Supine lower body negative pressure exercise during bed rest maintains upright exercise capacity

DONALD E. WATENPAUGH, 1 RICHARD E. BALLARD, 1 SUZANNE M. SCHNEIDER, 1 STEWART M. C. LEE, 2 ANDREW C. ERTL, 1 JACQUELINE M. WILLIAM, 1 WANDA L. BODA, 1 KAREN J. HUTCHINSON, 1 AND ALAN R. HARGENS 1

1Gravitational Research Branch, NASA Ames Research Center, Moffett Field, California 94035-1000; and 2Life Sciences Research Laboratories, NASA Johnson Space Center, Houston, Texas 77058

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Abstract—Bed rest and spaceflight reduce exercise fitness. Supine lower body negative pressure (LBNP) treadmill exercise provides integrated cardiovascular and musculoskeletal stimulation similar to that imposed by upright exercise in Earth gravity. We hypothesized that 40 min of supine exercise per day in a LBNP chamber at 1.0–1.2 body wt (58 ± 2 mmHg LBNP) maintains aerobic fitness and sprint speed during 15 days of 6° head-down bed rest (simulated microgravity). Seven male subjects underwent two such bed-rest studies in random order: one as a control study (no exercise) and one with daily supine LBNP treadmill exercise. After controlled bed-rest, time to exhaustion during an upright treadmill exercise test decreased 10%, peak oxygen consumption during the test decreased 14%, and sprint speed decreased 16% (all P < 0.05). Supine LBNP exercise during bed rest maintained all the above variables at pre-bed-rest levels. Our findings support further evaluation of LBNP exercise as a countermeasure against long-term microgravity-induced deconditioning.

Existence in microgravity leads to cardiovascular deconditioning in humans, as indicated by the postflight reduction of upright exercise capacity and orthostatic tolerance (6, 27, 35). Astronauts undergoing long-term spaceflight also experience loss of musculoskeletal integrity in load-bearing tissues (28) and reduced neuromuscular coordination during locomotion after flight (23, 39). Similar deconditioning occurs during bed rest (14, 15). Reduced upright exercise capacity, muscle strength, and orthostatic tolerance pose serious hazards to crew members during reentry, landing, and possible emergency egress from spacecraft.

Original submission in response to a special call for papers on “Physiology of a Microgravity Environment.” Address for reprint requests and other correspondence: D. Watenpaugh, Dept. of Integrative Physiology, Univ. of North Texas Health Science Center, 3500 Camp Bowie Blvd., Fort Worth, Texas 76107 (E-mail: dwatenpa@hsc.unt.edu).

Astronauts exercise during spaceflight to counteract its deconditioning effects. However, exercise protocols and equipment for astronauts remain subjects of research because no current regimen fully prevents deconditioning (9). During long stays in microgravity, crew members most commonly perform treadmill exercise with a harness and elastic (bungee) cords that pull them toward a treadmill. The bungee cord system provides comfortable lower body musculoskeletal loads equaling only ~60–70% of those present on Earth (11, 36). During the long-duration Mir Space Station missions, crew members perform treadmill, cycle, and resistive exercises for up to 2–3 h/day toward the end of a mission; however, this large expenditure of time and energy still does not fully prevent physiological deconditioning: Russian astronauts wear anti-G garments for up to 4 days after a long-duration flight, and some do not walk unaided for at least 2 days (16). Obviously, this level of deconditioning compromises an astronaut’s physical ability to cope with an emergency situation during return to Earth and delays return to normal 1-G activities.

Hypothetically, an integrated countermeasure to extended exposure to microgravity should simulate gravity by combining Earth-like loads on the musculoskeletal system (28, 37), normal regional distributions of transmural pressure across blood vessels (20), and stimulation of normal neuromuscular locomotor patterns. Lower body negative pressure (LBNP) treadmill exercise largely meets these criteria: LBNP produces Earth-like loading of the musculoskeletal system (21, 29), LBNP can approximate gravitational vascular transmural pressures and fluid redistribution (1, 29, 38), and treadmill exercise in a supine position in LBNP simulates metabolism, loading, and gait patterns of upright exercise on a treadmill (4). Therefore, we postulated that LBNP exercise may prevent bedrest-induced deconditioning by simulating upright exercise in gravity. In a previous 5-day bed-rest study,
METHODS

Subjects. The NASA Ames Research Center Institutional Review Board approved this study. Eight healthy and relatively fit male subjects participated after they provided informed, written consent. They exhibited the following characteristics as a group (means ± SD): weight = 74.2 ± 4.5 kg, height = 177 ± 7 cm, blood volume = 5,787 ± 856 ml, plasma volume = 3,768 ± 583 ml, peak VO$_2$ = 56.7 ± 7.0 ml·kg$^{-1}$·min$^{-1}$, and age range = 24–49 yr (mean = 34). Subjects underwent an extensive physical examination, exercise stress test, and clinical blood chemistry to establish their healthy status. Subjects abstained from caffeine and alcohol for at least 24 h before participation in the study and throughout its duration. No subject used tobacco. Only men were used because this investigation involved components that would be difficult to separate from effects of normal hormonal cycles in women. Also, the facility where this study was performed does not admit men and women simultaneously, and subjects were studied as a group for logistic and financial necessity.

Experimental design and conditions. Subjects were randomly divided into two groups of four each. We studied the same subjects in each of two 15-day 6° head-down tilt bed-rest studies; four subjects were assigned to the supine LBNP exercise countermeasure, whereas the remaining four subjects did not exercise. In the second bed-rest study, subjects reversed roles in a crossover design, such that each subject served as his own control. The 15-day bed-rest period approximates the duration of longer space shuttle flights. Eighty-six days separated the two bed-rest studies. We asked subjects to train at their habitual level during the period between studies.

Before the first baseline data collection session, subjects experienced LBNP exercise and all testing procedures to become fully familiarized with the study. A 1.5-day ambulatory control period provided baseline data before each bed-rest study, and a 1-day ambulatory recovery period allowed post-bed-rest measurements. Control measurements before bed rest took place in the following order: plantar flexor strength, plasma volume, orthostatic tolerance, sprint speed, and upright exercise capacity. The same sequence was followed after bed rest. Presentation of the orthostatic tolerance test results is beyond the scope of this paper. All tests took place at the same time of day for a given subject and were at least 2 h postprandial. Details of the individual measurements and tests are presented below.

Subjects’ diet (2,500–3,000 kcal/day), body weight (bed scale, ± 0.1 kg), fluid intake (± 10 ml), and urine volume (± 10 ml) were monitored. Fluid intake was ad libitum. The diet contained 180 mmol sodium/day and was the same during each bed-rest period. During the entire period of bed rest, subjects remained in a 6° head-down tilt except during periods for showers and exercise (0.5–1.5 h/day), when they were horizontal (0°). All testing and exercise sessions occurred at room temperature (21–23°C).

LBNP exercise training. The LBNP exercise device consists of a vacuum control system connected to a rectangular chamber containing a vertically oriented treadmill capable of speeds of up to 13 km/h (PaceMaster SX-Pro, Aerobics, Little Falls, NJ; Fig. 1). A high-capacity vacuum cleaner (model 360, H-P Products, Louisville, OH) reduces chamber pressure while providing some air flow through the chamber during exercise. This air flow helps attenuate chamber temperature elevation caused by exercise and by the treadmills. Personnel at NASA Ames Research Center custom-constructed the device specifically for bed-rest evaluations of LBNP exercise as a countermeasure.

Interchangeable plywood plates allow adjustment of the size of the elliptical opening through which a subject fits into the chamber. A broad, flexible neoprene waist seal spans the area between the subject and the edge of the elliptical opening. We set this waist seal area to equal twice the subject’s waist cross-sectional area, such that the negative pressure necessary to produce 1 body wt equaled 50–60 mmHg. This larger waist seal reduces orthostatic stress and risks of LBNP (petechiae, hernia, syncope) by decreasing the LBNP necessary to generate a given level of footward force (32). Shoulder straps attached to the waist seal prevent the negative chamber pressure from pulling the flexible seal footward past the subject’s hips. The shoulder straps also apply part of the suction force on the waist seal to the pectoral girdle, thus allowing spinal as well as lower-body loading.

To run while in a supine position, a subject’s back and buttocks were suspended in freely swinging supports. Subject’s legs were suspended across from each other via bungee cords attached to pulleys and cuffs at the ankles and lower thighs, such that one leg acted as a counterweight to the other during the gait cycle. This resulted in the leg in the stance phase of gait lifting the opposite leg through the swing phase of gait (Fig. 1). Neither the suspension system nor the waist seal imparted substantial frictional or other resistance to subject movements during normal gait.

Subjects wore specially designed shorts during LBNP exercise to prevent abnormal and excessive LBNP-induced pooling of blood and extravascular fluid in the relatively compliant lower abdomen and to minimize risk of hernia. These shorts consisted of lightweight, inelastic material, able to hold a 12 × 30-cm air bladder in place over the lower abdomen. This air bladder was connected to air outside the LBNP chamber via a tube through the waist seal. Therefore, the bladder automatically inflated to compress the lower abdomen in direct proportion to the magnitude of LBNP.

During the bed rest plus exercise trial in the present study, subjects performed 40 min of supine running exercise per day at 1.0–1.2 body wt of footward force. We determined the negative pressures necessary to produce this force range for each subject at supine rest in the chamber. A calibrated scale measured footward reaction force to ± 4 N. LBNP of 55 ± 2 mmHg (mean ± SD) produced 1.0 body wt of static footward force.
The exercise protocol was similar to that used by Greenleaf et al. (17) and Lee et al. (26), with target workloads and durations as follows: 7-min warm-up at 40% peak $V\dot{O}_2$, followed by 3 min at 60%, 2 min at 40%, 3 min at 70%, 2 min at 50%, 3 min at 80%, 2 min at 60%, 3 min at 80%, 2 min at 50%, 3 min at 70%, 2 min at 40%, and 3 min at 60%, and 5-min cool-down at 40% peak $V\dot{O}_2$. Target speeds were then calculated for each of the desired training workloads. Treadmill grade remained set at 0% during LBNP exercise. Exercise training commenced on the first day of bed rest; predicted speeds were used, and these were adjusted later as necessary to achieve target $V\dot{O}_2$ at $>1.0$ body wt of footward force and for subject tolerance. Subjects rated their perceived exertion on a 20-point scale before each change in workload (5). After the first few days of bed rest, we challenged all subjects to exercise at $>1.0$ body wt. On the seventh day of bed rest, exercising subjects did not exercise. Training $V\dot{O}_2$ was measured at the start, middle, and end of the 15-day bed-rest period.

Peak $V\dot{O}_2$. Peak $V\dot{O}_2$ and submaximal treadmill exercise responses were quantified with a protocol modified from Lee et al. (26) (treadmill model Q55, Quinton Instruments, Seattle, WA). On the basis of the results of a familiarization-graded peak exercise test, we designed a testing protocol that was specific to each subject. The protocol consisted of a walking warm-up at 4.8 and 6.4 km/h for 3 min each. Thereafter, subjects completed three 3-min, level running stages at $\sim70$, 80, and 90% of peak $V\dot{O}_2$ before bed rest. At the end of the third running stage, treadmill speed was held constant, whereas grade increased in 3% increments each minute until volitional fatigue. No subject exercised to $>9\%$ grade. Subjects were encouraged before and during the test to give their maximal effort.

$V\dot{O}_2$, carbon dioxide production, and ventilation were measured continuously using a calibrated IBM-compatible computer-based data acquisition system with an electronic spirometer (Vacumed, Vacumetrics, Ventura, CA) and $O_2$ and $CO_2$ analyzers (Applied Electrochemistry, models S3-A and CD-3A, respectively; Ametek, Thermox Instruments Division, Sunnyvale, CA). These variables were averaged over the last minute of each exercise stage. Heart rate was averaged from electrocardiograph recordings during the last 15 s of each minute.

Sprint speed. Subjects sprinted a distance of 27.4 m down a hallway from a standing start and were timed with a stopwatch. Two sprint trials were performed before bed rest, and two trials were performed $\sim10$ min after arising from bed rest. We took the faster of the two trials as the maximal sprint speed at each time.

Leg plantar flexor strength. Strength of the plantar flexor muscles, primarily the soleus, was determined by measurements of maximum isometric and isokinetic (concentric and eccentric) ankle joint torque (19) made before and after bed rest. The supine subject’s right leg was strapped to a dynamometer (Lidoactive, Loredan, Davis, CA), such that the hip was flexed at $\sim45^\circ$ and the knee was at 90°. The subject’s right foot was secured to the dynamometer foot plate such that the malleolus aligned with the axis of rotation of the dynamometer. The subject’s leg was secured to the dynamometer with a thigh cuff just proximal to the right knee. Once properly secured, full ankle range of motion was determined, and the subject warmed up briefly by performing $\sim10$ submaximal concentric plantar flexions at a velocity of 60° per second.

The isometric test was performed with the ankle at 90°. The subject performed three maximum plantar flexions during a 15-s interval. Maximal concentric torque was then determined with the subject applying maximum force during three full range-of-motion plantar flexions at a velocity of 60° per second. For determination of maximal eccentric torque, the foot plate moved at 30° per second in the plantar direction and 60° per second in the dorsal direction through full range of motion. The subject resisted dorsal foot movement.
with three maximal eccentric activations of the calf muscles. For each exercise type, the greatest of the three trials was taken as maximum torque. Subjects rested as necessary between tests.

**Hematocrit and plasma volume.** Plasma volume was measured before and after bed rest with Evan’s blue dye dilution, using a modification of a standard technique (31). An 18-gauge intravenous catheter was placed in an antecubital vein. Subjects were supine for a minimum of 25 min before injection of 2.5 mg of Evan’s blue dye (T-1824, New World Trading, De Bary, FL) in 2.5 ml of saline. Blood samples were obtained without stasis immediately before and 10 min after Evan’s blue injection, and plasma was collected from centrifuged blood. Elution of Evan’s blue was performed by acetone extraction through Sephadex G-25 M chromatograph columns (PD-10, Uppsala, Sweden). Eluate absorbance was read at a wavelength of 615 nm on a spectrophotometer. Hematocrit was measured in quadruplicate on a microcapillary tube reader (International Equipment, Needham Heights, MA) after 10 min of centrifugation at 11,500 rpm. Total erythrocyte and blood volume were calculated from measured plasma volume and microcapillary venous hematocrit corrected for trapped plasma (0.96) and to whole body hematocrit (0.91) (22).

**Statistical analyses.** Two-factor repeated-measures ANOVA assessed independent and interactive effects of bed rest and LBNP exercise for all dependent variables. For the peak treadmill exercise test variables, a third factor (time) was included to analyze data from all six exercise levels (2 walking speeds, 3 submaximal running speeds, and peak running exercise). Least significant difference post hoc tests determined which specific mean values differed from others for each variable. All reported changes or differences met the significance criterion of \( P < 0.05 \), unless otherwise noted. Software (Statistica) for Apple Macintosh computers performed all statistical analyses (StatSoft, Tulsa, OK). Values are expressed as means ± SE, unless noted otherwise. One subject did not complete the control (nonexercise) bed-rest study. Therefore, his results are presented separately, and they were not included in control vs. LBNP exercise statistical analyses and were also not included with mean data presented in the results (n = 7 men, unless indicated otherwise).

**RESULTS**

**LBNP exercise training.** LBNP during daily exercise sessions averaged 58 ± 2 mmHg LBNP and ranged from 52 to 67 mmHg overall. In terms of distance, the subjects walked and/or ran between 4.9 and 7.7 km per exercise session. Some subjects progressively increased their footward force (LBNP) levels up to 1.0 body wt during bed rest, whereas others only occasionally exercised at >1.0 body wt. When LBNP was increased to raise footward force above 1.0 body wt, they ran with the footward force (“weight”) equivalent of a 5- to 15-kg backpack. \( V_{O2} \) during the LBNP exercise protocol averaged between 41 ± 3 and 65 ± 3% of maximal \( V_{O2} \), and the exercise produced heart rates ranging between 102 ± 6 and 168 ± 4 beats/min (overall average = 145 beats/min; Fig. 2).

Treadmill speed limitations prevented some of the more fit subjects from reaching the higher target workloads. Also, the NASA Ames Medical Monitor mandated reduction of training workload if heart rate reached 90% of the subject’s maximum heart rate, which occurred occasionally. Heart rate increased 34 beats/min on average between the start and end of a training session (Fig. 2), yet treadmill speed was the same at the start and end of each session. An increase of LBNP chamber internal air temperature from 23°C to −26–29°C occurred during a typical exercise session, despite some air flow through the chamber due to intentional leakage.

Subject ratings of their perceived exertion (RPE) ranged between 10 ± 1 and 16 ± 0 on the 20-point Borg scale, and mean RPE equaled or exceeded 13 from min 15 through min 35 of the protocol. Some subjects rarely reported RPE up to 19. Daily LBNP exercise was well tolerated by all subjects after some initial individual comfort issues were resolved (e.g., ankle and leg chafing from suspension system, waist chafing from seal, waist seal sizing, shoulder strap vs. waist seal pressure distribution). One subject exercised for 30 instead of 40 min during bed-rest days 2 and 4 and missed training entirely on bed-rest day 5 because of abdominal discomfort. He resumed full training on bed-rest day 10 with no subsequent problems. Another subject did not feel well on bed-rest day 10 and walked 40 min at 6.4 km/h for that day’s exercise session. He resumed normal training on bed-rest day 11. No other substantial or unscheduled breaks from training occurred.

Daily supine LBNP exercise during bed rest preserved upright exercise capacity, sprint speed, and plantar flexor strength. Forty minutes per day of supine LBNP exercise during 15 days of bed rest maintained upright exercise capacity at levels observed before bed rest, whereas exercise capacity decreased after bed rest without daily exercise. Subjects’ time to volitional exhaustion during treadmill testing decreased 1.72 min (10%) on average after bed rest with no daily exercise (17.36 ± 0.19 and 15.64 ± 0.32 min before and after Fig. 2. LBNP exercise training increased heart rate as expected, with the exception that treadmill speed and medical monitoring limitations prevented some subjects from always reaching the higher target workloads (see text). Results are means ± SE; n = 7 men. Heart rate at the end of a training session averaged 34 beats/min greater than at the beginning, despite treadmill speed being the same at those 2 time points.
bed rest, respectively; \( P < 0.05 \); daily LBNP exercise during bed rest maintained exercise tolerance time at pre-bed-rest levels (17.27 ± 0.22 and 17.17 ± 0.22 min before and after bed rest, respectively; no significant difference). Daily LBNP exercise maintained peak upright \( \dot{V}O_2 \) at pre-bed-rest levels (59.5 ± 3.2 and 56.4 ± 3.4 ml min\(^{-1}\) kg\(^{-1}\) before and after bed rest, respectively; no significant difference). Mean peak \( \dot{V}O_2 \) decreased from 57.6 ± 2.6 to 49.8 ± 1.5 ml min\(^{-1}\) kg\(^{-1}\) (14%) after bed rest with no exercise \( (P < 0.05; \text{Fig. 3}). \) Analysis of absolute \( \dot{V}O_2 \) data (l/min) yielded similar results. Peak heart rate, minute ventilation, and respiratory exchange ratio (RER) remained unchanged by bed rest, regardless of daily exercise.

In addition to protection of peak upright exercise capacity, LBNP exercise during bed rest preserved submaximal exercise responses at pre-bed-rest levels. After 15 days of bed rest with no exercise, both RER (Fig. 4) and heart rate (Fig. 5) were consistently elevated at the three submaximal running speeds relative to measurements before bed rest \( (P < 0.05). \) Similar yet nonsignificant trends were seen during walking. Mean ventilation rate after bed rest was significantly elevated at the highest two submaximal running speeds (13 and 17%; \( P < 0.05 \)) relative to measurements before bed rest. These effects were not seen during submaximal exercise after bed rest with daily LBNP exercise; i.e., responses were not significantly different from those observed before bed rest.

Sprint speed from a standing start after bed rest was not significantly different from levels before bed rest when daily LBNP exercise accompanied 15 days of bed rest (Fig. 6). However, bed rest without daily exercise reduced sprint speed from 5.5 ± 0.2 to 4.6 ± 0.3 m/s or 16% below pre-bed-rest control levels \( (P < 0.05). \) Subjects appeared awkward when sprinting after bed rest with no exercise training, but this observation was not quantified.

Calf concentric, isometric, and eccentric muscle strength remained at control levels after bed rest with daily exercise (average across exercise type: 140 ± 6 and 143 ± 8 N m before and after bed rest, respectively; no significant difference). Plantar flexor strength tended to decrease after control bed rest, but the trend was not statistically significant (average across exercise type: 141 ± 7 and 131 ± 7 N m before and after bed rest, respectively; \( P > 0.07 \)).
Effects of LBNP exercise during bed rest on hematocrit and blood volume. Supine hematocrit increased from 39.7 ± 1.2 to 42.3 ± 0.9 hematocrit units (2.6 units; \( P < 0.05 \)) after 15 days of control bed rest without LBNP exercise, yet no significant change was seen in hematocrit after bed rest with exercise (39.7 ± 0.9 and 39.9 ± 1.1 before and after bed rest, respectively). Fifteen days of bed rest tended to reduce plasma volume, and LBNP exercise during bed rest appeared to counteract this effect to some extent, although these trends were not statistically significant (3,867 ± 322 and 3,337 ± 140 ml before and after bed rest without exercise, respectively; 3,708 ± 257 and 3,498 ± 214 ml before and after bed rest with exercise, respectively; \( P > 0.09; n = 6 \)). Calculated blood volume data exhibited similar tendencies (5,865 ± 482 and 5,247 ± 189 ml before and after bed rest without exercise, respectively; 5,600 ± 324 and 5,353 ± 411 ml before and after bed rest with exercise, respectively, \( P > 0.15; n = 6 \)). Five subjects lost plasma volume during control bed rest (average reduction was 18%). One subject exhibited an anomalous and large (~20%) increase in plasma and blood volume after 15 days of bed rest without exercise, despite an increase in hematocrit from 36 to 39 over the same period. Syringe leakage of Evan’s blue during injection led to loss of matocrit from 36 to 39 over the same period. Syringe leakage of Evan’s blue during injection led to loss of matocrit from 36 to 39 over the same period.

Daily exercise during bed rest increased fluid intake. Bed rest without exercise significantly reduced fluid intake 14% relative to pre-bed-rest conditions (overall average reduction of 295 ml/day from pre-bed-rest intake of 2,178 ± 245 to 1,883 ± 209 ml/day during bed rest; \( P < 0.05 \)). Exercise during bed rest significantly increased fluid intake, on average 423 ml/day (22%), relative to nonexercise bed-rest conditions, especially toward the end of the 15-day bed-rest period (576 ml/day increase during the last 5 days of bed rest; \( P < 0.05 \)). Fluid intake increased during the first recovery day after both exercise (21%) and nonexercise (42%) bed-rest periods relative to levels during bed rest \( (P < 0.05 \) for comparison to during bed rest and for comparison between nonexercise and exercise conditions). Urine output decreased similarly during bed rest without and with LBNP exercise (~600 ml, or 32%) relative to pre-bed-rest control levels \( (P < 0.05 \).

Other observations. The subject group displayed consistent baseline characteristics, in that no dependent variable changed significantly when the two pre-bed-rest baseline assessments were made. Body weight decreased during bed rest. Similar weight loss occurred during 15 days of bed rest without (1.4 kg, 1.9%) and with (1.6 kg, 2.2%) daily LBNP exercise \( (P < 0.05 \). Six of the eight subjects reported that daily LBNP exercise improved the quality of their sleep during bed rest. The other two subjects indicated that daily exercise neither improved nor worsened their sleep quality. All subjects reported that daily LBNP exercise made their recovery from bed rest “easier” than recovery from bed rest without concomitant exercise.

The single subject who completed only the LBNP exercise bed-rest period was the least aerobically conditioned subject before bed rest. He displayed responses to bed rest with daily exercise that were similar to those of the other seven subjects. For example, his peak upright \( V_O_2 \) equaled 48.2 ml·min\(^{-1}\)·kg\(^{-1}\) before and 49.2 ml·min\(^{-1}\)·kg\(^{-1}\) after bed rest. His sprint speed equaled 5.7 m/s before bed rest and 5.8 m/s after bed rest. His plantar flexion strength parameters either remained stable or increased.

DISCUSSION

Results from this 15-day bed-rest study clearly indicate that 40 min per day of supine LBNP treadmill exercise at 1.0–1.2 body wt and 41–65% of peak \( V_O_2 \) preserves submaximal and peak upright exercise function at pre-bed-rest levels. This study is the first to demonstrate maintenance of upright exercise capacity following 15 days of bed rest with a single daily exercise session of <1 h.

Acute responses to LBNP exercise training. The data indicate supine LBNP treadmill training provided a rigorous workout. We hoped subjects would reach 80% of peak \( V_O_2 \) at the highest workload, but they averaged 65% instead. Heart rate at a given treadmill speed and LBNP level at the end of an exercise session exceeded by 33% heart rate at the same speed and LBNP near the start of the session (after the 7-min warm-up). Multiple factors probably explain this observation. First, incomplete recovery from prior exercise at higher workloads almost certainly contributed. Furthermore, continued exposure to LBNP causes progressive blood and extravascular fluid accumulation in the lower body
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(1, 29, 33, 38). Also, heat accumulation inside the LBNP chamber during an exercise session imposed a progressively increasing, albeit small, thermal stress. These factors may have operated synergistically (e.g., thermal stress exacerbates cutaneous pooling). These factors acutely decrease central blood volume and thus cardiac stroke volume, thereby increasing the heart rate necessary to support metabolic demands for cardiac output.

Our subject suspension system sometimes caused discomfort, especially early in the bed-rest period. No such system would be necessary when exercising in LBNP in microgravity. In our experience to date, with this, previous, and ongoing studies, over 41 different subjects collectively have undergone over 153 hours of supine LBNP treadmill exercise without any serious acute mishap or long-term complication.

**LBNP exercise preserved upright exercise function.** The present exercise capacity results confirm and extend findings from a previous 5-day bed-rest study. In that work (26), control subjects who did not exercise during bed rest were compared with subjects who performed 30 min/day of supine treadmill exercise in LBNP at intensities of up to 90% peak heart rate, which was followed by 5 min of resting LBNP during recovery from exercise. The control subjects exhibited greater elevation of heart rate, RER, and ventilation rate during post-bed-rest submaximal upright treadmill exercise than those at the same workloads during pre-bed-rest exercise. Submaximal exercise responses remained at pre-bed-rest levels in subjects who performed daily LBNP exercise. Also, post-bed-rest time to exhaustion during upright treadmill exercise decreased in control but not in LBNP exercise subjects (26).

Other investigators previously reported successful exercise countermeasures that are pertinent to the present work. Convertino (8) demonstrated an extremely time-efficient means of reversing the bed-rest-induced reduction of upright exercise capacity. Subjects performed a single bout of supine maximal cycling exercise at the very end of 10 days of bed rest, and they experienced no post-bed-rest reduction of their upright treadmill exercise capacity, as measured 3 h later. The literature clearly indicates that 10 days of control (non-exercise) bed rest decreases upright exercise capacity (9, 15). Therefore, the maximal exercise results are interesting and attractive, yet it may be unrealistic to expect all crew members on a given flight to perform maximal exercise within 3 h of return from space, especially if return was emergent. Also, it is probably unreasonable to expect occasional bouts of maximal exercise to counter the type (e.g., bone degradation) and degree of deconditioning seen after spaceflights lasting months (16, 28).

Greenleaf and colleagues (17) found that two 30-min sessions per day of supine cycle ergometry maintained supine cycling exercise capacity during 30 days of head-down bed rest. However, as Lee et al. (26) stated, maintenance of upright exercise capacity is a more important concern than supine exercise capacity for patients reambulating after bed rest and for astronauts returning to Earth’s gravity after spaceflight. Upright exercise combines the stresses of exercise and gravity and therefore presents a greater cardiovascular stress than supine exercise both before and especially after bed rest (10, 15) and spaceflight (27). Upright exercise capacity provides a more physiologically and operationally relevant test of countermeasure efficacy because humans experience more aerobic exercise challenges when upright than when supine and because postflight emergencies would require astronauts to exert themselves while upright. Results of Bishop and colleagues (3) suggested a positive relationship between upright aerobic capacity and successful completion of a simulated emergency egress from the space shuttle.

It is also noteworthy that daily LBNP exercise maintained bed-rested subjects’ sprint speed at pre-bed-rest levels. Sprint speed assesses subjects’ functional leg strength and neuromuscular coordination and may also provide a crude indicator of one’s ability to perform emergency egress. Coping with such an emergency becomes still more stressful with the 26-kg launch-entry suit that astronauts wear during return from orbit (3). Because increasing LBNP generates linear increases in footward force (21), LBNP exercise offers the possibility of training for locomotion with the additional weight of the launch-entry suit. Such training would require ~65- to 75-mmHg LBNP, using our current waist-seal configuration.

We used relatively fit subjects (pre-bed-rest peak upright treadmill exercise Vo2 range was 48.2–70.0 ml·min⁻¹·kg⁻¹). Highly fit subjects experience greater loss of exercise capacity during bed rest than do less fit subjects (9). The daily supine LBNP exercise protected our subjects’ work capacity during bed rest, even though the highest training workload averaged only 65% of peak Vo2. LBNP exercise probably also protects less fit subjects from bed-rest-induced reductions of exercise capacity if they use similar relative workloads; however, this claim requires data beyond those presented here. The reduction in upright exercise capacity observed in control conditions in the present study matches previous bed-rest findings (15).

Leg plantar flexor strength results from our study were statistically inconclusive, in that we did not see significant reduction of strength after either control (nonexercise) bed rest or after bed rest accompanied by LBNP exercise. However, other studies indicate leg strength decreases significantly during 2 wk of control bed rest (2, 15), which agrees with the trend we saw for reduction of control bed-rest leg strength (P > 0.07).

*Effects of LBNP exercise during bed rest on hemocrit and blood volume.* In a previous 5-day bed-rest evaluation of LBNP exercise, Lee and co-workers (26) found that hematocrit increased 4.4 units in the control group during bed rest, indicating substantial hemoconcentration. Hematocrit did not increase significantly in the group performing daily LBNP exercise. These results suggested that LBNP exercise during bed rest prevented hemoconcentration and thereby helped
maintain fluid volume. In the present study, a trend existed for LBNP exercise to maintain plasma and blood volume chronically during bed rest relative to bed rest without exercise. In agreement with Lee and colleagues (26), hematocrit increased significantly in control bed-rest conditions yet remained unchanged when LBNP exercise accompanied bed rest. Therefore, the present and earlier findings collectively suggest that daily LBNP exercise maintains blood volume during bed rest. This effect provides an important mechanism for maintenance of upright exercise responses and capacity (9).

Implications of fluid metabolism results. Exercise increases fluid loss through sweat and expired air. During bed rest with exercise, the increased fluid intake we observed relative to nonexercise bed-rest conditions helped compensate for the substantial sweating and insensible respiratory fluid losses the subjects experienced during their daily exercise training. On a long-duration spaceflight, this increased intake and evaporative loss of fluid would require adequate environmental control and fluid-recycling systems.

Subjects drank significantly more after bed rest without exercise than after bed rest with exercise. This observation possibly reflects greater hypovolemia experienced by subjects during bed rest when they did not exercise. The reduced fluid intake and urine production seen under control (no exercise) bed-rest conditions in the present study agree with spaceflight results (25, 35). However, reduced urine production during the first days of bed rest does not agree with other bed-rest findings (15). We offer no explanation for this discrepancy.

Why use treadmill exercise? We used treadmill exercise for this long-term microgravity countermeasure concept, as opposed to alternatives such as cycle ergometry, for multiple reasons. First, treadmill exercise simulates the neuromuscular stimulation of upright walking and running across the ground, such as during an emergency egress. Second, the heelstrike of running provides impact loading of the skeleton, which is important for maintenance of bone strength (28). Third, running imposes concentric and eccentric activation of the large load-bearing muscle groups (24). Eccentric muscle activation generates greater forces than concentric activation but uses less oxygen and may therefore more efficiently protect muscle strength (12, 13, 18). Fourth, eventual integration of virtual environments with treadmill exercise may provide visual flow past the exerciser to simulate that experienced during walking and running across the ground. Nevertheless, our study does not exclude the possibility that other (nontreadmill) forms of exercise would produce similar results to those we report.

Why use LBNP to generate loading for supine treadmill exercise? We developed LBNP for this purpose because of the limitations of possible alternatives. We sought a loading mechanism capable of generating 1.0 or more body weight of footward force while supine, for reasons detailed in the introduction. Elastic (bungee) cords connecting an upper body harness to a treadmill (11) and centrifugation (7) comprise two other known loading mechanisms. Human centrifugation during spaceflight may not be possible or cost effective for many years. Use of elastic cord-harness systems at 1 body wt is essentially equivalent to exercising by wearing a backpack equivalent to the exerciser’s body weight. Pilot studies by our group found maximum supine treadmill exercise tolerance times of ~15–20 min using elastic cord-harness systems set to 1 body wt of footward force. Not surprisingly, the primary limiting factors were shoulder discomfort from shoulder strap compression and hip and gluteus pain from compression of working muscles by the waist belt of the elastic cord harness. This is why astronauts currently exercise at or below ~70% body weight with such systems (36). Similar to our ground-based experience and that of others (11), comments from crew members indicate that exercise at higher loads simply becomes too uncomfortable to sustain.

LBNP generates Earth-like vascular transmural pressures and fluid redistribution (1, 20, 38), which elastic cord systems do not produce. Therefore, integration of footward loading with LBNP cardiovascular effects may be an important element of this countermeasure’s success, just as integration of footward force with footward blood pressure and fluid distribution is an important element of our upright function in and adaptation to Earth gravity.

Would 40 min/day of LBNP without exercise protect exercise capacity during bed rest? We did not include an “LBNP alone” condition in the present study. Resting conditions do not impose the neuromuscular, biomechanical, metabolic, and cardiovascular demands of exercise; therefore, it is probably unreasonable to expect resting LBNP to protect exercise capacity during bed rest. Because supine, resting LBNP at moderate levels approximates systemic cardiovascular effects of quiet standing (33, 38), the idea of using resting LBNP during bed rest to protect exercise function is similar to postulating that standing quietly for a while every day during bed rest would maintain exercise capacity. Riviere and co-workers (30) evaluated effects of resting LBNP during 30 days of bed rest on submaximal exercise responses in five subjects. They employed three 20-min, 35-mmHg LBNP sessions per day for the first 3 wk of bed rest, and they increased the number of LBNP sessions to six per day (2 h total per day) by the end of the 30-day bed-rest period. Despite this substantial time commitment to resting LBNP exposure during bed rest, subjects experienced similar post-bed-rest hemoconcentration and relative heart rate elevation during submaximal exercise compared with those that underwent bed rest with no daily resting LBNP. Riviere and colleagues (30) did not assess exercise responses after a bed-rest period of only 2 wk; therefore, it remains technically possible that daily resting LBNP could preserve exercise responses and capacity during a bed-rest period similar to ours.

Another issue is LBNP tolerance: 40 min of 58-mmHg LBNP (the average level we employed during LBNP exercise) probably exceeds the resting LBNP...
tolerance of most subjects (1, 33, 38), even with the abdominal counterpressure we used (see METHODS, LBNP exercise training). Therefore, an appropriate “LBNP alone” condition for the present study may not be feasible. Subjects tolerate 50- to 60-mmHg LBNP with accompanying exercise partly because of the positive effects of exercise on LBNP tolerance (33). Exercise and LBNP performed separately could possibly have duplicated our results. However, we speculate that this strategy would require much longer than 40 min/day to achieve success.

In conclusion, these results show that daily supine LBNP treadmill exercise at 41–65% of maximal Vo2 during 15 days of bed rest preserves upright exercise responses and capacity. This finding possibly stems from the simultaneous and integrated musculoskeletal and cardiovascular stimulation provided by LBNP exercise, which is similar to the stimulation provided by upright exercise in Earth’s gravity. These positive bed-rest study results suggest that LBNP exercise may also prevent microgravity-induced reduction of upright exercise function and capacity.

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