MEAN E	8.33	11.29	6.79	6.27	5.90	7.49
STD. DEV. E	2.09	4.24	2.84	2.48	2.79	2.35
TOTAL MEAN	8.32	10.97	6.62	6.00	6.55	6.69
TOTAL STD. DEV.	2.47	3.58	1.89	1.76	2.47	2.09

GLUCOSE (mg/dl)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	97.90	83.10	68.10	78.40	71.40	77.40
407	66.30	71.90	84.30	90.10	76.20	53.70
409	106.20	83.00	83.90	75.00	73.30	90.90
397	73.60	79.30	77.10	67.70	75.00	82.70
391	70.40	114.40	80.50	32.30	90.70	75.70
MEAN C	82.88	86.34	78.78	68.70	77.32	76.08
STD. DEV. C	17.93	16.33	6.64	21.90	7.70	13.84
390	63.30	115.70	75.20	73.00	35.50	75.10
420	76.40	73.30	84.90	85.40	86.80	87.10
412	113.70	120.70	88.30	75.30	86.50	90.70
403	67.10		80.90	81.00	81.70	77.30
385	28.50	70.00	85.30	86.70	85.20	90.80
405	79.90	127.10	87.50	52.90	85.00	48.90
394	88.30	69.20	71.70	65.60	70.00	45.70
MEAN L	73.89	96.00	81.97	74.27	75.81	73.66
STD. DEV. L	25.99	27.84	6.36	11.96	18.71	19.04
381	100.70	120.10	82.40	82.90	77.90	81.50
408	71.00	96.00	78.40	79.20	90.70	92.80
422	136.90	102.00	91.30	77.50	88.00	115.10
392	80.80	77.60	64.20	73.30	76.40	82.80
372	128.00	124.20	59.50	81.50	82.50	76.10
399	68.10	89.50	83.10	82.10	82.70	84.20
402	78.60	78.80	88.80	93.80	90.10	89.90
MEAN E	94.87	98.31	78.24	81.47	84.04	88.91
STD. DEV. E	27.83	18.49	12.05	6.35	5.73	12.78
TOTAL MEAN	83.98	94.22	79.76	75.46	79.24	79.92
TOTAL STD. DEV.	25.32	20.92	8.65	13.96	12.47	16.39

PROTEIN (g/dl)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	7.20	7.60	6.90	7.10	7.00	7.50
407	7.80	8.00	7.30	7.20	7.40	7.50
409	7.90	7.80	7.70	7.80	7.90	7.70
397	6.90	8.00	6.90	7.00	7.20	7.50
391	6.30	6.50	6.40	6.40	6.50	6.50
MEAN C	7.22	7.58	7.04	7.10	7.20	7.34
STD. DEV. C	0.66	0.63	0.49	0.50	0.51	0.48
390	7.40	7.80	7.10	6.90	7.10	7.50
420	7.60	7.70	7.00	6.80	7.00	7.30
412	7.30	7.70	7.10	7.10	7.30	7.80
403	7.30		7.20	7.00	7.20	8.00
385	7.00	7.00	6.80	6.90	7.10	6.90
405	7.00	7.00	6.70	6.60	7.20	6.60
394	6.60	7.00	6.70	6.80	7.10	6.60
MEAN L	7.17	7.37	6.94	6.87	7.14	7.24
STD. DEV. L	0.33	0.40	0.21	0.16	0.10	0.56
381	7.70	8.10	7.20	7.30	7.20	7.30
408	7.70	8.10	7.10	7.20	7.00	7.50
422	7.80	7.80	7.70	7.60	7.60	7.70
392	7.80	8.40	7.50	7.40	7.70	8.00
372	7.50	6.70	6.60	6.60	6.90	6.20
399	7.30	7.00	7.00	7.00	7.50	7.20
402	7.70	7.70	7.00	7.30	7.00	7.40
MEAN E	7.64	7.69	7.16	7.20	7.27	7.33
STD. DEV. E	0.18	0.62	0.36	0.32	0.33	0.56
TOTAL MEAN	7.36	7.55	7.05	7.05	7.21	7.30
TOTAL STD. DEV.	0.44	0.54	0.35	0.35	0.32	0.51

CORTISOL (ug/dl)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	25.20	15.50	21.60	14.80	21.30	20.20
407	3.20	7.80	11.80	16.20	18.80	21.10
409	16.20	15.70	15.90	27.80	22.10	17.30
397	13.20	14.00	14.90	15.10	17.60	19.00
391	16.30	8.30	15.20	17.10	18.90	19.20
MEAN C	14.82	12.26	15.88	18.20	19.74	19.36
STD. DEV. C	7.90	3.90	3.56	5.44	1.88	1.43
390	11.30	19.30	14.70	23.00	15.30	15.40
420	10.50	17.30	17.60	11.60	19.00	13.60
412	20.90	18.90	14.80	21.40	16.40	18.00
403	13.40		19.50	20.80	22.70	21.80
385	14.20	10.00	19.50	17.60	17.70	15.80
405	12.50	15.70	19.20	14.40	18.00	22.30
394	15.60	15.90	15.60	16.40	15.90	12.40
MEAN L	14.06	16.18	17.27	17.89	17.86	17.04
STD. DEV.L	3.47	3.37	2.21	4.10	2.49	3.85
381	15.40	15.00	16.90	19.20	16.20	16.50
408	15.70	19.30	16.60	20.60	14.80	24.00
422	20.60	22.20	18.50	19.40	23.70	23.40
392	13.10	12.90	6.00	14.70	17.40	20.10
372	27.70	20.10	23.80	22.60	25.30	24.90
399	14.20	12.70	13.60	16.90	16.60	15.10
402	5.30	4.70	10.50	15.70	11.00	16.50
MEAN E	16.00	15.27	15.13	18.44	17.86	20.07
STD. DEV. E	6.89	5.94	5.76	2.81	5.01	4.08
TOTAL MEAN	14.97	14.74	16.12	18.17	18.35	18.77
TOTAL STD.	5.87	4.69	4.05	3.86	3.46	3.59

ALDOSTERONE (ng/dl)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	15.60	11.30	12.00	11.70	12.20	25.70
407	12.50	19.50	5.80	6.90	12.60	16.90
409	19.30	20.10	18.60	25.90	25.10	15.30
397	26.20	16.50	4.60	9.90	10.60	6.30
391	6.50	12.50	21.30	17.20	14.20	13.80
MEAN C	16.02	15.98	12.46	14.32	14.94	15.60
STD. DEV. C	7.38	3.99	7.45	7.48	5.82	6.96
390	9.60	8.40	10.60	24.70	8.70	9.00
420	17.60	24.10	11.10	18.30	16.70	22.00
412	8.90	16.80	13.00	16.90	11.80	7.10
403	8.40		9.50	12.60	13.50	10.10
385	13.50	5.20	10.30	7.60	6.30	9.10
405	12.10	10.00	10.70	7.10	9.90	8.50
394	13.90	19.90	18.30	23.20	11.60	12.30
MEAN L	12.00	14.07	11.93	15.77	11.21	11.16
STD. DEV. L	3.31	7.34	3.01	7.01	3.37	5.04
381	11.00	15.00	16.30	20.20	16.20	13.70
408	17.50	26.00	11.40	23.10	12.00	32.40
422	18.10	15.20	12.50	15.70	17.40	9.80
392	12.60	16.00	8.00	13.60	18.80	20.50
372	11.60	17.10	16.40	18.00	12.70	13.40
399	16.30	9.90	17.50	17.40	19.20	11.90
402	14.60	18.70	14.60	19.10	15.50	16.10
MEAN E	14.53	16.84	13.81	18.16	15.97	16.83
STD. DEV.	2.87	4.87	3.38	3.08	2.81	7.66
TOTAL MEAN	13.99	15.68	12.76	16.27	13.95	14.42
TOTAL STD. DEV.	4.61	5.43	4.46	5.87	4.33	6.75

ACTH (pg/ml)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	154.00	39.00	39.00	29.00	55.00	50.00
407	26.00	51.00	45.00	28.00	54.00	44.00
409	133.00	51.00	53.00	92.00	72.00	48.00
397	213.00	65.00	32.00	38.00	42.00	37.00
391	45.60	14.60	24.40	26.50	22.90	33.30
MEAN C	114.32	44.12	38.68	42.70	49.18	42.46
STD. DEV. C	77.76	18.90	11.11	27.92	18.17	7.13
390	18.00	32.00	30.00	69.00	33.00	16.00
420	59.00	17.00	7.00	19.00	23.00	23.00
412	60.00	53.00	53.00	61.00	80.00	52.00
403	48.00		29.00	43.00	53.00	44.00
385	79.30	30.80	46.90	40.70	61.40	54.50
405	27.20	25.00	26.80	27.50	39.70	53.70
394	74.40	74.20	73.60	75.50	63.20	74.00
MEAN L	52.27	38.67	38.04	47.96	50.47	45.31
STD. DEV. L	22.90	21.12	21.61	21.24	19.73	19.92
381	85.00	53.00	59.00	109.00	74.00	75.00
408	29.00	32.00		16.00	10.00	2.00
422	75.00	54.00	45.00	48.00	57.00	33.00
392	228.00	36.00	26.00	34.00	35.00	30.00
372	85.00	52.20	53.80	80.40	69.50	49.40
399	12.30	18.30	34.90	35.30	32.70	35.80
402	11.90	28.50	8.50	38.70	22.10	44.30
MEAN E	75.17	39.14	37.87	51.63	42.90	38.50
STD. DEV. E	74.88	14.09	18.78	32.01	24.34	22.09
TOTAL MEAN	77.04	40.37	38.16	47.93	47.34	42.05
TOTAL STD. DEV.	63.35	17.06	17.26	26.04	20.32	17.76

PLASMA RENIN ACTIVITY (ngA1/ml/hr)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	1.52	2.63	0.89	1.53	1.35	3.85
407	1.11	2.74	1.18	1.60	2.53	3.45
409	1.36	2.23	1.42	2.24	2.56	2.19
397	3.95	2.35	0.88	2.63	1.88	1.55
391	0.57	1.26	1.58	1.72	1.38	1.52
MEAN C.	1.70	2.24	1.19	1.94	1.94	2.51
STD. DEV. C	1.31	0.59	0.31	0.47	0.59	1.08
390	0.78	1.19	0.98	2.82	1.53	1.97
420	0.91	1.55	0.95	1.31	1.37	4.77
412	0.23	0.54	0.41	0.50	0.52	0.37
403	0.94	1.86	1.42	1.93	2.11	1.69
385	0.83	0.80	1.02	1.10	1.25	1.68
405	1.11	1.69	1.16	1.52	1.14	1.43
394	0.79	0.87	1.13	1.14	1.05	0.84
MEAN L	0.80	1.21	1.01	1.47	1.28	1.82
STD. DEV. L	0.28	0.50	0.31	0.74	0.48	1.41
381	0.70	1.50	0.26	0.46	0.35	2.71
408	2.04	3.76	2.30	4.33	2.32	8.49
422	3.08	1.39	1.08	1.50	2.11	0.94
392	4.69	1.51	0.91	1.30	1.44	1.25
372	0.82	1.26	0.93	0.90	0.77	1.31
399	2.75	1.55	2.56	2.00	2.17	2.11
402	6.97	1.50	1.48	2.30	1.30	1.23
MEAN E	3.01	1.78	1.36	1.83	1.49	2.58
STD. DEV. E	2.22	0.88	0.82	1.27	0.75	2.68
TOTAL MEAN	1.85	1.69	1.19	1.73	1.53	2.28
TOTAL STD. DEV.	1.73	0.77	0.55	0.90	0.64	1.86

AVP (pg/ml)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	10.10	4.90	1.90	0.20	2.30	1.70
407	1.10	0.60	0.60	0.60	0.90	1.00
409	15.20	4.40	2.00	2.50	5.00	2.30
397	43.20	2.10	1.60	1.20	0.80	1.10
391	1.30	1.30	1.30	1.10	0.90	1.30
MEAN C	14.18	2.66	1.48	1.12	1.98	1.48
STD. DEV. C	17.30	1.90	0.56	0.87	1.80	0.53
390	0.30	0.60	0.30	0.70	0.30	1.30
420	0.60	1.10	0.70	1.20	2.10	1.70
412	4.80	4.70	3.40	1.80	4.10	2.50
403	2.80		2.80	5.40	4.70	4.60
385	2.80	0.60	1.20	0.60	1.30	1.40
405	1.00	0.90	0.70	0.70	0.90	1.30
394	1.70	0.90	1.40	2.00	1.40	2.00
MEAN L	2.00	1.47	1.50	1.77	2.11	2.11
STD. DEV. L	1.58	1.60	1.16	1.69	1.66	1.18
381	1.70	1.40	1.70	3.40	3.30	1.70
408	1.30	1.20	2.20	2.70	1.30	1.40
422	2.80	1.50	0.70	1.90	2.40	0.80
392	28.70	1.60	1.00	1.50	0.60	1.30
372	1.30	0.80	0.90	0.70	0.70	0.70
399	1.30	1.30	1.30	1.10	0.90	1.30
402	3.30	3.30	3.10	4.90	4.40	3.20
MEAN E	5.77	1.59	1.56	2.31	1.94	1.49
STD. DEV. E	10.14	0.80	0.85	1.47	1.47	0.83
TOTAL MEAN	6.59	1.84	1.52	1.80	2.02	1.72
TOTAL STD. DEV.	11.23	1.45	0.87	1.44	1.54	0.92

NOREPINEPHRINE (pg/ml)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	328.00	595.00	169.00	59.00	161.00	856.00
407	220.00	341.00	99.00	67.00	92.00	336.00
409	275.00	341.00	111.00	251.00	171.00	273.00
397	308.00	514.00	248.00	191.00	352.00	612.00
391	456.00	336.00	202.00	155.00	142.00	326.00
MEAN C	317.40	425.40	165.80	144.60	183.60	480.60
STD. DEV. C	87.60	121.30	62.34	82.05	98.93	248.04
390	289.00	294.00	59.00	130.00		350.00
420	514.00	401.00	178.00	157.00	179.00	626.00
412	338.00	383.00	160.00	85.00	169.00	396.00
403	364.00	448.00	145.00	56.00	129.00	389.00
385	245.00	300.00	82.00	92.00	116.00	306.00
405	160.00	172.00	119.00	32.00	26.00	119.00
394	356.00	289.00	97.00	121.00	98.00	344.00
MEAN L	323.71	326.71	120.00	96.14	119.50	361.43
STD. DEV. L	110.52	91.78	43.37	43.46	55.31	149.57
381	127.00	250.00	26.00	57.00	62.00	238.00
408	247.00	405.00	106.00	107.00	62.00	208.00
422	320.00	330.00	231.00	294.00	204.00	442.00
392	162.00	338.00	111.00	110.00	67.00	194.00
372	328.00	247.00	134.00	35.00	176.00	291.00
399	329.00	353.00	308.00	264.00		522.00
402	165.00	202.00	97.00	91.00	65.00	241.00
MEAN E	239.71	303.57	144.71	136.86	106.00	305.14
STD. DEV. E	88.12	71.88	94.19	101.10	65.69	126.73
TOTAL MEAN	291.11	344.16	141.16	123.89	133.59	372.05
TOTAL STD. DEV.	99.99	101.94	69.25	77.57	76.77	177.60

EPINEPHRINE (pg/ml)

SUBJECT	DAY					
	-3	1	8	14	21	+4
376	40.00	51.00	34.00	24.00	44.00	48.00
407	38.00	50.00	24.00	26.00	24.00	33.00
409	56.00	44.00	15.00	42.00	28.00	39.00
397	554.00	70.00	42.00	37.00	57.00	78.00
391	13.00	73.00	22.00	33.00	18.00	39.00
MEAN C	140.20	57.60	27.40	32.40	34.20	47.40
STD. DEV C	231.83	13.01	10.62	7.50	15.97	17.92
390	16.00		10.00	15.00		
420	13.00	22.00	11.00	15.00	7.00	17.00
412	41.00	79.00	39.00	49.00	111.00	54.00
403	29.00	133.00	21.00	26.00	45.00	29.00
385	32.00	24.00	18.00	14.00	16.00	28.00
405	34.00	32.00	27.00	8.00	9.00	80.00
394	3.00	11.00	12.00	27.00	3.00	41.00
MEAN L	24.00	50.17	19.71	22.00	31.83	41.50
STD. DEV. L	13.56	46.98	10.48	13.71	41.62	22.70
381	47.00	66.00		28.00	29.00	48.00
408	21.00	50.00	34.00	18.00	18.00	32.00
422	39.00	47.00	23.00	24.00	25.00	32.00
392	93.00	39.00	27.00	37.00	17.00	33.00
372	24.00	55.00	21.00	34.00	39.00	21.00
399	11.00	42.00	14.00	12.00		30.00
402	35.00	44.00	63.00	41.00	51.00	29.00
MEAN E	38.57	49.00	30.33	27.71	29.83	32.14
STD. DEV. E	26.86	9.17	17.32	10.47	13.12	8.07
TOTAL MEAN	59.95	51.78	25.39	26.84	31.82	39.50
TOTAL STD. DEV.	121.30	27.07	13.29	11.39	25.73	17.10

Appendix F

TILT STUDY

SODIUM (mEq/l)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	138.30	137.60	137.00	137.00
407	138.80	138.80	136.50	137.00
409	135.70	135.20	135.70	134.90
397	138.90	138.80	137.00	137.00
391	135.60	135.60	138.50	138.80
MEAN C	137.46	137.20	136.94	136.94
STD. DEV. C	1.67	1.72	1.02	1.38
390	139.00	139.20	137.80	137.80
420	139.20	138.80	136.20	136.10
412	141.60	141.60	137.00	137.00
403	139.90	138.10	135.80	135.60
385	140.30	141.80	140.00	138.80
405	138.10	137.70	137.60	138.70
394	135.80	135.90	137.80	137.40
MEAN L	139.13	139.01	137.46	137.34
STD. DEV. L	1.84	2.11	1.37	1.22
381	138.20	138.50	136.20	137.00
408	137.60	138.60	136.80	136.80
422	139.40	140.10	136.90	137.40
392	138.20	137.70	135.90	135.30
372	138.90	139.60	137.30	138.00
399	135.80	139.50	138.40	138.50
402	135.00	135.50	139.00	139.10
MEAN E	137.59	138.50	137.21	137.44
STD. DEV. E	1.61	1.55	1.13	1.25
TOTAL MEAN	138.12	138.35	137.23	137.27
TOTAL STD. DEV.	1.80	1.87	1.15	1.22

POTASSIUM (mEq/l)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	4.38	4.18	4.43	4.57
407	3.64	3.66	4.23	4.61
409	4.28	4.84	4.24	4.04
397	3.73	3.90	3.78	3.79
391	4.43	4.37	4.41	4.49
MEAN C	4.09	4.19	4.22	4.30
STD. DEV. C	0.38	0.45	0.26	0.36
390	3.81	3.82	3.79	3.84
420	3.98	3.87	4.01	4.06
412	4.14	4.21	4.08	4.03
403	4.33	4.63	3.94	3.98
385	4.11	4.10	4.21	4.27
405	4.12	4.05	4.09	4.21
394	3.67	3.75	3.80	3.77
MEAN L	4.02	4.06	3.99	4.02
STD. DEV. L	0.22	0.30	0.16	0.18
381	3.88	3.88	3.77	3.91
408	4.15	4.56	3.98	4.22
422	4.00	4.16	3.99	3.91
392	4.12	4.12	4.27	4.27
372	4.10	4.21	3.97	4.08
399	4.20	4.51	4.30	4.32
402	4.02	4.03	4.26	4.17
MEAN E	4.07	4.21	4.08	4.13
STD. DEV. E	0.11	0.25	0.20	0.17
TOTAL MEAN	4.06	4.15	4.08	4.13
TOTAL STD. DEV.	0.23	0.32	0.21	0.25

OSMOLALITY (mosm/kg)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	285.00	287.00	291.00	290.00
407	292.00	294.00	294.00	293.00
409	286.00	286.00	290.00	290.00
397	289.00	291.00	290.00	292.00
391	289.00	284.00	288.00	291.00
MEAN C	288.20	288.40	290.60	291.20
STD. DEV. C	2.77	4.04	2.19	1.30
390	284.00	289.00	292.00	290.00
420	288.00	291.00	292.00	290.00
412	293.00	294.00	292.00	293.00
403	289.00	288.00	288.00	289.00
385	275.00	287.00	295.00	294.00
405	290.00	291.00	291.00	293.00
394	286.00	289.00	289.00	290.00
MEAN L	286.43	289.86	291.29	291.29
STD. DEV. L	5.80	2.34	2.29	1.98
381	286.00	286.00	293.00	292.00
408	291.00	292.00	294.00	284.00
422	289.00	289.00	294.00	293.00
392	286.00	289.00	295.00	290.00
372	282.00	284.00	287.00	292.00
399	283.00	285.00	294.00	294.00
402	287.00	284.00	295.00	293.00
MEAN E	286.29	287.00	293.14	291.14
STD. DEV. E	3.15	3.06	2.79	3.39
TOTAL MEAN	286.84	288.42	291.79	291.21
TOTAL STD. DEV.	4.11	3.19	2.57	2.35

CPK (IU/l)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	94 00	80.90	91.90	91.20
407	137.90	144.90	105.20	130.60
409	172.50	197.80	105.60	141.40
397	8.18	83.30	37.70	49.80
391	55.60	60.40	68.50	77.40
MEAN C	93.64	113.46	81.78	98.08
STD. DEV. C	65.05	56.76	28.89	37.88
390	141.90	153.50	410.10	122.40
420	86.00	84.90	85.40	85.40
412	98.20	106.90	94.10	95.60
403	225.60	220.00	106.30	110.70
385	209.20	192.80	89.70	90.10
405	269.50	232.30	195.40	208.30
394	159.40	160.70	86.90	87.60
MEAN L	169.97	164.44	152.56	114.30
STD. DEV. L	67.87	55.18	120.06	43.59
381	121.70	127.50	51.30	72.60
408	136.30	162.30	76.20	91.50
422	103.90	109.20	95.20	63.50
392	43.80	55.70	81.10	89.40
372	58.40	62.90	57.10	56.40
399	160.10	166.50	123.10	125.40
402	136.70	145.60	134.10	116.70
MEAN E	108.70	118.53	88.30	87.93
STD. DEV. E	43.05	45.02	31.35	26.05
TOTAL MEAN	127.31	134.11	110.26	100.32
TOTAL STD. DEV.	65.20	54.56	80.17	36.27

LDH (IU/l)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	120.70	101.50	110.20	155.80
407	98.30	104.40	100.80	192.30
409	137.10	206.60	78.40	109.50
397	93.40	99.00	103.60	110.50
391	105.20	126.20	122.90	160.90
MEAN C	110.94	127.54	103.18	145.80
STD. DEV. C	17.89	45.50	16.26	35.55
390	143.90	150.90	105.80	120.10
420	142.40	145.20	120.10	126.50
412	88.20	109.40	113.50	120.30
403	182.00	170.30	93.70	87.10
385	120.90	121.60	98.60	88.60
405	118.50	130.10	120.70	109.50
394	97.90	98.80	117.80	113.90
MEAN L	127.69	128.47	107.46	109.43
STD. DEV. L	31.64	27.29	9.97	15.68
381	132.64	135.30	119.80	136.50
408	118.40	170.80	90.50	151.40
422	112.20	133.40	106.50	98.30
392	78.80	87.10	98.60	113.00
372	128.30	144.20	149.00	153.30
399	153.70	153.40	114.80	113.80
402	190.90	200.60	170.20	130.20
MEAN E	130.63	146.40	121.34	128.07
STD. DEV. E	34.99	35.11	28.54	20.71
TOTAL MEAN	124.36	134.83	111.45	125.87
TOTAL STD. DEV.	29.71	34.67	20.65	26.89

LACTATE (mg/dl)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	Postrest
376	4.30	3.90	4.90	6.50
407	4.70	5.20	4.90	5.70
409	4.40	5.10	5.80	6.70
397	3.90	3.60	3.50	4.10
391	4.30	4.10	5.60	6.10
MEAN C	4.32	4.38	4.94	5.82
STD. DEV. C	0.29	0.73	0.90	1.04
390	5.30	5.80	7.50	8.00
420	6.20	6.70	6.50	6.80
412	5.90	6.00	6.20	6.40
403	4.80	6.40	10.00	10.20
385	4.20	4.50	4.40	4.80
405	6.10	5.80	4.20	4.70
394	2.40	1.80	5.10	5.30
MEAN L	4.99	5.29	6.27	6.60
STD. DEV. L	1.35	1.69	2.03	1.98
381	4.90	4.50	6.20	6.40
408	7.10	6.60	6.20	7.60
422	3.60	3.60	4.50	5.00
392	5.30	5.30	5.00	5.70
372	6.20	6.60	4.50	5.30
399	5.70	4.40	5.50	5.30
402	4.70	4.60	6.40	6.40
MEAN E	5.36	5.09	5.47	5.96
STD. DEV. E	1.13	1.15	0.82	0.91
TOTAL MEAN	4.95	4.97	5.63	6.16
TOTAL STD. DEV.	1.11	1.28	1.44	1.39

GLUCOSE (mg/dl)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	85.40	88.00	83.20	78.70
407	81.60	80.40	83.80	87.00
409	81.70	87.00	92.70	98.60
397	83.60	85.90	83.00	91.00
391	79.70	83.50	80.90	73.40
MEAN C	82.40	84.96	84.72	85.74
STD. DEV. C	2.17	3.05	4.59	9.96
390	83.30	82.80	82.60	83.70
420	82.10	83.30	42.30	108.50
412	79.10	78.70	90.50	89.10
403	78.60	71.20	84.40	88.30
385	77.40	77.50	92.80	93.80
405	88.60	92.10	91.20	81.80
394	63.50	71.10	68.70	73.00
MEAN L	78.94	79.53	78.93	88.31
STD. DEV. L	7.78	7.40	18.10	11.08
381	88.00	95.30	79.20	77.50
408	84.10	97.70	105.80	102.50
422	87.30	89.00	86.60	88.80
392	82.20	80.90	82.70	89.90
372	98.30	91.30	87.40	93.90
399	63.90	82.70	83.80	87.70
402	85.90	88.60	96.40	106.60
MEAN E	84.24	89.36	88.84	92.41
STD. DEV. E	10.34	6.13	9.20	9.74
TOTAL MEAN	81.81	84.58	84.11	89.15
TOTAL STD. DEV.	7.90	7.19	12.70	10.11

PROTEIN (g/dl)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	6.80	6.70	7.10	7.30
407	6.90	7.20	7.60	7.60
409	6.90	6.70	7.90	8.10
397	6.50	6.60	6.90	7.60
391	6.40	6.40	6.30	6.40
MEAN C	6.70	6.72	7.16	7.40
STD. DEV. C	0.23	0.29	0.62	0.63
390	7.40	7.40	7.80	7.50
420	6.80	7.00	7.10	7.20
412	6.80	6.80	7.10	7.20
403	6.90	7.50	7.60	8.00
385	6.00	5.90	6.70	6.90
405	7.20	7.30	6.50	6.60
394	7.00	6.90	6.50	6.60
MEAN L	6.87	6.97	7.04	7.14
STD. DEV. L	0.44	0.54	0.52	0.50
381	6.90	7.00	7.30	7.40
408	7.10	7.20	7.20	7.30
422	7.80	7.90	7.50	7.50
392	7.40	7.30	7.70	7.90
372	6.30	6.60	6.20	6.20
399	7.00	6.90	7.00	7.00
402	7.30	7.20	7.80	7.40
MEAN E	7.11	7.16	7.24	7.24
STD. DEV. E	0.47	0.40	0.54	0.53
TOTAL MEAN	6.92	6.97	7.15	7.25
TOTAL STD. DEV.	0.42	0.45	0.53	0.53

CORTISOL (ug/dl)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	23.30	23.40	15.50	14.30
407	10.40	8.50	4.30	5.60
409	13.50	12.30	11.60	9.70
397	15.50	19.70	17.20	15.90
391	11.60	15.20	11.60	10.20
MEAN C	14.86	15.82	12.04	11.14
STD. DEV. C	5.10	5.89	4.97	4.07
390	10.60	10.40	12.60	13.30
420	15.00	7.50	15.50	10.10
412	16.40	15.00	16.60	15.70
403	15.60	19.20	16.70	15.10
385	8.60	9.80	11.40	9.50
405	6.40	5.30	9.10	9.40
394	14.20	13.60	10.50	9.20
MEAN L	12.40	11.54	13.20	11.76
STD. DEV. L	3.87	4.73	3.08	2.86
381	10.80	9.50	12.50	11.80
408	16.20	15.10	17.30	16.80
422	23.80	22.70	14.00	13.30
392	7.10	7.40	8.70	10.00
372	25.80	25.00	28.40	29.40
399	12.50	12.60	14.00	14.80
402	7.30	8.20	11.50	12.00
MEAN E	14.79	14.36	15.20	15.44
STD. DEV.	7.54	7.03	6.39	6.54
TOTAL MEAN	13.93	13.71	13.63	12.95
TOTAL STD. DEV.	5.58	5.91	4.90	4.95

ALDOSTERONE (ng/dl)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	26.10	23.10	6.80	7.90
407	2.90	3.30	8.80	10.40
409	13.80	11.60	19.00	15.40
397	6.00	7.10	5.80	5.80
391	10.00	10.60	8.80	10.30
MEAN C	11.76	11.14	9.84	9.96
STD. DEV. C	9.01	7.44	5.28	3.59
390	4.70	5.50	4.20	5.10
420	6.80	6.10	8.90	11.40
412	11.60	11.80	9.60	9.00
403	9.20	11.10	5.00	4.50
385	4.90	4.60	4.30	4.80
405	4.30	4.50	3.60	4.20
394	11.40	11.90	8.40	8.00
MEAN L	7.56	7.93	6.29	6.71
STD. DEV. L	3.17	3.49	2.56	2.78
381	9.80	8.30	10.40	9.20
408	10.20	9.70	9.40	10.40
422	9.50	9.60	6.60	5.80
392	2.80	3.30	4.30	5.80
372	5.30	4.00	8.10	8.90
399	6.70	6.80	6.10	5.50
402	7.90	8.10	6.90	9.40
MEAN E	7.46	7.11	7.40	7.86
STD. DEV. E	2.72	2.57	2.07	2.07
TOTAL MEAN	8.63	8.47	7.63	7.99
TOTAL STD. DEV.	5.25	4.62	3.45	2.93

ACTH (pg/ml)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	57.00	47.00	17.00	23.00
407	55.00	53.00	53.00	64.00
409	62.00	58.00	47.00	81.00
397	47.00	49.00	31.00	38.00
391	24.30	25.20	15.60	29.00
MEAN C	49.06	46.44	32.72	47.00
STD. DEV. C	14.86	12.60	17.02	24.63
390	28.00	30.00	22.00	40.00
420	36.00	36.00		11.00
412	55.00	60.00	31.00	43.00
403	69.00	44.00	24.00	44.00
385	27.30	31.10	29.70	30.60
405	3.60	14.50	19.20	28.60
394	49.90	58.10	49.10	56.90
MEAN L	38.40	39.10	29.17	36.30
STD. DEV. L	21.57	16.24	10.76	14.57
381	42.00	49.00	28.00	50.00
408	16.00	26.00	14.00	50.00
422	34.00	47.00	28.00	34.00
392	52.00	89.00	9.00	186.00
372	55.60	71.10	65.40	95.20
399	12.40	21.70	19.70	24.60
402	24.70	31.60	26.70	25.20
MEAN E	33.81	47.91	27.26	66.43
STD. DEV. E	16.99	24.70	18.36	57.97
TOTAL MEAN	39.52	44.28	29.41	50.22
TOTAL STD. DEV.	18.41	18.53	15.04	38.81

PLASMA RENIN ACTIVITY (ngA1/ml/hr)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	0.86	0.81	0.93	1.12
407	0.61	0.63	2.63	4.40
409	0.60	0.47	1.90	2.65
397	0.14	0.43	1.95	2.61
391	0.40	0.78	1.05	1.29
MEAN C	0.52	0.62	1.69	2.41
STD. DEV. C	0.27	0.17	0.70	1.32
390	0.24	0.20	0.56	0.90
420	0.47	0.52	1.62	1.30
412	0.32	0.20	0.39	0.51
403	0.88	0.89	0.70	3.47
385	0.48	0.34	0.87	1.32
405	0.28	0.31	0.98	1.00
394	0.81	0.73	0.81	0.96
MEAN L	0.50	0.46	0.85	1.35
STD. DEV. L	0.25	0.27	0.39	0.97
381	0.63	0.68	1.38	2.26
408	1.03	1.02	1.42	1.70
422	0.94	0.85	1.22	1.51
392	0.07	0.12	0.42	0.59
372	0.18	0.15	1.01	1.95
399	0.50	0.49	1.54	0.95
402	0.69	0.80	1.16	1.75
MEAN E	0.58	0.59	1.16	1.53
STD. DEV. E	0.36	0.35	0.37	0.58
TOTAL MEAN	0.53	0.55	1.19	1.70
TOTAL STD. DEV.	0.29	0.28	0.57	1.01

AVP (pg/ml)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	1.90	3.90	0.50	0.40
407	1.70	1.20	0.30	0.50
409	7.40	2.90	1.20	4.60
397	3.00	4.60	1.10	2.10
391	1.10	1.50	0.40	0.30
MEAN C	3.02	2.82	0.70	1.58
STD. DEV. C	2.54	1.48	0.42	1.84
390	0.20	0.20	0.50	0.80
420	0.50	1.30	0.50	0.50
412	1.90	2.20	1.30	5.30
403	2.30	0.80	3.80	8.00
385	0.40	0.70	0.70	0.90
405	1.00	1.20	0.60	0.60
394	1.40	2.30	1.30	27.40
MEAN L	1.10	1.24	1.24	4.28
STD. DEV. L	0.80	0.78	1.18	7.69
381	2.90	3.10	1.30	5.20
408	1.50	0.00	0.50	2.00
422	1.20	1.30	0.90	1.10
392	1.30	2.50	0.60	22.10
372	0.70	1.80	0.90	2.20
399	1.10	1.50	0.40	0.30
402	1.00	1.40	0.50	1.00
MEAN E	1.39	1.66	0.73	4.49
STD. DEV. E	0.71	0.98	0.32	7.51
TOTAL MEAN	1.71	1.81	0.91	4.46
TOTAL STD. DEV.	1.58	1.19	0.78	7.52

NOREPINEPHRINE (pg/ml)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	174.00	564.00	124.00	483.00
407	38.00	170.00	164.00	372.00
409	87.00	230.00	103.00	418.00
397	142.00	245.00	84.00	381.00
391	181.00	315.00	106.00	418.00
MEAN C	124.40	304.80	116.20	414.40
STD. DEV. C	60.90	153.81	30.25	43.72
390	70.00	226.00	70.00	219.00
420	119.00	308.00		472.00
412	75.00	337.00	132.00	427.00
403	303.00	351.00	143.00	438.00
385	75.00	222.00	48.00	293.00
405	22.00	134.00	84.00	207.00
394	189.00	464.00	90.00	356.00
MEAN L	121.86	291.71	94.50	344.57
STD. DEV. L	95.20	107.68	36.47	107.43
381	97.00		71.00	508.00
408	166.00	328.00	101.00	442.00
422	207.00	464.00	185.00	509.00
392	55.00	225.00	40.00	55.00
372	130.00	266.00	116.00	552.00
399	368.00	429.00	225.00	515.00
402	57.00	163.00	106.00	277.00
MEAN E	154.29	312.50	120.57	408.29
STD. DEV. E	109.38	117.42	64.06	180.42
TOTAL MEAN	134.47	302.28	110.67	386.42
TOTAL STD. DEV.	89.87	117.47	46.87	127.31

EPINEPHRINE (pg/ml)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	22.00	61.00	27.00	83.00
407	19.00	35.00	22.00	53.00
409	27.00	31.00	43.00	215.00
397	18.00	48.00	32.00	113.00
391	26.00	39.00	23.00	62.00
MEAN C	22.40	42.80	29.40	105.20
STD. DEV. C	4.04	11.97	8.56	65.58
390	6.00	41.00	47.00	
420	13.00	11.00		25.00
412	14.00	21.00	42.00	57.00
403	50.00	21.00	64.00	154.00
385	24.00	16.00	23.00	40.00
405	18.00	28.00	30.00	59.00
394	8.00	24.00	14.00	199.00
MEAN L	19.00	23.14	36.67	89.00
STD. DEV. L	14.93	9.58	18.04	70.30
381	25.00	0.00	31.00	65.00
408	16.00	45.00	71.00	96.00
422	51.00	87.00	43.00	59.00
392	15.00	33.00	31.00	37.00
372	21.00	86.00	41.00	48.00
399	14.00	22.00	19.00	28.00
402	33.00	33.00	81.00	105.00
MEAN E	25.00	43.71	45.29	62.57
STD. DEV. E	13.28	32.34	22.58	28.86
TOTAL MEAN	22.11	35.89	38.00	83.22
TOTAL STD. DEV.	11.99	22.61	18.36	55.59

HEART RATE (b/min)

SUBJECT	Pre Bedrest		30th day of Bedrest	
	pre-tilt	post-tilt	pre-tilt	post-tilt
376	56.00	69.00	69.00	91.00
407	64.00	83.00	69.00	107.00
409	59.00	61.00	72.00	116.00
397	66.00	77.00	84.00	107.00
391	65.00	94.00	58.00	68.00
MEAN C	62.00	76.80	70.40	97.80
STD. DEV. C	4.30	12.70	9.29	18.94
390	54.00	66.00	65.00	99.00
420	60.00	75.00	68.00	96.00
412	56.00	65.00	60.00	85.00
403	43.00	50.00	53.00	136.00
385	45.00	54.00	48.00	84.00
405	59.00	70.00	61.00	93.00
394	54.00	72.00	58.00	78.00
MEAN L	53.00	64.57	59.00	95.86
STD. DEV. L	6.58	9.31	6.83	19.18
381	54.00	64.00	56.00	80.00
408	67.00	75.00	82.00	100.00
422	60.00	70.00	69.00	100.00
392	61.00	64.00	75.00	110.00
372	57.00	80.00	57.00	112.00
399	53.00	61.00	63.00	81.00
402	68.00	86.00	66.00	70.00
MEAN E	60.00	71.43	66.86	93.29
STD. DEV. E	5.89	9.31	9.41	16.28
TOTAL MEAN	57.95	70.32	64.89	95.42
TOTAL STD. DEV.	6.77	10.89	9.36	17.15

Appendix G

EXERCISE STUDY

SODIUM (mEq/l)

SUBJECT	DAY -4 pre	-4 post	+4 pre	+4 post	+27 pre	+27 post
376	138.60	138.70	136.80	136.80	136.10	136.10
407	138.90	138.50	136.20	137.60	136.20	136.50
409	136.80	136.70	137.00	137.40	135.70	135.30
397	137.70	137.60	139.30	140.30	138.20	137.90
391	139.20	139.50	136.90	137.50	136.80	137.40
MEAN C	138.24	138.20	137.24	137.92	136.60	136.64
STD. DEV. C	0.98	1.08	1.19	1.37	0.98	1.03
390	138.70	138.50	138.10	136.30	134.60	135.40
420	137.60	138.50	136.30	137.60	136.00	136.40
412	137.90	140.70	136.20	137.70	135.50	137.20
403	139.30	139.60	140.10	139.90	136.40	136.70
385	136.90	135.90	138.30	138.30	138.10	139.20
405	134.40	135.20	138.10	138.90	138.80	139.50
394	137.20	141.20	137.00	138.10	136.60	137.90
MEAN L	137.43	138.51	137.73	138.11	136.57	137.47
STD. DEV. L	1.57	2.27	1.36	1.12	1.45	1.49
381	137.80	139.40	137.10	136.80	137.10	136.60
408	138.00	137.50	140.10	139.70	135.20	136.20
422	138.90	137.00	137.40	138.50	136.40	138.40
392	136.90	137.70	137.30	136.00	135.30	135.70
372	134.10	135.50	136.50	138.50	138.20	138.30
399	134.60	136.20	139.20	139.10	138.40	137.80
402	135.50	136.30	139.20	139.40	135.50	137.60
MEAN E	136.54	137.09	138.11	138.29	136.59	137.23
STD. DEV. E	1.84	1.28	1.36	1.38	1.35	1.06
TOTAL MEAN	137.32	137.91	137.74	138.13	136.58	137.16
TOTAL STD. DEV.	1.62	1.72	1.29	1.22	1.24	1.21

POTASSIUM (mEq/l)

SUBJECT	DAY -4		DAY +4		DAY +27	
	pre	post	pre	post	pre	post
376	4.79	4.66	4.37	4.42	4.24	4.47
407	4.86	4.52	3.83	3.88	3.96	4.01
409	4.80	4.68	4.19	3.92	4.63	4.35
397	4.11	4.26	3.98	4.01	3.94	4.06
391	4.48	4.55	4.11	4.09	4.18	4.22
MEAN C	4.61	4.53	4.10	4.06	4.19	4.22
STD. DEV. C	0.32	0.17	0.21	0.22	0.28	0.19
390	4.30	4.05	3.79	3.94	4.20	3.96
420	4.57	3.89	4.01	3.88	3.98	4.03
412	4.60	4.37	4.12	4.03	4.67	4.31
403	4.63	4.33	4.24	4.32	4.83	3.95
385	4.29	4.24	4.07	4.16	3.86	3.86
405	4.30	4.40	4.21	4.03	4.06	4.06
394	4.28	4.69	4.05	4.36	4.35	4.30
MEAN L	4.42	4.28	4.07	4.10	4.28	4.07
STD. DEV. L	0.17	0.26	0.15	0.18	0.36	0.17
381	4.47	4.47	4.18	4.33	4.46	4.19
408	4.36	4.45	3.92	4.29	3.98	4.16
422	4.76	3.95	4.15	4.33	4.37	4.78
392	4.58	4.76	4.47	4.85	4.27	4.34
372	4.24	4.36	4.35	4.27	4.36	4.27
399	4.09	4.03	3.46	3.83	3.81	4.14
402	4.26	4.17	3.97	3.95	3.86	4.00
MEAN E	4.39	4.31	4.07	4.26	4.16	4.27
STD. DEV. E	0.23	0.28	0.33	0.33	0.27	0.25
TOTAL MEAN	4.46	4.36	4.08	4.15	4.21	4.18
TOTAL STD. DEV.	0.24	0.26	0.23	0.26	0.30	0.22

OSMOLALITY (mosm/kg)

SUBJECT	DAY -4 pre	-4 post	+4 pre	+4 post	+27 pre	+27 post
376	289.00	288.00	292.00	290.00	289.00	286.00
407	290.00	290.00	294.00	291.00	286.00	289.00
409	286.00	289.00	293.00	293.00	288.00	286.00
397	292.00	289.00	294.00	291.00	294.00	294.00
391	287.00	284.00	291.00	290.00	291.00	295.00
MEAN C	288.80	288.00	292.80	291.00	289.60	290.00
STD. DEV. C	2.39	2.35	1.30	1.22	3.05	4.30
390	286.00	291.00	290.00	288.00	281.00	287.00
420	290.00	295.00	289.00	291.00	287.00	290.00
412	293.00	298.00	290.00	292.00	294.00	294.00
403	289.00	294.00	294.00	296.00	290.00	291.00
385	290.00	291.00	291.00	291.00	295.00	297.00
405	284.00	288.00	288.00	287.00	296.00	298.00
394	289.00	287.00	283.00	288.00	295.00	294.00
MEAN L	288.71	292.00	289.29	290.43	291.14	293.00
STD. DEV. L	2.93	3.92	3.35	3.10	5.52	3.92
381	289.00	292.00	292.00	293.00	287.00	291.00
408	291.00	289.00	300.00	297.00	290.00	290.00
422	291.00	291.00	292.00	296.00	290.00	290.00
392	295.00	290.00	289.00	286.00	285.00	285.00
372	287.00	289.00	285.00	285.00	291.00	294.00
399	289.00	290.00	289.00	288.00	292.00	293.00
402	293.00	290.00	290.00	291.00	294.00	296.00
MEAN E	290.71	290.14	291.00	290.86	289.86	291.29
STD. DEV. E	2.69	1.07	4.62	4.74	3.02	3.55
TOTAL MEAN	289.47	290.26	290.84	290.74	290.26	291.58
TOTAL STD. DEV.	2.74	3.05	3.64	3.33	3.97	3.86

CPK (IU/l)

SUBJECT	DAY -4 pre	-4 post	+4 pre	+4 post	+27 pre	+27 post
376	129.40	150.70	70.50	70.40	52.80	57.10
407	179.60	211.90	135.10	126.80	118.40	77.00
409	169.90	194.20	155.40	90.80	183.60	121.20
397	94.60	72.40	79.30	115.70	64.00	67.60
391	109.90	113.30	43.30	40.90	57.50	66.20
MEAN C	136.68	148.50	96.72	88.92	95.26	77.82
STD. DEV. C	37.04	57.32	46.80	34.66	56.00	25.26
390	150.00	125.60	167.20	193.00	118.90	134.00
420	220.30	226.90	154.70	127.80	115.80	159.70
412	166.90	224.30	178.00	183.90	99.30	113.80
403	198.60	155.20	111.70	154.70	119.80	81.70
385	144.60	155.20	146.10	139.80	84.00	84.20
405	219.90	227.80	206.40	254.30	166.40	186.40
394	104.80	114.70	92.30	110.70	111.90	104.00
MEAN L	172.16	175.67	150.91	166.31	116.59	123.40
STD. DEV. L	43.03	49.61	38.92	48.61	25.43	39.04
381	113.50	120.00	76.50	92.40	83.30	73.10
408	180.80	183.30	176.10	459.40	92.50	125.20
422	148.00	186.30	138.70	108.00	52.90	139.00
392	116.40	121.60	95.90	87.10	70.90	98.80
372	99.30	123.70	3102.50	3469.20	72.50	76.60
399	138.70	148.10	103.10	114.60	99.00	104.00
402	113.80	174.80	114.50	80.60	112.60	136.60
MEAN E	130.07	151.11	543.90	630.19	83.39	107.61
STD. DEV. E	27.82	30.10	1128.70	1259.22	19.93	27.01
TOTAL MEAN	147.32	159.47	281.44	316.85	98.74	105.59
TOTAL STD. DEV.	39.59	44.89	684.50	768.78	35.55	35.10

LDH (IU/l)

SUBJECT	DAY -4		DAY +4		DAY +27	
	pre	post	pre	post	pre	post
376	130.50	145.60	110.00	135.80	87.30	110.10
407	103.90	95.80	94.60	84.80	70.70	68.80
409	139.20	143.00	126.70	162.20	120.20	115.60
397	104.30	99.20	70.60	90.40	83.70	82.10
391	134.80	121.50	110.60	111.00	105.80	102.20
MEAN C	122.54	121.02	102.50	116.84	93.54	95.76
STD. DEV. C	17.11	23.45	21.14	32.31	19.48	19.71
390	168.90	134.70	132.40	168.20	138.70	130.20
420	148.70	156.10	138.20	127.30	117.20	149.30
412	155.10	130.40	129.40	114.10	120.00	126.50
403	169.50	130.10	107.90	104.70	215.60	96.60
385	118.60	145.50	105.40	93.90	91.30	84.60
405	127.10	117.40	114.80	122.70	104.50	116.00
394	96.40	105.10	79.20	103.20	172.40	129.20
MEAN L	140.61	131.33	115.33	119.16	137.10	118.91
STD. DEV. L	27.48	16.88	20.30	24.53	43.32	21.98
381	159.70	208.70	158.10	161.50	197.90	152.50
408	154.60	151.90	129.90	130.10	86.40	108.30
422	116.70	145.00	151.20	259.50	97.00	130.60
392	90.50	106.90	136.50	112.60	98.20	100.90
372	148.30	166.80	258.60	284.80	138.40	144.70
399	128.10	135.60	136.20	134.60	128.80	104.70
402	75.50	82.60	97.30	116.20	95.20	135.00
MEAN E	124.77	142.50	152.54	171.33	120.27	125.24
STD. DEV. E	32.51	40.76	50.61	71.04	39.23	20.60
TOTAL MEAN	130.02	132.73	125.66	137.77	119.44	115.15
TOTAL STD. DEV.	27.19	29.11	39.52	53.00	39.12	23.20

LACTATE (mg/dl)

SUBJECT	DAY -4		DAY +4		DAY +27	
	pre	post	pre	post	pre	post
376	4.20	5.50	9.90	9.00	5.20	6.00
407	5.40	5.60	8.40	8.30	5.30	4.90
409	14.00	11.10	14.30	12.60	9.20	9.80
397	8.90	5.90	9.50	8.00	7.40	6.10
391	10.00	7.70	11.70	6.60	13.30	9.90
MEAN C	8.50	7.16	10.76	8.90	8.08	7.34
STD. DEV.	3.90	2.38	2.31	2.24	3.35	2.34
390	7.10	24.30	8.00	16.70	6.90	18.80
420	4.20	67.50	4.90	34.90	5.70	29.70
412	13.30	68.80	13.50	32.30	11.60	38.70
403	10.60	20.50	8.10	21.50	10.50	14.90
385	8.80	20.90	5.90	8.70	5.10	20.30
405	4.40	11.70	6.50	21.60	8.40	33.60
394	9.40	7.10	11.70	12.10	10.70	15.00
MEAN L	8.26	31.54	8.37	21.11	8.41	24.43
STD. DEV. L	3.30	25.69	3.14	9.75	2.59	9.52
381	9.90	34.30	9.80	31.50	13.20	28.50
408	5.70	20.80	6.40	23.10	6.60	22.60
422	10.20	36.90	12.30	40.60	8.90	27.50
392	6.90	15.20	6.20	12.90	6.30	14.50
372	7.90	18.40	5.80	29.40	6.50	32.00
399	5.00	31.50	24.30	9.50	8.00	18.60
402	6.60	40.40	9.60	36.60	11.80	28.80
MEAN E	7.46	28.21	10.63	26.23	8.76	24.64
STD. DEV. E	1.99	9.94	6.48	11.68	2.75	6.30
TOTAL MEAN	8.03	23.90	9.83	19.78	8.45	20.01
TOTAL STD. DEV.	2.92	19.03	4.45	11.32	2.71	10.26

GLUCOSE (mg/dl)

SUBJECT	DAY -4		DAY +4		DAY +27	
	pre	post	pre	post	pre	post
376	83.70	96.40	90.90	87.90	64.40	75.50
407	77.40	64.20	67.80	70.10	62.60	69.90
409	84.40	89.60	101.90	83.60	101.40	99.80
397	101.30	89.20	72.50	88.60	83.10	74.30
391	74.30	76.60	121.80	62.60	87.30	79.10
MEAN C	84.22	83.20	90.98	78.56	79.76	79.72
STD. DEV. C	10.45	12.80	22.07	11.62	16.33	11.70
390	70.20	84.40	79.70	82.40	68.80	80.10
420	75.00	80.00	69.10	81.00	101.20	89.30
412	141.10	85.90	116.20	84.30	122.30	62.10
403	67.60	80.80	83.60	87.80	89.60	77.50
385	84.80	72.90	80.40	103.30	82.80	96.30
405	81.90	83.80	96.60	88.80	90.40	48.90
394	76.30	58.00	87.50	37.80	80.10	79.50
MEAN L	85.27	77.97	87.59	80.77	90.74	76.24
STD. DEV. L	25.34	9.79	15.12	20.34	17.15	16.06
381	108.60	74.40	114.80	76.80	96.10	78.00
408	74.00	77.70	83.20	59.30	91.40	79.00
422	72.00	77.80	89.50	80.40	89.70	79.60
392	99.00	74.30	88.60	80.80	80.70	63.50
372	98.70	64.60	118.70	81.20	97.90	82.40
399	78.20	75.80	57.90	78.40	82.20	77.90
402	94.40	74.60	81.10	74.20	129.70	84.40
MEAN E	89.27	74.17	90.54	75.87	95.39	77.83
STD. DEV. E	14.36	4.47	20.80	7.72	16.44	6.76
TOTAL MEAN	86.47	77.95	89.57	78.38	89.56	77.74
TOTAL STD. DEV.	17.67	9.39	18.19	13.87	16.97	11.56

PROTEIN (g/dl)

SUBJECT	DAY -4 pre	-4 post	+4 pre	+4 post	+27 pre	+27 post
376	6.90	6.80	6.90	7.00	7.10	7.00
407	7.40	7.20	7.60	7.50	7.60	7.60
409	7.30	7.30	7.60	7.50	7.60	7.60
397	6.50	6.30	7.00	7.00	7.20	7.30
391	6.00	6.00	6.00	6.20	6.20	6.30
MEAN C	6.82	6.72	7.02	7.04	7.14	7.16
STD. DEV. C	0.58	0.56	0.66	0.53	0.57	0.54
390	7.00	7.50	7.10	7.60	7.30	7.80
420	7.20	7.90	6.90	7.50	6.90	7.50
412	6.80	7.60	6.70	6.30	6.80	7.50
403	7.40	7.50	7.30	7.70	7.30	7.50
385	6.40	6.90	6.70	7.00	6.60	7.00
405	6.60	7.30	6.50	7.00	6.40	7.00
394	6.10	6.90	6.30	6.80	6.70	7.00
MEAN L	6.79	7.37	6.79	7.13	6.86	7.33
STD. DEV. L	0.46	0.37	0.34	0.50	0.34	0.33
381	7.70	8.10	7.10	8.00	7.60	7.90
408	7.40	7.80	7.20	7.80	7.10	7.70
422	7.80	8.10	7.30	8.10	7.40	8.20
392	7.30	7.60	7.60	7.90	7.30	8.00
372	6.80	7.40	6.00	7.00	6.30	7.00
399	7.00	8.00	6.80	7.30	6.80	7.40
402	7.10	8.00	7.00	8.00	7.30	6.80
MEAN E	7.30	7.86	7.00	7.73	7.11	7.57
STD. DEV. E	0.37	0.27	0.51	0.42	0.44	0.53
TOTAL MEAN	6.98	7.38	6.93	7.33	7.03	7.37
TOTAL STD. DEV.	0.50	0.59	0.48	0.55	0.44	0.47

CORTISOL (ug/dl)

SUBJECT	DAY -4		DAY +4		DAY +27	
	pre	post	pre	post	pre	post
376	25.50	18.90	22.60	17.30	19.20	13.50
407	5.80	9.30	8.90	10.10	14.20	6.90
409	10.90	8.30	16.70	5.80	17.60	10.90
397	22.50	19.20	12.00	9.40	18.70	18.30
391	18.80	12.50	17.90	13.80	12.90	12.90
MEAN C	16.70	13.64	15.62	11.28	16.52	12.50
STD. DEV. C	8.18	5.18	5.32	4.40	2.81	4.14
390	9.10	8.20	10.30	10.00	10.20	9.20
420	14.10	9.90	9.60	11.50	12.80	11.70
412	16.90	11.60	15.70	11.30	15.60	13.70
403	11.50	10.00	13.20	8.60	12.90	11.40
385	15.70	9.60	9.70	7.60	11.70	10.00
405	9.50	7.50	11.00	13.20	11.30	12.60
394	15.70	16.20	12.50	10.50	16.90	10.80
MEAN L	13.21	10.43	11.71	10.39	13.06	11.34
STD. DEV. L	3.17	2.87	2.23	1.88	2.40	1.53
381	11.60	14.80	12.20	15.90	15.90	13.20
408	12.80	8.50	19.50	8.70	13.70	13.40
422	16.30	17.10	15.80	16.30	17.40	17.00
392	24.20	15.90	16.50	5.50	11.90	8.90
372	23.90	18.50	23.40	28.70	24.70	23.00
399	10.40	13.50	13.70	19.40	13.10	18.40
402	5.50	9.50	6.70	9.00	7.80	6.60
MEAN E	14.96	13.97	15.40	14.79	14.93	14.36
STD. DEV. E	6.99	3.76	5.34	7.91	5.28	5.63
TOTAL MEAN	14.77	12.58	14.10	12.24	14.66	12.76
TOTAL STD. DEV.	6.04	4.03	4.58	5.52	3.87	4.12

ALDOSTERONE (ng/dl)

SUBJECT	DAY -4		DAY +4		DAY +27	
	pre	post	pre	post	pre	post
376	15.40	9.60	11.90	9.80	13.20	11.30
407	11.00	8.40	10.10	10.40	8.50	7.40
409	12.60	11.80	16.40	14.20	12.50	9.80
397	33.20	15.00	13.00	20.20	8.70	14.20
391	7.90	7.00	10.20	13.70	8.20	8.40
MEAN C	16.02	10.36	12.32	13.66	10.22	10.22
STD. DEV. C	9.98	3.13	2.58	4.14	2.42	2.67
390	8.70	7.40	6.30	7.30	9.70	9.50
420	12.60	19.00	15.80	18.20	16.30	21.00
412	8.40	8.80	8.30	13.50	8.60	16.80
403	7.90	6.00	8.30	13.20	6.80	19.50
385	8.60	5.60	5.30	14.70	5.60	17.40
405	9.00	7.30	7.30	9.50	5.00	11.50
394	12.30	8.80	8.30	11.90	8.90	8.80
MEAN L	9.64	8.99	8.51	12.61	8.70	14.93
STD. DEV. L	1.95	4.58	3.41	3.54	3.78	4.94
381	6.50	11.40	11.00	19.40	19.30	28.20
408	15.30	28.10	7.70	23.80	12.90	35.40
422	18.20	32.40	7.40	20.50	8.10	24.40
392	14.90	10.90	11.30	18.20	7.10	17.20
372	6.90	21.10	7.80	31.90	11.40	27.40
399	16.10	24.90	5.70	17.10	7.20	20.90
402	16.40	28.60	10.50	31.30	9.20	26.80
MEAN E	13.47	22.49	8.77	23.17	10.74	25.76
STD. DEV. E	4.74	8.49	2.15	6.13	4.35	5.79
TOTAL MEAN	12.73	14.32	9.61	16.78	9.85	17.68
TOTAL STD. DEV.	6.15	8.63	3.11	6.77	3.64	8.04

ACTH (pg/ml)

SUBJECT	DAY -4		DAY +4		DAY +27	
	pre	post	pre	post	pre	post
376	45.00	22.00	31.00	12.00	21.00	6.00
407	54.00	31.00	60.00	27.00	42.00	44.00
409	71.00	59.00	64.00	77.00	55.00	55.00
397	116.00	51.00	40.00	38.00	52.00	57.00
391	25.20	6.40	14.40	12.00	19.10	8.90
MEAN C	62.24	33.88	41.88	33.20	37.82	34.18
STD. DEV. C	34.29	21.38	20.58	26.83	16.93	24.92
390	18.00	14.00	10.00	21.00	22.00	21.00
420	23.00	90.00	14.00	33.00	7.00	18.00
412	46.00	51.00	36.00	43.00	44.00	39.00
403	40.00	42.00	27.00	22.00	18.00	20.00
385	36.40	35.20	37.50	34.80	25.50	41.80
405	19.50	14.90	17.50	38.40	33.30	55.60
394	63.30	76.70	46.10	50.30	58.60	58.10
MEAN L	35.17	46.26	26.87	34.64	29.77	36.21
STD. DEV. L	16.44	28.94	13.57	10.63	17.23	16.93
381	55.00	74.00	52.00	194.00	37.00	37.00
408	13.00	15.00	10.00	7.00	12.00	8.00
422	39.00	64.00	31.00	37.00	20.00	52.00
392	82.00	26.00	32.00	29.00	26.00	26.00
372	44.10	44.30	81.80	67.10	72.50	65.40
399	8.90	33.90	8.20	37.60	22.70	46.70
402	3.00	30.40	8.30	34.00	1.50	25.20
MEAN E	35.00	41.09	31.90	57.96	27.39	37.19
STD. DEV. E	28.57	21.18	27.37	62.52	22.78	19.26
TOTAL MEAN	42.23	41.09	32.67	42.85	31.01	36.04
TOTAL STD. DEV.	27.83	23.56	21.02	40.51	18.82	18.94

PLASMA RENIN ACTIVITY (ngA1/ml/hr)

SUBJECT	DAY -4 pre	-4 post	+4 pre	+4 post	+27 pre	+27 post
376	0.89	0.77	1.66	1.62	2.27	2.05
407	0.84	0.50	2.64	2.30	2.16	1.85
409	1.22	0.96	2.10	3.10	1.13	1.17
397	1.88	1.08	3.14	3.09	5.83	4.08
391	0.61	0.50	1.42	1.28	1.00	1.16
MEAN C	1.09	0.76	2.19	2.28	2.48	2.06
STD. DEV. C	0.49	0.26	0.70	0.83	1.96	1.20
390	0.51	0.61	1.06	1.03	1.27	1.44
420	0.63	0.62	0.99	0.97	1.35	1.60
412	0.14	0.28	0.35	0.90	0.38	1.12
403	0.92	1.05	1.81	3.52	3.24	3.68
385	0.62	0.76	1.29	2.02	1.12	1.92
405	0.78	0.77	0.87	1.92	1.17	3.08
394	0.41	0.41	1.00	1.03	1.20	1.53
MEAN L	0.57	0.64	1.05	1.63	1.39	2.05
STD. DEV. L	0.25	0.25	0.44	0.96	0.88	0.95
381	0.50	0.51	1.27	0.47	1.88	2.60
408	1.59	3.34	2.51	4.18	2.28	5.33
422	1.36	2.59	0.90	2.58	1.76	4.09
392	1.21	0.92	1.06	1.59	0.75	2.15
372	0.59	1.34	0.67	3.02	0.90	2.77
399	1.76	2.48	1.70	2.06	1.23	2.02
402	1.00	7.09	1.22	2.54	1.37	2.98
MEAN E	1.14	2.61	1.33	2.35	1.45	3.13
STD. DEV. E	0.48	2.22	0.61	1.16	0.55	1.18
TOTAL MEAN	0.92	1.40	1.46	2.06	1.70	2.45
TOTAL STD. DEV.	0.48	1.61	0.72	1.01	1.20	1.17

AVP (pg/ml)

SUBJECT	DAY -4 pre	-4 post	+4 pre	+4 post	+27 pre	+27 post
376	1.70	1.40	0.70	0.40	0.30	0.40
407	0.60	0.80	0.60	0.40	0.70	0.50
409	5.60	2.20	4.50	4.50	0.70	3.70
397	11.40	3.40	1.10	1.20	6.80	3.10
391	1.30	0.60	0.60	0.60	0.50	0.60
MEAN C	4.12	1.68	1.50	1.42	1.80	1.66
STD. DEV. C	4.51	1.15	1.69	1.75	2.80	1.60
390	0.30	0.30	0.30		0.40	0.30
420	0.60	5.70	0.50	2.10	1.00	2.10
412	1.40	3.30	0.70	1.50	0.60	3.20
403	3.30	2.40	4.60	6.10	2.50	2.30
385	0.60	0.60	0.80	0.70	0.80	0.90
405	0.80	0.80	0.40	0.90	0.60	1.20
394	1.00	0.90	0.90	0.90		0.90
MEAN L	1.14	2.00	1.17	2.03	0.98	1.56
STD. DEV. L	1.01	1.96	1.53	2.06	0.77	1.01
381	1.40	2.30	1.50	5.30	2.20	4.10
408	0.40	1.10	1.90	3.20	1.10	1.00
422	1.30	1.60		1.00	2.70	1.40
392	3.40	1.00	0.20	1.10	0.40	0.60
372	0.60	1.10	1.10	0.70	0.70	1.20
399	1.30	0.60	0.60	0.60	0.50	
402	0.80	4.20	0.80	4.90	0.80	1.40
MEAN E	1.31	1.70	1.02	2.40	1.20	1.62
STD. DEV. E	1.00	1.23	0.62	2.04	0.89	1.25
TOTAL MEAN	1.99	1.81	1.21	2.01	1.29	1.61
TOTAL STD. DEV.	2.63	1.45	1.28	1.90	1.55	1.20

NOREPINEPHRINE (pg/ml)

SUBJECT	DAY -4 pre	-4 post	+4 pre	+4 post	+27 pre	+27 post
376	130.00	123.00	155.00	234.00	61.00	122.00
407	114.00	96.00	96.00	89.00	145.00	132.00
409	181.00	152.00	279.00	263.00	113.00	181.00
397	85.00	82.00	176.00	160.00	245.00	208.00
391	242.00	174.00	252.00	223.00	142.00	176.00
MEAN C	150.40	125.40	191.60	193.80	141.20	163.80
STD. DEV. C	61.94	38.15	74.18	69.61	67.11	35.91
390	175.00	248.00	78.00		53.00	202.00
420	252.00	563.00	101.00	398.00	165.00	574.00
412	147.00	561.00	124.00	341.00	71.00	410.00
403	180.00	352.00	118.00	319.00	139.00	184.00
385	81.00	111.00	120.00	190.00	105.00	182.00
405	35.00	147.00	100.00	375.00	94.00	225.00
394	127.00	176.00	97.00	303.00	87.00	249.00
MEAN L	142.43	308.29	105.43	321.00	102.00	289.43
STD. DEV. L	70.77	190.05	16.27	73.12	38.73	148.10
381	108.00	227.00	150.00	261.00	79.00	186.00
408	211.00	275.00	198.00	267.00	136.00	251.00
422	159.00	356.00	116.00	290.00	13.00	398.00
392	75.00	147.00	107.00	174.00	71.00	152.00
372	183.00	319.00	98.00	310.00	83.00	272.00
399	178.00	389.00	172.00	373.00	295.00	382.00
402	103.00	278.00	94.00	261.00	69.00	213.00
MEAN E	145.29	284.43	133.57	276.57	106.57	264.86
STD. DEV. E	50.20	81.21	40.30	60.13	90.48	94.28
TOTAL MEAN	145.58	251.37	138.47	268.39	114.00	247.32
TOTAL STD. DEV.	58.07	143.72	55.41	81.42	67.18	115.36

EPINEPHRINE (pg/ml)

SUBJECT	DAY -4		+4		+27	
	pre	post	pre	post	pre	post
376	25.00	33.00	10.00	19.00	23.00	26.00
407	29.00	18.00	17.00	20.00	13.00	15.00
409	37.00	21.00	13.00	14.00	27.00	27.00
397	29.00	29.00	9.00	9.00	64.00	55.00
391	16.00	7.00	406.00	19.00	3.00	9.00
MEAN C	27.20	21.60	91.00	16.20	26.00	26.40
STD. DEV. C	7.63	10.14	176.12	4.66	23.19	17.69
390	28.00	60.00	22.00		29.00	36.00
420	10.00	32.00	13.00	19.00	12.00	38.00
412	39.00	103.00	13.00	38.00	27.00	79.00
403	29.00	71.00	44.00	73.00	27.00	70.00
385	23.00	42.00	24.00	28.00	15.00	32.00
405	29.00	45.00	10.00	30.00	20.00	44.00
394	100.00	16.00		19.00	12.00	51.00
MEAN L	36.86	52.71	21.00	34.50	20.29	50.00
STD. DEV. L	29.17	28.48	12.55	20.19	7.43	17.99
381	57.00	63.00		57.00	58.00	53.00
408		30.00	22.00	30.00	33.00	43.00
422	27.00	36.00	14.00	21.00	105.00	29.00
392	24.00	22.00	13.00	21.00	16.00	23.00
372	25.00	96.00	20.00	74.00	20.00	54.00
399	10.00	39.00	6.00	20.00	20.00	18.00
402	38.00	61.00	31.00	45.00	17.00	61.00
MEAN E	30.17	49.57	17.67	38.29	38.43	40.14
STD. DEV. E	15.89	25.51	8.64	21.10	32.88	16.88
TOTAL MEAN	31.94	43.37	40.41	30.89	28.47	40.16
TOTAL STD. DEV.	20.15	26.28	94.67	19.31	23.76	19.04

HEART RATE (b/min)

SUBJECT	DAY -4 pre	-4 post	+4 pre	+4 post	+27 pre	+27 post
376	52.00	52.00	64.00	60.00	56.00	52.00
407	60.00	60.00	72.00	68.00	72.00	72.00
409	76.00	72.00	68.00	64.00	64.00	64.00
397	68.00	68.00	68.00	64.00	92.00	96.00
391	72.00	74.00	64.00	68.00	64.00	64.00
MEAN C	65.60	65.20	67.20	64.80	69.60	69.60
STD. DEV. C	9.63	9.12	3.35	3.35	13.74	16.40
390	52.00	88.00	56.00	60.00	60.00	70.00
420	56.00	90.00	68.00	86.00	68.00	84.00
412	76.00	120.00	60.00	84.00	64.00	114.00
403	46.00	108.00	52.00	108.00	48.00	126.00
385	60.00	72.00	56.00	60.00	60.00	120.00
405	66.00	84.00	60.00	72.00	64.00	120.00
394	60.00	60.00	60.00	108.00	66.00	96.00
MEAN L	59.43	88.86	58.86	82.57	61.43	104.29
STD. DEV. L	9.71	20.33	5.01	20.16	6.60	21.27
381	66.00	142.00	60.00	132.00	60.00	136.00
408	64.00	108.00	76.00	120.00	72.00	136.00
422	72.00	163.00	64.00	132.00	64.00	120.00
392	76.00	144.00	76.00	138.00	72.00	126.00
372	60.00	144.00	60.00	162.00	56.00	132.00
399	68.00	132.00	80.00	150.00	68.00	126.00
402	64.00	156.00	60.00	126.00	64.00	150.00
MEAN E	67.14	141.29	68.00	137.14	65.14	132.29
STD. DEV. E	5.40	17.78	8.94	14.46	5.98	9.76
TOTAL MEAN	63.89	101.95	64.42	98.00	64.95	105.47
TOTAL STD. DEV.	8.63	36.13	7.53	34.67	8.90	29.66

SYSTOLIC (mmHg)

SUBJECT	DAY -4 pre	-4 post	+4 pre	+4 post	+27 pre	+27 post
376	120.00	120.00	118.00	112.00	106.00	106.00
407	126.00		106.00	110.00	112.00	108.00
409	132.00	120.00	106.00	130.00	118.00	140.00
397	112.00		110.00	110.00	106.00	96.00
391	120.00	118.00	112.00	108.00	112.00	126.00
MEAN C	122.00	119.33	110.40	114.00	110.80	115.20
STD. DEV. C	7.48	1.15	4.98	9.06	5.02	17.58
390	102.00	180.00	106.00	116.00	108.00	
420	108.00	178.00	110.00		108.00	128.00
412	134.00	136.00	118.00	148.00	130.00	144.00
403	128.00	168.00	112.00	150.00	126.00	144.00
385	98.00	124.00	118.00	132.00	10	
405	98.00	116.00	116.00	138.00	106.00	154.00
394	128.00	128.00	120.00	154.00	128.00	152.00
MEAN L	113.71	147.14	114.29	139.67	115.14	141.67
STD. DEV. L	5.72	27.27	5.09	14.17	12.38	11.34
381	124.00	190.00	122.00	168.00	110.00	182.00
408	106.00	180.00	110.00	176.00	120.00	194.00
422	122.00	180.00	126.00	204.00	108.00	76.00
392	118.00	158.00	122.00	186.00	122.00	168.00
372	112.00	198.00	118.00	186.00	110.00	172.00
399	124.00	190.00	132.00	190.00	130.00	192.00
402	122.00	212.00	112.00	188.00	120.00	208.00
MEAN E	118.29	186.86	120.29	185.43	117.14	170.29
STD. DEV. E	6.87	16.85	7.70	11.30	8.07	43.76
TOTAL MEAN	117.58	158.59	115.47	150.33	114.74	145.44
TOTAL STD. DEV.	11.05	32.88	7.11	32.54	9.22	36.26

DIASTOLIC (mmHg)

SUBJECT	DAY -4		DAY +4		DAY +27	
	pre	post	pre	post	pre	post
376	70.00	78.00	68.00	70.00	74.00	74.00
407	84.00		76.00	76.00	78.00	78.00
409	80.00	80.00	60.00	80.00	78.00	90.00
397	68.00		60.00	66.00	60.00	60.00
391	78.00	86.00	68.00	64.00	68.00	74.00
MEAN C	76.00	81.33	66.40	71.20	71.60	75.20
STD. DEV. C	6.78	4.16	6.69	6.72	7.67	10.73
390	70.00	80.00	64.00	80.00	68.00	
420	68.00	84.00	68.00		70.00	60.00
412	80.00	68.00	72.00	72.00	78.00	70.00
403	78.00	70.00	76.00	76.00	80.00	62.00
385	68.00	80.00	78.00	88.00	70.00	80.00
405	68.00	86.00	80.00	90.00	76.00	98.00
394	90.00	86.00	92.00	78.00	88.00	92.00
MEAN L	74.57	79.14	75.71	80.67	75.71	77.00
STD. DEV. L	8.46	7.38	9.12	7.00	7.06	15.74
381	84.00	80.00	88.00	84.00	76.00	88.00
408	78.00	78.00	76.00	80.00	76.00	88.00
422	86.00	82.00	86.00	96.00	78.00	100.00
392	72.00	78.00	70.00	98.00	80.00	96.00
372	78.00	90.00	78.00	90.00	74.00	88.00
399	90.00	108.00	90.00	90.00	94.00	88.00
402	70.00	80.00	76.00	68.00	70.00	70.00
MEAN E	79.71	85.14	80.57	86.57	78.29	88.29
STD. DEV. E	7.34	10.88	7.46	10.31	7.61	9.41
TOTAL MEAN	76.84	82.00	75.05	80.33	75.58	80.89
TOTAL STD. DEV.	7.58	8.66	9.44	10.16	7.50	12.98

HEMATOCRIT

SUBJECT	DAY -4 pre	-4 post	+4 pre	+4 post	+27 pre	+27 post
376	45.20	45.40	48.30	48.80	48.50	48.40
407	41.90	42.00	44.90	45.00	45.10	45.10
409	46.00	45.50	49.20	48.10	47.40	47.20
397	38.20	37.20	41.20	41.00	43.70	43.70
391	41.20	42.70	44.20	44.80	43.20	43.10
MEAN C	42.50	42.56	45.56	45.54	45.58	45.50
STD. DEV. C	3.17	3.38	3.24	3.11	2.31	2.26
390	38.70	40.20	41.30	43.50	41.10	43.40
420	40.50	44.30	40.70	42.80	41.50	43.70
412	44.70	44.60	45.70	47.30	45.90	48.60
403	39.70	41.70	42.50	43.80	41.80	41.80
385	40.60	42.00	43.30	44.10	41.00	42.60
405	42.20	43.20	42.60	44.20	40.40	42.00
394	44.70	46.00	46.10	47.40	46.50	47.90
MEAN L	41.59	43.14	43.17	44.73	42.60	44.29
STD. DEV. L	2.37	1.99	2.06	1.85	2.50	2.80
381	41.30	44.30	44.10	46.30	44.30	45.60
408	42.50	44.90	42.80	43.90	42.80	45.10
422	45.20	48.30	44.10	47.30	43.60	46.30
392	43.70	44.40	44.80	46.30	43.50	45.40
372	47.00	48.80	47.70	51.00	45.40	48.30
399	44.00	46.20	42.50	43.70	43.00	44.50
402	41.80	44.90	40.80	43.40	41.80	44.60
MEAN E	43.64	45.97	43.83	45.99	43.49	45.69
STD. DEV. E	2.00	1.87	2.16	2.69	1.15	1.31
TOTAL MEAN	42.58	44.03	44.04	45.41	43.71	45.12
TOTAL STD. DEV.	2.50	2.72	2.50	2.45	2.28	2.18

HEMOGLOBIN

SUBJECT	DAY -4		DAY +4		DAY +27	
	pre	post	pre	post	pre	post
376	16.00	16.00	16.70	16.70	17.00	17.00
407	14.30	14.20	15.50	15.10	15.70	15.80
409	15.50	15.00	17.10	16.50	16.50	16.80
397	12.70	12.00	13.90	13.50	15.40	15.30
391	15.00	15.20	16.30	16.80	15.90	15.70
MEAN C	14.70	14.48	15.90	15.72	16.10	16.12
STD. DEV. C	1.28	1.53	1.26	1.42	0.64	0.74
390	13.20	13.60	13.50	14.40	13.60	14.50
420	13.70	15.10	14.30	14.90	14.20	15.20
412	14.10	15.10	15.10	15.90	15.50	16.60
403	13.30	13.50	14.20	14.70	14.60	14.70
385	14.00	14.60	15.50	15.90	14.60	15.00
405	15.00	15.50	15.20	15.90	14.90	15.60
394	15.90	16.60	16.60	17.00	16.50	16.70
MEAN L	14.17	14.86	14.91	15.53	14.84	15.47
STD. DEV. L	0.97	1.08	1.02	0.91	0.94	0.88
381	14.60	16.60	15.10	15.70	15.00	15.60
408	14.30	14.80	14.70	15.30	14.10	15.40
422	15.50	16.70	16.10	18.10	16.10	17.40
392	14.90	15.40	15.60	17.00	16.00	16.90
372	17.00	17.80	17.20	18.50	16.50	17.70
399	15.40	16.40	14.70	15.70	14.90	15.30
402	14.30	14.40	14.60	16.30	14.50	14.90
MEAN E	15.14	16.01	15.43	16.66	15.30	16.17
STD. DEV. E	0.95	1.20	0.96	1.25	0.90	1.13
TOTAL MEAN	14.67	15.18	15.36	15.99	15.34	15.90
TOTAL STD. DEV.	1.08	1.35	1.08	1.23	0.96	0.96

EXERCISE STUDY
URINE DATA

VOLUME (ml)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	74.0	40.0	390.0	74.0	40.0	390.0	74.0	40.0	390.0
407	815.0	340.0	270.0	815.0	340.0	270.0	815.0	340.0	270.0
409	89.0	90.0	242.0	89.0	90.0	242.0	89.0	90.0	242.0
397	43.0	23.0	226.0	43.0	23.0	226.0	43.0	23.0	226.0
391	443.0	42.0	125.0	443.0	42.0	125.0	443.0	42.0	125.0
MEAN	292.8	107.0	250.6	292.8	107.0	250.6	292.8	107.0	250.6
STDEV	334.3	132.6	95.2	334.3	132.6	95.2	334.3	132.6	95.2
390	275.0	290.0	180.0	275.0	290.0	180.0	275.0	290.0	180.0
420	495.0	210.0	124.0	495.0	210.0	124.0	495.0	210.0	124.0
412	62.0	57.0	107.0	62.0	57.0	107.0	62.0	57.0	107.0
403	25.0	130.0	132.0	25.0	130.0	132.0	25.0	130.0	132.0
385	180.0	68.0	174.0	180.0	68.0	174.0	180.0	68.0	174.0
405	118.0	50.0	172.0	118.0	50.0	172.0	118.0	50.0	172.0
394	92.0	65.0	180.0	92.0	65.0	180.0	92.0	65.0	180.0
MEAN	178.1	124.3	152.7	178.1	124.3	152.7	178.1	124.3	152.7
STDEV	162.2	92.7	30.7	162.2	92.7	30.7	162.2	92.7	30.7
381	312.0	157.0	356.0	312.0	157.0	356.0	312.0	157.0	356.0
408	82.0	82.0	106.0	82.0	82.0	106.0	82.0	82.0	106.0
422	51.0	39.0	70.0	51.0	39.0	70.0	51.0	39.0	70.0
392	194.0	57.0	188.0	194.0	57.0	188.0	194.0	57.0	188.0
372	76.0	74.0	105.0	76.0	74.0	105.0	76.0	74.0	105.0
399	242.0	315.0	90.0	242.0	315.0	90.0	242.0	315.0	90.0
402	168.0	100.0	140.0	168.0	100.0	140.0	168.0	100.0	140.0
MEAN	160.7	117.7	150.7	160.7	117.7	150.7	160.7	117.7	150.7
STDEV	96.7	94.7	98.3	96.7	94.7	98.3	96.7	94.7	98.3
T MEAN	201.9	117.3	177.7	201.9	117.3	177.7	201.9	117.3	177.7
T STDEV	199.7	99.1	86.9	199.7	99.1	86.9	199.7	99.1	86.9

TIME (min)

DAY-		-4			+5			+28	
TIME- SUBJECT	pre	3'	120'	pre	3'	120'	pre	3'	120'
376	90.0	40.0	155.0	90.0	40.0	155.0	90.0	40.0	155.0
407	228.0	35.0	115.0	228.0	35.0	115.0	228.0	35.0	115.0
409	115.0	40.0	122.0	115.0	40.0	122.0	115.0	40.0	122.0
397	75.0	35.0	122.0	75.0	35.0	122.0	75.0	35.0	122.0
391	245.0	170.0	318.0	245.0	170.0	318.0	245.0	170.0	318.0
MEAN	150.6	64.0	166.4	150.6	64.0	166.4	150.6	64.0	166.4
STDEV	79.9	59.3	86.2	79.9	59.3	86.2	79.9	59.3	86.2
390	116.0	64.0	104.0	116.0	64.0	104.0	116.0	64.0	104.0
420	239.0	125.0	121.0	239.0	125.0	121.0	239.0	125.0	121.0
412	60.0	67.0	120.0	60.0	67.0	120.0	60.0	67.0	120.0
403	111.0	52.0	120.0	111.0	52.0	120.0	111.0	52.0	120.0
385	118.0	60.0	120.0	118.0	60.0	120.0	118.0	60.0	120.0
405	135.0	60.0	140.0	135.0	60.0	140.0	135.0	60.0	140.0
394	130.0	70.0	128.0	130.0	70.0	128.0	130.0	70.0	128.0
MEAN	129.9	71.1	121.9	129.9	71.1	121.9	129.9	71.1	121.9
STDEV	54.0	24.4	10.8	54.0	24.4	10.8	54.0	24.4	10.8
381	155.0	55.0	141.0	155.0	55.0	141.0	155.0	55.0	141.0
408	90.0	55.0	70.0	90.0	55.0	70.0	90.0	55.0	70.0
422	112.0	50.0	120.0	112.0	50.0	120.0	112.0	50.0	120.0
392	95.0	50.0	120.0	95.0	50.0	120.0	95.0	50.0	120.0
372	115.0	47.0	113.0	115.0	47.0	113.0	115.0	47.0	113.0
399	301.0	91.0	125.0	301.0	91.0	125.0	301.0	91.0	125.0
402	205.0	80.0	120.0	205.0	80.0	120.0	205.0	80.0	120.0
MEAN	153.3	61.1	115.6	153.3	61.1	115.6	153.3	61.1	115
STDEV	76.5	17.2	21.9	76.5	17.2	21.9	76.5	17.2	21.9
T MEAN	143.9	65.6	131.3	143.9	65.6	131.3	143.9	65.6	131.3
T STDEV	66.8	33.2	48.2	66.8	33.2	48.2	66.8	33.2	48.2

URINE FLOW RATE (ml/min)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	0.8	1.0	2.5	0.8	1.0	2.5	0.8	1.0	2.5
407	3.6	9.7	2.3	3.6	9.7	2.3	3.6	9.7	2.3
409	0.8	2.2	2.0	0.8	2.2	2.0	0.8	2.2	2.0
397	0.6	0.7	1.9	0.6	0.7	1.9	0.6	0.7	1.9
391	1.8	0.2	0.4	1.8	0.2	0.4	1.8	0.2	0.4
MEAN	1.5	2.8	1.8	1.5	2.8	1.8	1.5	2.8	1.8
STDEV	1.2	4.0	0.8	1.2	4.0	0.8	1.2	4.0	0.8
390	2.4	4.5	1.7	2.4	4.5	1.7	2.4	4.5	1.7
420	2.1	1.7	1.0	2.1	1.7	1.0	2.1	1.7	1.0
412	1.0	0.9	0.9	1.0	0.9	0.9	1.0	0.9	0.9
403	0.2	2.5	1.1	0.2	2.5	1.1	0.2	2.5	1.1
385	1.5	1.1	1.4	1.5	1.1	1.4	1.5	1.1	1.4
405	0.9	0.8	1.2	0.9	0.8	1.2	0.9	0.8	1.2
394	0.7	0.9	1.4	0.7	0.9	1.4	0.7	0.9	1.4
MEAN	1.3	1.8	1.3	1.3	1.8	1.3	1.3	1.8	1.3
STDEV	0.8	1.4	0.3	0.8	1.4	0.3	0.8	1.4	0.3
381	2.0	2.9	2.5	2.0	2.9	2.5	2.0	2.9	2.5
408	0.9	1.5	1.5	0.9	1.5	1.5	0.9	1.5	1.5
422	0.5	0.8	0.6	0.5	0.8	0.6	0.5	0.8	0.6
392	2.0	1.1	1.6	2.0	1.1	1.6	2.0	1.1	1.6
372	0.7	1.6	0.9	0.7	1.6	0.9	0.7	1.6	0.9
399	0.8	3.5	0.7	0.8	3.5	0.7	0.8	3.5	0.7
402	0.8	1.3	1.2	0.8	1.3	1.2	0.8	1.3	1.2
MEAN	1.1	1.8	1.3	1.1	1.8	1.3	1.1	1.8	1.3
STDEV	0.6	1.0	0.7	0.6	1.0	0.7	0.6	1.0	0.7
T MEAN	1.3	2.0	1.4	1.3	2.0	1.4	1.3	2.0	1.4
T STDEV	0.8	2.1	0.6	0.8	2.1	0.6	0.8	2.1	0.6

PLASMA CREATININE (mg/dl)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	0.9	0.8		0.9	0.8		0.9	0.8	
407	0.8	0.8		0.8	0.8		0.8	0.8	
409	0.9	0.8		0.9	0.8		0.9	0.8	
397	0.5	0.4		0.5	0.4		0.5	0.4	
391	1.0	0.8		1.0	0.8		1.0	0.8	
MEAN	0.8	0.7		0.8	0.7		0.8	0.7	
STDEV	0.2	0.2		0.2	0.2		0.2	0.2	
390	1.0	1.0		1.0	1.0		1.0	1.0	
420	0.9	1.0		0.9	1.0		0.9	1.0	
412	1.0	1.0		1.0	1.0		1.0	1.0	
403	0.9	0.9		0.9	0.9		0.9	0.9	
385	0.8	0.9		0.8	0.9		0.8	0.9	
405	1.0	1.0		1.0	1.0		1.0	1.0	
394	1.0	1.0		1.0	1.0		1.0	1.0	
MEAN	0.9	1.0		0.9	1.0		0.9	1.0	
STDEV	0.1	0.1		0.1	0.1		0.1	0.1	
381	1.0	1.0		1.0	1.0		1.0	1.0	
408	1.0	1.0		1.0	1.0		1.0	1.0	
422	0.8	0.9		0.8	0.9		0.8	0.9	
392	0.6	0.7		0.6	0.7		0.6	0.7	
372	0.9	1.0		0.9	1.0		0.9	1.0	
399	0.8	0.8		0.8	0.8		0.8	0.8	
402	0.9	0.9		0.9	0.9		0.9	0.9	
MEAN	0.9	0.9		0.9	0.9		0.9	0.9	
STDEV	0.1	0.1		0.1	0.1		0.1	0.1	
T MEAN	0.9	0.9		0.9	0.9		0.9	0.9	
T STDEV	0.1	0.1		0.1	0.1		0.1	0.1	

URINE CREATININE (mg/ml)

DAY-	-4			+5			+28		
TIMEANE-	pre	3'	120'	pre	3'	120'	pre	3'	1.
SUBJECT									
376	1.5	1.3	0.3	1.5	1.3	0.3	1.5	1.3	0.3
407	0.4	0.2	0.6	0.4	0.2	0.6	0.4	0.2	0.6
409	1.7	1.3	0.9	1.7	1.3	0.9	1.7	1.3	0.9
397	1.1	1.5	0.8	1.1	1.5	0.8	1.1	1.5	0.8
391	0.9	0.9	0.3	0.9	0.9	0.3	0.9	0.9	0.3
MEAN	1.1	1.1	0.6	1.1	1.1	0.6	1.1	1.1	0.6
STDEV	0.5	0.5	0.3	0.5	0.5	0.3	0.5	0.5	0.3
390	0.6	0.3	0.8	0.6	0.3	0.8	0.6	0.3	0.8
420	0.3	0.8	1.5	0.3	0.8	1.5	0.3	0.8	1.5
412	2.3	1.5	1.4	2.3	1.5	1.4	2.3	1.5	1.4
403	1.3	1.2	1.4	1.3	1.2	1.4	1.3	1.2	1.4
385	0.9	1.1	1.0	0.9	1.1	1.0	0.9	1.1	1.0
405	1.5	1.2	1.3	1.5	1.2	1.3	1.5	1.2	1.3
394	1.8	1.1	0.9	1.8	1.1	0.9	1.8	1.1	0.9
MEAN	1.2	1.0	1.2	1.2	1.0	1.2	1.2	1.0	1.2
STDEV	0.7	0.4	0.3	0.7	0.4	0.3	0.7	0.4	0.3
381	0.7	0.5	0.7	0.7	0.5	0.7	0.7	0.5	0.7
408	0.7	0.5	0.8	0.7	0.5	0.8	0.7	0.5	0.8
422	2.3	1.6	2.3	2.3	1.6	2.3	2.3	1.6	2.3
392	0.6	1.3	0.9	0.6	1.3	0.9	0.6	1.3	0.9
372	1.8	0.8	1.1	1.8	0.8	1.1	1.8	0.8	1.1
399	0.8	0.9	1.7	0.8	0.9	1.7	0.8	0.9	1.7
402	1.5	1.0	1.0	1.5	1.0	1.0	1.5	1.0	1.0
MEAN	1.2	0.9	1.2	1.2	0.9	1.2	1.2	0.9	1.2
STDEV	0.7	0.4	0.6	0.7	0.4	0.6	0.7	0.4	0.6
T MEAN	1.2	1.0	1.0	1.2	1.0	1.0	1.2	1.0	1.0
T STDEV	0.6	0.4	0.5	0.6	0.4	0.5	0.6	0.4	0.5

CREATININE EXCRETION RATE (mg/ml)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	1.2	1.3	0.8	1.2	1.3	0.8	1.2	1.3	0.8
407	1.3	2.1	1.4	1.3	2.1	1.4	1.3	2.1	1.4
409	1.3	3.0	1.8	1.3	3.0	1.8	1.3	3.0	1.8
397	0.6	1.0	1.4	0.6	1.0	1.4	0.6	1.0	1.4
391	1.7	0.2	0.1	1.7	0.2	0.1	1.7	0.2	0.1
MEAN	1.2	1.5	1.1	1.2	1.5	1.1	1.2	1.5	1.1
STDEV	0.4	1.1	0.7	0.4	1.1	0.7	0.4	1.1	0.7
390	1.4	1.3	1.4	1.4	1.3	1.4	1.4	1.3	1.4
420	0.7	1.3	1.6	0.7	1.3	1.6	0.7	1.3	1.6
412	2.4	1.3	1.2	2.4	1.3	1.2	2.4	1.3	1.2
403	0.3	3.0	1.6	0.3	3.0	1.6	0.3	3.0	1.6
385	1.3	1.2	1.5	1.3	1.2	1.5	1.3	1.2	1.5
405	1.3	1.0	1.6	1.3	1.0	1.6	1.3	1.0	1.6
394	1.3	1.0	1.2	1.3	1.0	1.2	1.3	1.0	1.2
MEAN	1.2	1.5	1.4	1.2	1.5	1.4	1.2	1.5	1.4
STDEV	0.6	0.7	0.2	0.6	0.7	0.2	0.6	0.7	0.2
381	1.4	1.5	1.7	1.4	1.5	1.7	1.4	1.5	1.7
408	0.6	0.8	1.2	0.6	0.8	1.2	0.6	0.8	1.2
422	1.0	1.2	1.3	1.0	1.2	1.3	1.0	1.2	1.3
392	1.3	1.4	1.3	1.3	1.4	1.3	1.3	1.4	1.3
372	1.2	1.3	1.0	1.2	1.3	1.0	1.2	1.3	1.0
399	0.6	3.0	1.2	0.6	3.0	1.2	0.6	3.0	1.2
402	1.3	1.3	1.1	1.3	1.3	1.1	1.3	1.3	1.1
MEAN	1.1	1.5	1.3	1.1	1.5	1.3	1.1	1.5	1.3
STDEV	0.3	0.7	0.2	0.3	0.7	0.2	0.3	0.7	0.2
T MEAN	1.2	1.5	1.3	1.2	1.5	1.3	1.2	1.5	1.3
T STDEV	0.5	0.8	0.4	0.5	0.8	0.4	0.5	0.8	0.4

CREATININE CLEARANCE RATE (ml/min)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	137.0	162.5		137.0	162.5		137.0	162.5	
407	160.9	267.1		160.9	267.1		160.9	267.1	
409	146.2	349.4		146.2	349.4		146.2	349.4	
397	126.1	249.7		126.1	249.7		126.1	249.7	
391	175.1	27.3		175.1	27.3		175.1	27.3	
MEAN	149.1	211.2		149.1	211.2		149.1	211.2	
STDEV	19.3	122.4		19.3	122.4		19.3	122.4	
390	131.0	126.9		131.0	126.9		131.0	126.9	
420	78.2	134.4		78.2	134.4		78.2	134.4	
412	250.2	129.3		250.2	129.3		250.2	129.3	
403	32.5	333.3		32.5	333.3		32.5	333.3	
385	164.0	134.7		164.0	134.7		164.0	134.7	
405	131.1	102.5		131.1	102.5		131.1	102.5	
394	127.4	99.0		127.4	99.0		127.4	99.0	
MEAN	130.6	151.5		130.6	151.5		130.6	151.5	
STDEV	68.0	81.5		68.0	81.5		68.0	81.5	
381	140.9	156.2		140.9	156.2		140.9	156.2	
408	60.1	77.5		60.1	77.5		60.1	77.5	
422	129.8	136.9		129.8	136.9		129.8	136.9	
392	211.0	205.2		211.0	205.2		211.0	205.2	
372	131.4	139.2		131.4	139.2		131.4	139.2	
399	76.4	372.1		76.4	372.1		76.4	372.1	
402	140.2	138.9		140.2	138.9		140.2	138.9	
MEAN	127.1	175.2		127.1	175.2		127.1	175.2	
STDEV	49.1	94.6		49.1	94.6		49.1	94.6	
T MEAN	134.2	175.9		134.2	175.9		134.2	175.9	
T STDEV	50.2	95.4		50.2	95.4		50.2	95.4	

PLASMA OSMOLALITY (mOsm/kg)

DAY-	-4			+5			+28		
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	289.0	288.0		289.0	288.0		289.0	288.0	
407	290.0	290.0		290.0	290.0		290.0	290.0	
409	286.0	289.0		286.0	289.0		286.0	289.0	
397	292.0	289.0		292.0	289.0		292.0	289.0	
391	287.0	284.0		287.0	284.0		287.0	284.0	
MEAN	288.8	288.0		288.8	288.0		288.8	288.0	
STDEV	2.4	2.3		2.4	2.3		2.4	2.3	
390	286.0	291.0		286.0	291.0		286.0	291.0	
420	290.0	295.0		290.0	295.0		290.0	295.0	
412	293.0	298.0		293.0	298.0		293.0	298.0	
403	289.0	294.0		289.0	294.0		289.0	294.0	
385	290.0	291.0		290.0	291.0		290.0	291.0	
405	284.0	288.0		284.0	288.0		284.0	288.0	
394	289.0	287.0		289.0	287.0		289.0	287.0	
MEAN	288.7	292.0		288.7	292.0		288.7	292.0	
STDEV	2.9	3.9		2.9	3.9		2.9	3.9	
381	289.0	292.0		289.0	292.0		289.0	292.0	
408	291.0	289.0		291.0	289.0		291.0	289.0	
422	291.0	291.0		291.0	291.0		291.0	291.0	
392	295.0	290.0		295.0	290.0		295.0	290.0	
372	287.0	289.0		287.0	289.0		287.0	289.0	
399	289.0	290.0		289.0	290.0		289.0	290.0	
402	293.0	290.0		293.0	290.0		293.0	290.0	
MEAN	290.7	290.1		290.7	290.1		290.7	290.1	
STDEV	2.7	1.1		2.7	1.1		2.7	1.1	
T MEAN	289.5	290.3		289.5	290.3		289.5	290.3	
T STDEV	2.7	3.1		2.7	3.1		2.7	3.1	

URINE OSMOLALITY (mOsm/kg)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	680.0	697.0	206.0	680.0	697.0	206.0	680.0	697.0	206.0
407	233.0	211.0	365.0	233.0	211.0	365.0	233.0	211.0	365.0
409	783.0	760.0	684.0	783.0	760.0	684.0	783.0	760.0	684.0
397	643.0	927.0	570.0	643.0	927.0	570.0	643.0	927.0	570.0
391	871.0	610.0	367.0	871.0	610.0	367.0	871.0	610.0	367.0
MEAN	642.0	641.0	438.4	642.0	641.0	438.4	642.0	641.0	438.4
STDEV	245.5	266.9	188.5	245.5	266.9	188.5	245.5	266.9	188.5
390	309.0	171.0	401.0	309.0	171.0	401.0	309.0	171.0	401.0
420	245.0	456.0	727.0	245.0	456.0	727.0	245.0	456.0	727.0
412	1012.0	810.0	863.0	1012.0	810.0	863.0	1012.0	810.0	863.0
403	817.0	807.0	859.0	817.0	807.0	859.0	817.0	807.0	859.0
385	581.0	639.0	697.0	581.0	639.0	697.0	581.0	639.0	697.0
405	752.0	682.0	720.0	752.0	682.0	720.0	752.0	682.0	720.0
394	818.0	808.0	773.0	818.0	808.0	773.0	818.0	808.0	773.0
MEAN	647.7	624.7	720.0	647.7	624.7	720.0	647.7	624.7	720.0
STDEV	283.6	237.7	155.4	283.6	237.7	155.4	283.6	237.7	155.4
381	323.0	275.0	397.0	323.0	275.0	397.0	323.0	275.0	397.0
408	494.0	371.0	499.0	494.0	371.0	499.0	494.0	371.0	499.0
422	893.0	801.0	902.0	893.0	801.0	902.0	893.0	801.0	902.0
392	340.0	696.0	735.0	340.0	696.0	735.0	340.0	696.0	735.0
372	776.0	383.0	677.0	776.0	383.0	677.0	776.0	383.0	677.0
399	503.0	532.0	908.0	503.0	532.0	908.0	503.0	532.0	908.0
402	808.0	677.0	793.0	808.0	677.0	793.0	808.0	677.0	793.0
MEAN	591.0	533.6	701.6	591.0	533.6	701.6	591.0	533.6	701.6
STDEV	232.6	197.7	194.4	232.6	197.7	194.4	232.6	197.7	194.4
T MEAN	625.3	595.4	639.1	625.3	595.4	639.1	625.3	595.4	639.1
T STDEV	242.8	223.8	209.3	242.8	223.8	209.3	242.8	223.8	209.3

OSMOTIC CLEARANCE RATE (ml/min)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	1.9	2.4		1.9	2.4		1.9	2.4	
407	2.9	7.1		2.9	7.1		2.9	7.1	
409	2.1	5.9		2.1	5.9		2.1	5.9	
397	1.3	2.1		1.3	2.1		1.3	2.1	
391	5.5	0.5		5.5	0.5		5.5	0.5	
MEAN	2.7	3.6		2.7	3.6		2.7	3.6	
STDEV	1.6	2.8		1.6	2.8		1.6	2.8	
390	2.6	2.7		2.6	2.7		2.6	2.7	
420	1.7	2.6		1.7	2.6		1.7	2.6	
412	3.6	2.3		3.6	2.3		3.6	2.3	
403	0.6	6.9		0.6	6.9		0.6	6.9	
385	3.1	2.5		3.1	2.5		3.1	2.5	
405	2.3	2.0		2.3	2.0		2.3	2.0	
394	2.0	2.6		2.0	2.6		2.0	2.6	
MEAN	2.3	3.1		2.3	3.1		2.3	3.1	
STDEV	0.9	1.7		0.9	1.7		0.9	1.7	
381	2.2	2.7		2.2	2.7		2.2	2.7	
408	1.5	1.9		1.5	1.9		1.5	1.9	
422	1.4	2.1		1.4	2.1		1.4	2.1	
392	2.4	2.7		2.4	2.7		2.4	2.7	
372	1.8	2.1		1.8	2.1		1.8	2.1	
399	1.4	6.4		1.4	6.4		1.4	6.4	
402	2.3	2.9		2.3	2.9		2.3	2.9	
MEAN	1.9	3.0		1.9	3.0		1.9	3.0	
STDEV	0.4	1.5		0.4	1.5		0.4	1.5	
T MEAN	2.2	3.2		2.2	3.2		2.2	3.2	
T STDEV	1.0	1.9		1.0	1.9		1.0	1.9	

PLASMA SODIUM (mEq/l)

DAY-	-4			+5			+28		
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	138.6	138.7		138.6	138.7		138.6	138.7	
407	138.9	138.5		138.9	138.5		138.9	138.5	
409	136.8	136.7		136.8	136.7		136.8	136.7	
397	137.7	137.6		137.7	137.6		137.7	137.6	
391	139.2	139.5		139.2	139.5		139.2	139.5	
MEAN	138.2	138.2		138.2	138.2		138.2	138.2	
STDEV	1.0	1.1		1.0	1.1		1.0	1.1	
390	138.7	138.5		138.7	138.5		138.7	138.5	
420	137.6	138.5		137.6	138.5		137.6	138.5	
412	137.9	140.7		137.9	140.7		137.9	140.7	
403	139.3	139.6		139.3	139.6		139.3	139.6	
385	136.9	135.9		136.9	135.9		136.9	135.9	
405	134.4	135.2		134.4	135.2		134.4	135.2	
394	137.2	141.2		137.2	141.2		137.2	141.2	
MEAN	137.4	138.5		137.4	138.5		137.4	138.5	
STDEV	1.6	2.3		1.6	2.3		1.6	2.3	
381	137.8	139.4		137.8	139.4		137.8	139.4	
408	138.0	137.5		138.0	137.5		138.0	137.5	
422	138.9	137.0		138.9	137.0		138.9	137.0	
392	136.9	137.7		136.9	137.7		136.9	137.7	
372	134.1	135.5		134.1	135.5		134.1	135.5	
399	134.6	136.2		134.6	136.2		134.6	136.2	
402	135.5	136.3		135.5	136.3		135.5	136.3	
MEAN	136.5	137.1		136.5	137.1		136.5	137.1	
STDEV	1.8	1.3		1.8	1.3		1.8	1.3	
T MEAN	137.3	137.9		137.3	137.9		137.3	137.9	
T STDEV	1.6	1.7		1.6	1.7		1.6	1.7	

URINE SODIUM (mEq/l)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	102.0	117.9	38.6	102.0	117.9	38.6	102.0	117.9	38.6
407	43.7	45.6	69.1	43.7	45.6	69.1	43.7	45.6	69.1
409	112.8	146.9	164.9	112.8	146.9	164.9	112.8	146.9	164.9
397	89.2	134.1	96.2	89.2	134.1	96.2	89.2	134.1	96.2
391	153.3	124.2	79.4	153.3	124.2	79.4	153.3	124.2	79.4
MEAN	100.2	113.7	89.6	100.2	113.7	89.6	100.2	113.7	89.6
STDEV	39.7	39.6	47.0	39.7	39.6	47.0	39.7	39.6	47.0
390	47.1	33.0	71.5	47.1	33.0	71.5	47.1	33.0	71.5
420	42.2	83.8	134.8	42.2	83.8	134.8	42.2	83.8	134.8
412	159.7	124.3	122.1	159.7	124.3	122.1	159.7	124.3	122.1
403	146.8	153.1	160.0	146.8	153.1	160.0	146.8	153.1	160.0
385	119.8	109.5	141.7	119.8	109.5	141.7	119.8	109.5	141.7
405	102.3	83.2	115.0	102.3	83.2	115.0	102.3	83.2	115.0
394	119.4	149.1	185.6	119.4	149.1	185.6	119.4	149.1	185.6
MEAN	105.3	105.1	133.0	105.3	105.1	133.0	105.3	105.1	133.0
STDEV	45.6	42.3	36.1	45.6	42.3	36.1	45.6	42.3	36.1
381	53.4	54.7	77.7	53.4	54.7	77.7	53.4	54.7	77.7
408	87.1	63.9	76.8	87.1	63.9	76.8	87.1	63.9	76.8
422	71.3	105.1	73.5	71.3	105.1	73.5	71.3	105.1	73.5
392	56.0	91.9	144.9	56.0	91.9	144.9	56.0	91.9	144.9
372	78.7	33.1	71.3	78.7	33.1	71.3	78.7	33.1	71.3
399	90.3	96.9	50.7	90.3	96.9	50.7	90.3	96.9	50.7
402	98.6	80.3	129.5	98.6	80.3	129.5	98.6	80.3	129.5
MEAN	76.5	75.1	89.2	76.5	75.1	89.2	76.5	75.1	89.2
STDEV	17.2	25.8	34.3	17.2	25.8	34.3	17.2	25.8	34.3
T MEAN	93.4	96.3	105.4	93.4	96.3	105.4	93.4	96.3	105.4
T STDEV	36.3	38.2	42.2	36.3	38.2	42.2	36.3	38.2	42.2

FREE WATER CLEARANCE (ml/min)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	-1.1	-1.4		-1.1	-1.4		-1.1	-1.4	
407	0.7	2.6		0.7	2.6		0.7	2.6	
409	-1.3	-3.7		-1.3	-3.7		-1.3	-3.7	
397	-0.7	-1.5		-0.7	-1.5		-0.7	-1.5	
391	-3.7	-0.3		-3.7	-0.3		-3.7	-0.3	
MEAN	-1.2	-0.8		-1.2	-0.8		-1.2	-0.8	
STDEV	1.6	2.3		1.6	2.3		1.6	2.3	
390	-0.2	1.9		-0.2	1.9		-0.2	1.9	
420	0.3	-0.9		0.3	-0.9		0.3	-0.9	
412	-2.5	-1.5		-2.5	-1.5		-2.5	-1.5	
403	-0.4	-4.4		-0.4	-4.4		-0.4	-4.4	
385	-1.5	-1.4		-1.5	-1.4		-1.5	-1.4	
405	-1.4	-1.1		-1.4	-1.1		-1.4	-1.1	
394	-1.3	-1.7		-1.3	-1.7		-1.3	-1.7	
MEAN	-1.0	-1.3		-1.0	-1.3		-1.0	-1.3	
STDEV	1.0	1.8		1.0	1.8		1.0	1.8	
381	-0.2	0.2		-0.2	0.2		-0.2	0.2	
408	-0.6	-0.4		-0.6	-0.4		-0.6	-0.4	
422	-0.9	-1.4		-0.9	-1.4		-0.9	-1.4	
392	-0.3	-1.6		-0.3	-1.6		-0.3	-1.6	
372	-1.1	-0.5		-1.1	-0.5		-1.1	-0.5	
399	-0.6	-2.9		-0.6	-2.9		-0.6	-2.9	
402	-1.4	-1.7		-1.4	-1.7		-1.4	-1.7	
MEAN	-0.8	-1.2		-0.8	-1.2		-0.8	-1.2	
STDEV	0.4	1.0		0.4	1.0		0.4	1.0	
T MEAN	-1.0	-1.1		-1.0	-1.1		-1.0	-1.1	
T STDEV	1.0	1.6		1.0	1.6		1.0	1.6	

SODIUM EXCRETION RATE (mEq/l)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	83.9	117.9	97.1	83.9	117.9	97.1	83.9	117.9	97.1
407	156.2	443.0	162.2	156.2	443.0	162.2	156.2	443.0	162.2
409	87.3	330.5	327.1	87.3	330.5	327.1	87.3	330.5	327.1
397	51.1	88.1	178.2	51.1	88.1	178.2	51.1	88.1	178.2
391	277.2	30.7	31.2	277.2	30.7	31.2	277.2	30.7	31.2
MEAN	131.1	202.0	159.2	131.1	202.0	159.2	131.1	202.0	159.2
STDEV	90.2	176.1	110.4	90.2	176.1	110.4	90.2	176.1	110.4
390	111.7	149.5	123.7	111.7	149.5	123.7	111.7	149.5	123.7
420	87.4	140.8	138.1	87.4	140.8	138.1	87.4	140.8	138.1
412	165.0	105.7	108.9	165.0	105.7	108.9	165.0	105.7	108.9
403	33.1	382.7	176.0	33.1	382.7	176.0	33.1	382.7	176.0
385	182.7	124.1	205.5	182.7	124.1	205.5	182.7	124.1	205.5
405	89.4	69.3	141.3	89.4	69.3	141.3	89.4	69.3	141.3
394	84.5	138.4	261.0	84.5	138.4	261.0	84.5	138.4	261.0
MEAN	107.7	158.7	164.9	107.7	158.7	164.9	107.7	158.7	164.9
STDEV	51.3	102.5	53.4	51.3	102.5	53.4	51.3	102.5	53.4
381	107.5	156.1	196.2	107.5	156.1	196.2	107.5	156.1	196.2
408	79.4	95.3	116.3	79.4	95.3	116.3	79.4	95.3	116.3
422	32.5	82.0	42.9	32.5	82.0	42.9	32.5	82.0	42.9
392	114.4	104.8	227.0	114.4	104.8	227.0	114.4	104.8	227.0
372	52.0	52.1	66.3	52.0	52.1	66.3	52.0	52.1	66.3
399	72.6	335.4	36.5	72.6	335.4	36.5	72.6	335.4	36.5
402	80.8	100.4	151.1	80.8	100.4	151.1	80.8	100.4	151.1
MEAN	77.0	132.3	119.5	77.0	132.3	119.5	77.0	132.3	119.5
STDEV	28.8	94.8	75.3	28.8	94.8	75.3	28.8	94.8	75.3
T MEAN	102.6	160.4	146.7	102.6	160.4	146.7	102.6	160.4	146.7
T STDEV	58.7	119.1	77.5	58.7	119.1	77.5	58.7	119.1	77.5

% FILTERED SODIUM EXCRETED

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	44.2	52.3		44.2	52.3		44.2	52.3	
407	69.9	119.7		69.9	119.7		69.9	119.7	
409	43.7	69.2		43.7	69.2		43.7	69.2	
397	29.4	25.6		29.4	25.6		29.4	25.6	
391	113.7	80.5		113.7	80.5		113.7	80.5	
MEAN	60.2	69.5		60.2	69.5		60.2	69.5	
STDEV	33.3	34.9		33.3	34.9		33.3	34.9	
390	61.5	85.1		61.5	85.1		61.5	85.1	
420	81.2	75.6		81.2	75.6		81.2	75.6	
412	47.8	58.1		47.8	58.1		47.8	58.1	
403	73.0	82.3		73.0	82.3		73.0	82.3	
385	81.4	67.8		81.4	67.8		81.4	67.8	
405	50.7	50.0		50.7	50.0		50.7	50.0	
394	48.3	99.0		48.3	99.0		48.3	99.0	
MEAN	63.4	74.0		63.4	74.0		63.4	74.0	
STDEV	15.1	16.8		15.1	16.8		15.1	16.8	
381	55.4	71.7		55.4	71.7		55.4	71.7	
408	95.6	89.4		95.6	89.4		95.6	89.4	
422	18.0	43.7		18.0	43.7		18.0	43.7	
392	39.6	37.1		39.6	37.1		39.6	37.1	
372	29.5	27.6		29.5	27.6		29.5	27.6	
399	70.6	66.2		70.6	66.2		70.6	66.2	
402	42.5	53.0		42.5	53.0		42.5	53.0	
MEAN	50.2	55.5		50.2	55.5		50.2	55.5	
STDEV	26.3	21.5		26.3	21.5		26.3	21.5	
T MEAN	57.7	66.0		57.7	66.0		57.7	66.0	
T STDEV	24.3	24.3		24.3	24.3		24.3	24.3	

PLASMA POTASSIUM (mEq/l)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	4.8	4.7		4.8	4.7		4.8	4.7	
407	4.9	4.5		4.9	4.5		4.9	4.5	
409	4.8	4.7		4.8	4.7		4.8	4.7	
397	4.1	4.3		4.1	4.3		4.1	4.3	
391	4.5	4.5		4.5	4.5		4.5	4.5	
MEAN	4.6	4.5		4.6	4.5		4.6	4.5	
STDEV	0.3	0.2		0.3	0.2		0.3	0.2	
390	4.3	4.0		4.3	4.0		4.3	4.0	
420	4.6	3.9		4.6	3.9		4.6	3.9	
412	4.6	4.4		4.6	4.4		4.6	4.4	
403	4.6	4.3		4.6	4.3		4.6	4.3	
385	4.3	4.2		4.3	4.2		4.3	4.2	
405	4.3	4.4		4.3	4.4		4.3	4.4	
394	4.3	4.7		4.3	4.7		4.3	4.7	
MEAN	4.4	4.3		4.4	4.3		4.4	4.3	
STDEV	0.2	0.3		0.2	0.3		0.2	0.3	
381	4.5	4.5		4.5	4.5		4.5	4.5	
408	4.4	4.4		4.4	4.4		4.4	4.4	
422	4.8	4.0		4.8	4.0		4.8	4.0	
392	4.6	4.8		4.6	4.8		4.6	4.8	
372	4.2	4.4		4.2	4.4		4.2	4.4	
399	4.1	4.0		4.1	4.0		4.1	4.0	
402	4.3	4.2		4.3	4.2		4.3	4.2	
MEAN	4.4	4.3		4.4	4.3		4.4	4.3	
STDEV	0.2	0.3		0.2	0.3		0.2	0.3	
T MEAN	4.5	4.4		4.5	4.4		4.5	4.4	
T STDEV	0.2	0.3		0.2	0.3		0.2	0.3	

URINE POTASSIUM (mEq/l)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	78.1	56.9	21.1	78.1	56.9	21.1	78.1	56.9	21.1
407	26.3	28.2	38.0	26.3	28.2	38.0	26.3	28.2	38.0
409	42.5	41.0	39.4	42.5	41.0	39.4	42.5	41.0	39.4
397	78.8	58.7	50.6	78.8	58.7	50.6	78.8	58.7	50.6
391	53.1	40.2	34.9	53.1	40.2	34.9	53.1	40.2	34.9
MEAN	55.8	45.0	36.8	55.8	45.0	36.8	55.8	45.0	36.8
STDEV	22.8	12.8	10.6	22.8	12.8	10.6	22.8	12.8	10.6
390	33.3	18.1	43.1	33.3	18.1	43.1	33.3	18.1	43.1
420	34.9	50.1	62.1	34.9	50.1	62.1	34.9	50.1	62.1
412	65.5	32.3	66.7	65.5	32.3	66.7	65.5	32.3	66.7
403	87.1	87.9	79.5	87.1	87.9	79.5	87.1	87.9	79.5
385	78.0	100.1	86.2	78.0	100.1	86.2	78.0	100.1	86.2
405	84.6	85.7	77.3	84.6	85.7	77.3	84.6	85.7	77.3
394	58.0	65.7	59.0	58.0	65.7	59.0	58.0	65.7	59.0
MEAN	63.1	62.8	67.7	63.1	62.8	67.7	63.1	62.8	67.7
STDEV	22.3	30.7	14.6	22.3	30.7	14.6	22.3	30.7	14.6
381	32.4	22.6	45.0	32.4	22.6	45.0	32.4	22.6	45.0
408	55.5	47.2	71.8	55.5	47.2	71.8	55.5	47.2	71.8
422	75.1	81.2	128.8	75.1	81.2	128.8	75.1	81.2	128.8
392	48.6	68.3	76.3	48.6	68.3	76.3	48.6	68.3	76.3
372	64.9	30.1	88.2	64.9	30.1	88.2	64.9	30.1	88.2
399	44.5	49.1	8.0	44.5	49.1	8.0	44.5	49.1	8.0
402	83.9	75.3	76.6	83.9	75.3	76.6	83.9	75.3	76.6
MEAN	57.8	53.4	70.7	57.8	53.4	70.7	57.8	53.4	70.7
STDEV	18.0	22.4	37.3	18.0	22.4	37.3	18.0	22.4	37.3
T MEAN	59.2	54.7	60.7	59.2	54.7	60.7	59.2	54.7	60.7
T STDEV	20.0	23.9	27.9	20.0	23.9	27.9	20.0	23.9	27.9

URINE EXCRETION RATE (mEq/min)

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	64.2	56.9	53.1	64.2	56.9	53.1	64.2	56.9	53.1
407	94.0	273.9	89.2	94.0	273.9	89.2	94.0	273.9	89.2
409	32.9	92.3	78.2	32.9	92.3	78.2	32.9	92.3	78.2
397	45.2	38.6	93.7	45.2	38.6	93.7	45.2	38.6	93.7
391	96.0	9.9	13.7	96.0	9.9	13.7	96.0	9.9	13.7
MEAN	66.5	94.3	65.6	66.5	94.3	65.6	66.5	94.3	65.6
STDEV	28.4	104.8	33.0	28.4	104.8	33.0	28.4	104.8	33.0
390	78.9	82.0	74.6	78.9	82.0	74.6	78.9	82.0	74.6
420	72.3	84.2	63.6	72.3	84.2	63.6	72.3	84.2	63.6
412	67.7	27.5	59.5	67.7	27.5	59.5	67.7	27.5	59.5
403	19.6	219.7	87.5	19.6	219.7	87.5	19.6	219.7	87.5
385	119.0	113.4	125.0	119.0	113.4	125.0	119.0	113.4	125.0
405	73.9	71.4	95.0	73.9	71.4	95.0	73.9	71.4	95.0
394	41.0	61.0	83.0	41.0	61.0	83.0	41.0	61.0	83.0
MEAN	67.5	94.2	84.0	67.5	94.2	84.0	67.5	94.2	84.0
STDEV	31.2	61.2	22.1	31.2	61.2	22.1	31.2	61.2	22.1
381	65.2	64.5	113.6	65.2	64.5	113.6	65.2	64.5	113.6
408	50.6	70.4	108.7	50.6	70.4	108.7	50.6	70.4	108.7
422	34.2	63.3	75.1	34.2	63.3	75.1	34.2	63.3	75.1
392	99.2	77.9	119.5	99.2	77.9	119.5	99.2	77.9	119.5
372	42.9	47.4	82.0	42.9	47.4	82.0	42.9	47.4	82.0
399	35.8	170.0	5.8	35.8	170.0	5.8	35.8	170.0	5.8
402	68.8	94.1	89.4	68.8	94.1	89.4	68.8	94.1	89.4
MEAN	56.7	83.9	84.9	56.7	83.9	84.9	56.7	83.9	84.9
STDEV	23.1	40.5	38.7	23.1	40.5	38.7	23.1	40.5	38.7
T MEAN	63.2	90.4	79.5	63.2	90.4	79.5	63.2	90.4	79.5
T STDEV	26.6	65.3	31.2	26.6	65.3	31.2	26.6	65.3	31.2

%FILTERED POTASSIUM EXCRETED

DAY-		-4			+5			+28	
TIME-	pre	3'	120'	pre	3'	120'	pre	3'	120'
SUBJECT									
376	9.8	7.5		9.8	7.5		9.8	7.5	
407	12.0	22.7		12.0	22.7		12.0	22.7	
409	4.7	5.6		4.7	5.6		4.7	5.6	
397	8.7	3.6		8.7	3.6		8.7	3.6	
391	12.2	8.0		12.2	8.0		12.2	8.0	
MEAN	9.5	9.5		9.5	9.5		9.5	9.5	
STDEV	3.1	7.6		3.1	7.6		3.1	7.6	
390	14.0	16.0		14.0	16.0		14.0	16.0	
420	20.2	16.1		20.2	16.1		20.2	16.1	
412	5.9	4.9		5.9	4.9		5.9	4.9	
403	13.0	15.2		13.0	15.2		13.0	15.2	
385	16.9	19.9		16.9	19.9		16.9	19.9	
405	13.1	15.8		13.1	15.8		13.1	15.8	
394	7.5	13.1		7.5	13.1		7.5	13.1	
MEAN	13.0	14.4		13.0	14.4		13.0	14.4	
STDEV	5.0	4.7		5.0	4.7		5.0	4.7	
381	10.4	9.2		10.4	9.2		10.4	9.2	
408	19.3	20.4		19.3	20.4		19.3	20.4	
422	5.5	11.7		5.5	11.7		5.5	11.7	
392	10.3	8.0		10.3	8.0		10.3	8.0	
372	7.7	7.8		7.7	7.8		7.7	7.8	
399	11.5	11.3		11.5	11.3		11.5	11.3	
402	11.5	16.3		11.5	16.3		11.5	16.3	
MEAN	10.9	12.1		10.9	12.1		10.9	12.1	
STDEV	4.3	4.7		4.3	4.7		4.3	4.7	
T MEAN	11.3	12.3		11.3	12.3		11.3	12.3	
T STDEV	4.3	5.6		4.3	5.6		4.3	5.6	

Appendix H

Publications from This Study

Extant

Arnaud, S., P. Berry, M. Cohen, J. Danellis, C. DeRoshia, J. Greenleaf, B. Harris, L. Keil, E. Bernauer, M. Bond, S. Ellis, P. Lee, R. Selzer, and C. Wade. Exercise countermeasures for bed rest deconditioning. NASA Space Life Sciences Symposium: Three Decades of Life Science Research in Space. Washington, DC, June 21-26, 1987. p. 59-60. Abstract.

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In Preparation

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	June 1993	Technical Memorandum

4. TITLE AND SUBTITLE
Exercise Countermeasures for Bed-Rest Deconditioning (1986): Final Report

5. FUNDING NUMBERS
199-21-12-07

6. AUTHOR(S)
Editor: John Greenleaf

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Ames Research Center
Moffett Field, CA 94035-1000

8. PERFORMING ORGANIZATION REPORT NUMBER
A-93008

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
National Aeronautics and Space Administration
Washington, DC 20546-0001

10. SPONSORING/MONITORING AGENCY REPORT NUMBER
NASA TM-103987

11. SUPPLEMENTARY NOTES
Point of Contact: John Greenleaf, Ames Research Center, MS 239-11, Moffett Field, CA 94035-1000
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12a. DISTRIBUTION/AVAILABILITY STATEMENT
Unclassified — Unlimited
Subject Category 51

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

The purpose for this 30-day bed rest study was to investigate the effects of short-term, high-intensity isotonic and isokinetic exercise training on maintenance of working capacity (peak oxygen uptake), muscular strength and endurance, and on orthostatic tolerance, posture and gait. Other data were collected on muscle atrophy, bone mineralization and density, endocrine analyses concerning vasoactivity and fluid-electrolyte balance, muscle intermediary metabolism, and on performance and mood of the subjects.

It was concluded that: (1) The subjects maintained a relatively stable mood, high morale, and high esprit de corps throughout the study. Performance improved in nearly all tests in almost all the subjects. Isotonic training, as opposed to isokinetic exercise training, was associated more with decreasing levels of psychological tension, concentration, and motivation; and improvement in the quality of sleep. (2) Working capacity (peak oxygen uptake) was maintained during bed rest with isotonic exercise training; it was not maintained with isokinetic or no exercise training. (3) In general, there was no significant decrease in strength or endurance of arm or leg muscles during bed rest, in spite of some reduction in muscle size (atrophy) of some leg muscles. (4) There was no effect of isotonic exercise training on orthostasis, since tilt-table tolerance was reduced similarly in all three groups following bed rest. (5) Bed rest resulted in significant decreases of postural stability and self-selected step length, stride length, and walking velocity, which were not influenced by either exercise training regimen. Most pre-bed rest responses were restored by the fourth day of recovery.

14. SUBJECT TERMS	15. NUMBER OF PAGES
Bed rest, Deconditioning, Exercise training	228
	16. PRICE CODE: A11

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified		