

# Long-Duration Head-Down Bed Rest: Project Overview, Vital Signs, and Fluid Balance

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**Introduction:** Spaceflight has profound effects on the human body. Many of these effects can be induced with head-down bed rest, which has been a useful ground-based analog. With limited resources aboard the International Space Station for human research, the bed rest analog will be a primary platform on which countermeasures will be developed and tested for lunar and Mars mission scenarios. **Methods:** NASA Johnson Space Center, in conjunction with the University of Texas Medical Branch (UTMB), has created the NASA Flight Analogs Project (FAP), a research program with the overall objective of using head-down bed rest to evaluate, compare, and refine candidate countermeasures to spaceflight deconditioning. This paper serves as an overview and describes the standard conditions, the standard set of subject screening criteria, and the standard set of measurements for all FAP bed rest subjects. **Results:** Heart rate and diastolic pressures decreased transiently at the onset of bed rest. Fluid balance showed an early diuresis, which stabilized within 3 d. In this supplement, detailed results from multiple disciplines are presented in a series of reports. **Discussion:** The following reports describe multi-disciplinary results from the standard measurements by which the responses to bed rest will be assessed and by which countermeasures will be evaluated. The data presented in this overview are meant to serve as a context in which to view the data presented in the discipline specific manuscripts. The dietary support and behavioral health papers provide additional information regarding those aspects of implementing bed rest studies successfully.

**Keywords:** fluid balance, blood pressure, heart rate.

SPACEFLIGHT HAS PROFOUND multi-system effects on the human body which include bone demineralization, muscle atrophy, cardiovascular deconditioning, and altered sensorimotor coordination. The severity of these effects generally increases as spaceflight duration increases. NASA's Vision for Space Exploration requires planning for human exploration missions to the Moon, Mars, and beyond. Extending the time-distance aspect of space exploration will challenge human health, safety, and performance more than any spaceflight endeavor to date.

Preparations for exploration-class missions must include development of or improvement of countermeasures to mitigate expected deleterious physiological deconditioning. Since current in-flight resources for countermeasure development and validation are limited, NASA must rely on ground-based analogs to the greatest extent possible. To this purpose, the NASA Johnson Space Center has created the NASA Flight Analogs Project (FAP), with the overall objective of using head-down bed rest to evaluate, compare, and refine candi-

date countermeasures to the greatest extent possible in bed rest studies. Spaceflight resources will be requested only for final validation, or for systems for which it is not feasible to test countermeasures in bed rest studies.

The NASA FAP, in collaboration with the University of Texas Medical Branch at Galveston (UTMB), established the NASA Flight Analogs Research Unit (FARU), a satellite of the NIH-sponsored General Clinical Research Center (GCRC) at UTMB. The FAP provides NASA with a long-term capability to conduct bed rest studies by providing the infrastructure to support integrated investigations while maximizing subject utilization and reducing expense.

Although head-down bed rest has been used as a spaceflight analog to study changes in physiologic function associated with spaceflight for many years at many different institutions (2,5), standards for conducting such studies have not previously been established. Conditions of bed rest have been investigation or site specific. Some studies strictly control diet, others feed subjects ad libitum. Some studies require strict bed rest, others allow subjects to use bedside commodes. Some physiologic disciplines have been studied extensively while others have received little attention. Most studies have had no direct comparisons of bed rest data with spaceflight data. As a consequence, systematic, multi-disciplinary comparisons across studies and comparisons of bed rest and actual spaceflight data have not been possible. To address these issues, the FAP has developed standard conditions for implementation of all NASA-funded bed rest studies and a set of standard measurements to be collected from all bed rest subjects.

The standard measures (Table I) replicate, for the most part, measurements obtained on astronauts before and after long-duration missions. Spaceflight and bed rest measurements are taken by researchers at the Johnson Space Center laboratories and are used for three purposes.

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TABLE I. STANDARD MEASURES FOR PARTICIPANTS IN THE NASA FLIGHT ANALOGS PROJECT.

Discipline	Test Performed	Measurement
Psychology	Cognitive Assessment	Sustained concentration, verbal working memory, attention, short-term memory testing, spatial processing, and math skills
Bone	Dual Energy X-ray Absorptiometry	Bone density of whole body, lumbar spine, proximal femora (hips), calcaneus (heel), and forearm
Exercise Physiology	Iso-inertial Strength and Endurance Isokinetic Testing	Skeletal muscle strength, endurance, and flexibility Muscle strength and endurance of the knee, ankle, and back muscles
Nutritional Biochemistry	Cycle Ergometry Nutritional Status Assessment	Aerobic capacity ( $\dot{V}O_2$ ), heart rate, ECG, blood pressure, work load General blood and urine chemistry, electrolytes, selected markers of hematological, vitamin, and mineral status, markers of oxidative damage, and markers of bone metabolism
Neuroscience	Computerized Dynamic Posture Functional Mobility	Sensorimotor balance control Locomotor performance including otolith-spinal reflex function, integrated balance control performance, and functional mobility
	Functional Stretch Reflex	Motor and sensorimotor responses at the central, vestibular nuclei and cerebellar, and peripheral levels.
Cardiovascular	Arterial Function Cardiac Function Plasma Volume	Endothelium-dependent and -independent vasodilation Echocardiography Assessment of blood volume
Immunology	Cardiovascular Tilt Test Stress Measures	Evaluation of orthostatic intolerance Neuroendocrine hormones and cytokines in response to biochemical and psychological stress
	Immune Status	Leukocyte subset distribution, T cell function, and T cell cytokine production profiles.
	Latent Virus Reactivation	Number and function of virus-specific T cells. Viral reactivation determined by the level of viral DNA in saliva and urine including plasma viral antibody levels.

First, they make possible a direct comparison between responses to spaceflight and responses to head-down bed rest. Second, they provide a characterization of human responses to long-duration head-down bed rest. Third, they provide the ability to assess candidate countermeasures in a multi-disciplinary manner, by evaluating the effects on the targeted systems as well as possible unexpected effects on non-targeted systems. Reported here are the results from 13 control subjects who have completed long-duration bed rest in a series of four subgroups. The purpose of this initial study is to establish control data against which countermeasures will be evaluated. The papers resulting from the standard measures data are included within this supplement. They are, in order: "Dietary Support of Long-Duration Head-Down Bed Rest" (3); "Nutritional Status Assessment Before, During, and After Long-Duration Head-Down Bed Rest" (12); "Skeletal Effects of Long-Duration Head-Down Bed Rest" (11); "Cardiovascular Adaptations to Long-Duration Head-Down Bed Rest" (6); "Immune Status, Latent Viral Reactivation, and Stress During Long-Duration Head-Down Bed Rest" (1); "Postural Reflexes, Balance Control, and Functional Mobility With Long-Duration Head-Down Bed Rest" (7); "Behavioral and Psychological Issues in Long-Duration Head-Down Bed Rest" (8); and "Cognitive Functioning in Long-Duration Head-Down Bed Rest" (9). Most unfortunately, due in part to the inability to obtain data during the hurricane evacuation (Hurricane Rita, September 2005) and in part to problems with subject compliance and hardware changes, the exercise data are not included in this set of papers.

## METHODS

All study protocols were reviewed and approved by the NASA Johnson Space Center Committee for the

Protection of Human Subjects (CPHS), the UTMB Institutional Review Board (IRB), and the UTMB General Clinical Research Center Advisory Committee. Subjects received verbal and written explanations of all bed rest and test protocols prior to providing written informed consent.

Candidate subjects were recruited and screened by personnel at the Johnson Space Center Human Test Subject Facility (HTSF). Recruitment advertising, approved by the CPHS and IRB, included radio, television, and newspaper announcements in Houston, Dallas, and San Antonio, TX. Recruiting personnel also visited a local air show, a Star Trek convention, and an American College of Sports Medicine annual meeting. A website at [www.bedreststudy.com](http://www.bedreststudy.com) was established for informational and preliminary screening purposes. In addition, a toll-free number was provided for interested individuals to contact the HTSF.

## Subjects

We report on 13 subjects who participated in this study. Subjects 1, 2, and 3 experienced 60 d of head-down bed rest. It was subsequently decided to extend the standard bed rest duration to 90 d to accommodate bone countermeasure investigations. Subjects 4, 5, 6, and 7 experienced 90 d of head-down bed rest. Unfortunately, the next group of subjects was evacuated when Hurricane Rita approached the Texas Gulf Coast and Galveston Island in September of 2005. As a result, subjects 8, 9, 10, and 11 experienced only 52, 49, 44, and 42 d of head-down bed rest, respectively, so not all data were obtained. Details regarding what data were obtained and how it was analyzed are provided in the individual manuscripts.

Potential subjects were pre-screened via telephone interviews by HTSF nurses. Those who satisfied the basic

inclusion criteria traveled to the Johnson Space Center for a NASA-modified Air Force Class III physical examination. Candidates were excluded from the study if they had any of the following: a) hypertension; b) electrocardiogram abnormalities; c) required medication that might interfere with the interpretation of the results; d) recent sub-standard nutritional status; e) metal implants which could interfere with MRI imaging; f) a history of thyroid dysfunction, renal stones, mental illness, gastroesophageal reflux, cardiovascular disease, musculoskeletal or sensorimotor dysfunction, or had smoked within 6 m prior to the start of the study; g) a personal or family history of thrombosis; h) a body mass index (BMI) outside of 20-30; i) abnormal blood or urine values; or j) inability to clear a criminal background check.

Blood chemistry testing included fasting glucose, blood urea nitrogen (BUN), uric acid, creatinine, total bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase, glutamyl transferase, sodium, potassium, chloride, phosphorous, calcium, magnesium, CO<sub>2</sub>, total protein, cholesterol, triglyceride, high density lipoprotein, low density lipoprotein, and high sensitivity C-reactive protein. The hematology profile included white cell count and differential, red cell count, hemoglobin, hematocrit, ferritin, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet count, and red cell distribution width. Urinalysis included pH, specific gravity, color, appearance, protein, glucose, ketones, blood, bilirubin, urobilinogen, nitrite, and leukocyte esterase.

Following physical screening, candidate subjects were tested and interviewed by a psychologist for assessment of their ability to complete the study. Psychological screening methods used commercial, off-the-shelf psychological tests and International Classification of Diseases (ICD) criteria for psychiatric disorders derived from current astronaut select-out and select-in procedures. Subjects were also assessed for roommate compatibility. Details can be found in the behavioral and psychological issues paper by Seaton et al. within this supplement (8). From approximately 1200 initial phone interviews, 8 men and 5 women were entered into this study. Demo-

graphic data for these subjects are presented in **Table II**. Although all subjects initially passed the exclusion criteria, by the time they were admitted to the study some subjects had weight changes that moved them slightly outside of the BMI criteria. We chose to keep them in the study, given the difficulty of replacing them in a timely manner.

Each candidate subject met with the Principal Investigator or her designee and received a detailed briefing regarding all aspects of the study protocol. As part of study orientation, subjects visited the facility and were given a briefing by the GCRC nursing staff. Subjects were also provided with a Test Subject Handbook, which contained details of the study requirements, instructions on preparing themselves for the study, and a list of personal items that should be brought with them upon admission to the FARU.

### Study Protocol

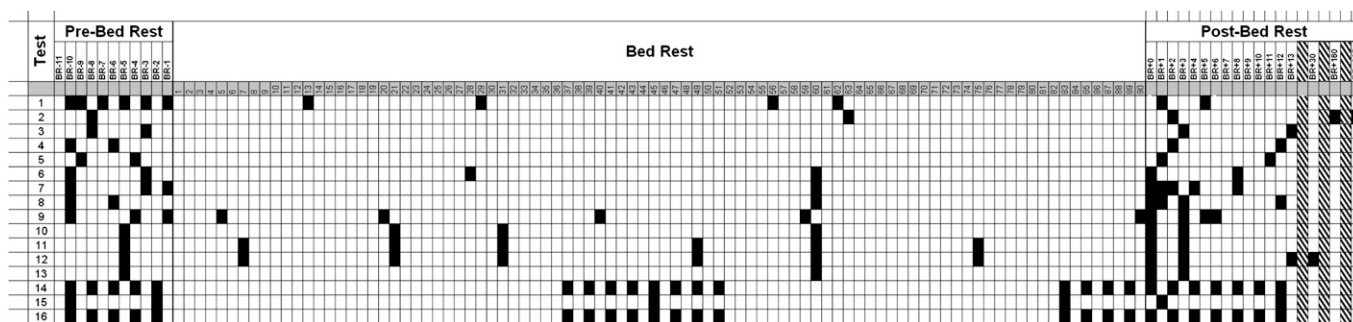
The study was divided into three phases: a pre-bed rest phase of 11–14 d for acclimation and baseline data collection, a bed rest phase, and a post-bed rest recovery phase of 14 d for post-bed rest testing and reconditioning. For scheduling consistency, each study day was referred to with a conventional naming system. Pre-bed rest days began at ~BR-14 and ended on BR-1. Days in bed rest began on BR1. Post-bed rest days began on BR+0 and subjects were released on BR+13. A general overview schedule of tests is provided in **Fig. 1**. Discipline-specific testing schedules can be found in the individual discipline papers within this supplement. Notice that many tests were performed around bed rest day 60 (BR60). This was done to compare responses to 60 and 90 d, to assess the possibility of shortening the studies to reduce costs. Three of these tests—postural stability, tilt testing, and functional mobility—were performed in the upright position. Subjects were kept head-down at all times between testing. There appeared to be no effect on the end of bed rest measures as a result of this. Data from these tests are presented in the individual manuscripts.

Male subjects were admitted to the unit as soon as possible after they provided informed consent, to begin the pre-bed rest phase of the study. Female subjects were

TABLE II. DEMOGRAPHIC DATA FOR PARTICIPANTS IN THE NASA FLIGHT ANALOGS PROJECT.

Subject Number	Age	Sex	Height (cm)	Weight (kg)	BMI*	Bed Rest Duration (days)
1	41	M	175	73.9	24.05	60
2	54	M	165	80	29.38	60
3	26	M	177	73.6	23.58	60
4	44	F	160	57.5	22.46	90
5	27	M	170	89	30.8	90
6	42	M	165	72.18	26.81	90
7	26	F	156	44	18.08	90
8	27	F	155	56.2	23.41	52
9	33	M	184	97.5	28.8	49
10	27	M	169	82.2	28.78	44
11	38	M	179	90.5	28.25	42
12	28	F	160	51	19.92	90
13	48	F	172	76.4	25.82	90

\* Body Mass Index (BMI) = Kg/(cm/100)<sup>2</sup>.



**Fig. 1.** Testing schedule for NASA Flight Analogs Project Standard Measures. Test 1: Cognitive Assessment; Test 2: Dual Energy X-ray Absorptiometry; Test 3: Iso-Inertial Strength and Endurance; Test 4: Isokinetic Testing; Test 5: Cycle Ergometry; Test 6: Nutritional Status Assessment; Test 7: Computerized Dynamic Posture; Test 8: Functional Mobility Test; Test 9: Functional Stretch Reflex; Test 10: Plasma Volume; Test 11: Arterial Function; Test 12: Cardiac Function; Test 13: Cardiovascular Tilt Test; Test 14: Stress Measures; Test 15: Immune Status; Test 16: Latent Virus Reactivation.

admitted so that the estimated time of their next menses would occur 2 d prior to their entering the bed rest phase of the study. Upon admission, subjects began to acclimate to their environment. They remained ambulatory, but were made familiar with the head-down shower procedures, practiced using a bedpan in the head-down position, became accustomed to the sleep/wake schedule, began consumption of the prescribed standard diet and fluid intake, were instructed on the required stretching exercises, and became familiar with the routine at the facility. On the standard sleep/wake schedule lights were turned on at 0600 and were turned off at 2200. Subjects were expected to wake at lights on and to cease activity at lights out. Sleep during the wake period was not permitted, except on occasions when it was necessary to interrupt the sleep period for early-morning test procedures. On those occasions, subjects were allowed to nap for a period of time equal to their sleep loss.

Details of the standardized diet and prescribed water intake can be found in the dietary support paper by Inniss et al. within this supplement (3). Nominally, subjects received a controlled diet of three meals per day on a 7-d or 10-d meal rotation cycle. Occasionally, the experimental protocol required that meals be divided into a smaller portion plus a snack. Caloric requirements were individualized for each subject to maintain bodyweight. Subjects were required to meet minimum daily water consumption ( $28.5 \text{ ml} \cdot \text{kg}^{-1}$ ), but were allowed to drink ad libitum beyond that which was prescribed. All fluid consumption, including the water content of food, was measured or calculated.

Same-sex subjects were housed two to a room except when there were an odd number of men or women admitted. Room temperatures were maintained at  $72 \pm 2^\circ \text{ F}$ . Each subject was provided with a personal television and an internet-accessible laptop computer with DVD capability, both mounted on reticulated arms for ease of use in the head-down position. Subjects were also provided a mechanical reach aid on an extension arm for reaching purposes. Also available were telephone calling cards, an on-site collection of movies, books, magazines, music, games, and PlayStation™ game system. Additional entertainment was provided when possible, including group activities for holidays, subject birthdays,

and study milestones. Special visits from astronauts and NASA VIPs were arranged and one group of subjects received a phone call from a crewmember aboard the International Space Station. Manicurists and hair stylists were available, at subjects' expense, to provide services on the unit.

Subjects were cared for 24/7 by the GCRC nursing staff. The nurses made daily measurements of heart rate (radial pulse), blood pressure, and bodyweight (bedside scale) [see Inniss et al. (3)] before breakfast at about the same time every day. The attending physician examined the subjects daily and also was on call 24/7. Subject health status was monitored with blood and urine testing performed during the study by Johnson Space Center Clinical Laboratory personnel.

Test subject monitors were present 24/7 to observe subjects for compliance with the standard conditions, assist subjects with non-nursing activities, perform small errands, visit with subjects, play games, etc. There was one subject monitor for every two subjects. Additionally, each subject was monitored via remote cameras.

A clinical psychologist and a psychiatrist visited subjects at least once a week throughout the study and were also available 24/7. Psychological support was provided for all known subject personal and/or family issues that arose. Details of the types of issues that arose can be found in Seaton et al. (8).

During the pre-bed rest phase of the study, baseline ambulatory measurements were taken. Following the pre-bed rest phase, subjects were confined to strict head-down bed rest. During bed rest, subjects were encouraged to move about in their beds and could lie in the prone, supine, or lateral position. Subjects were allowed to elevate themselves on one elbow to eat, but for no longer than 30 min per meal. A waterproof head-down gurney was used for showers. All subjects performed mandatory stretching exercises (hip, gluteal, abdominal, leg, arm, low back, wrist, shoulder, neck, and ankle isometric and stretch movements) for 15 min twice per day, and were provided 1 h of massage therapy every other day.

Bedpans were used for urination and defecation. Each urine void was measured for weight and specific gravity and volumes were calculated. Fluid intake minus urine output was calculated daily for each subject. To

prevent constipation, subjects were prescribed docusate sodium as a stool softener. Other medications were provided as necessary, with consideration of the impact on science objectives. If necessary, testing schedules were modified.

During the post-bed rest portion of the study, subjects remained in the unit for 14 d. During this phase of the study, recovery data were collected and the subjects underwent a reconditioning protocol that was designed and implemented by NASA's Astronaut Strength, Conditioning, and Rehabilitation group (ASCR). The protocol included treadmill walking, sitting to standing tasks, single leg balancing, abdomen and back exercises, shoulder stability exercises, modified push-ups and pull-ups, object pick-ups, and functional lifting tasks.

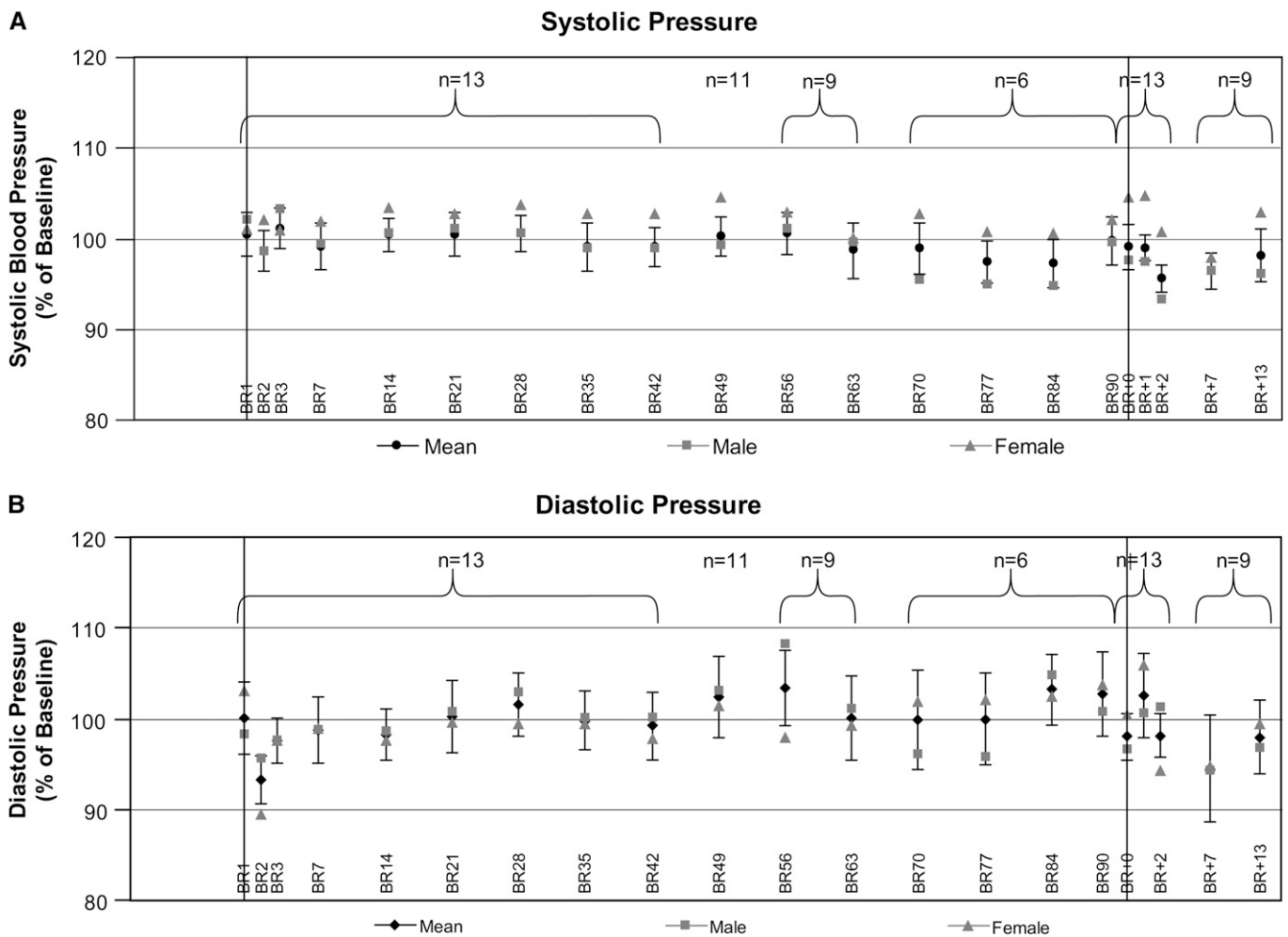
The four subjects who were evacuated for the hurricane received less than 24 h of reconditioning before they were released. Unfortunately, recovery data were not obtained on those subjects and in some cases, no data were used from these subjects. Details are provided in the individual manuscripts. As soon as study personnel returned from their own evacuations, the subjects

were brought back to Johnson Space Center for evaluation by a physician and the ASCR team. This occurred about 10 d after their release. With the exception of some minor muscle discomforts, the subjects appeared to be recovering very well. Functional fitness levels were near pre-bed rest levels and no formal reconditioning was recommended.

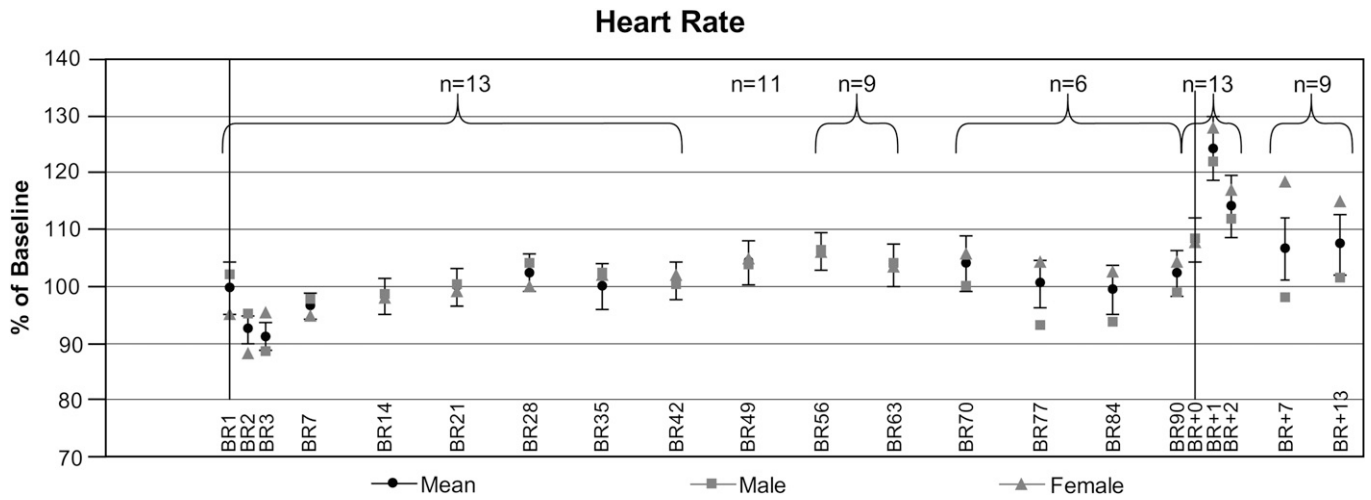
**RESULTS**

*Arterial Pressure and Heart Rate*

For systolic and diastolic pressure, heart rate, and fluid balance, percent changes from pre-bed rest were calculated. Means and SE were calculated for men and women. **Fig. 2** and **Fig. 3** present systolic and diastolic pressures and heart rates as a percent of pre-bed rest values. The average baseline systolic pressure was  $119 \pm 4$  mmHg for men and  $108 \pm 3$  mmHg for women (significant gender difference,  $P < 0.01$ ). The average baseline diastolic pressure was  $72 \pm 4$  mmHg for men and  $66 \pm 4$  mmHg for women (significant gender difference,  $P < 0.01$ ). Baseline heart rate was  $61 \pm 4$  bpm in the men and  $72 \pm 4$  bpm



**Fig. 2.** A) Systolic and B) diastolic pressures as a percent of baseline (average of daily measurements obtained during the pre-bed rest phase) are summarized (mean  $\pm$  SE;  $N$  for each data point is indicated). At the beginning and end of head-down bed rest, each of the first 3 d is shown. Otherwise, data points represent weekly averages. As described in the text, subjects experienced different durations of bed rest. For illustrative purposes, BR+0 represents the first day out of bed, regardless of the duration of head-down bed rest.



**Fig. 3.** Heart rate as a percent of baseline (average of daily measurements obtained during the pre-bed rest phase) are summarized (mean  $\pm$  SE; *N* for each data point is indicated). At the beginning and end of head-down bed rest, each of the first 3 d is shown. Otherwise, data points represent weekly averages. As described in the text, subjects experienced different durations of bed rest. For illustrative purposes, BR+0 represents the first day out of bed, regardless of the duration of head-down bed rest.

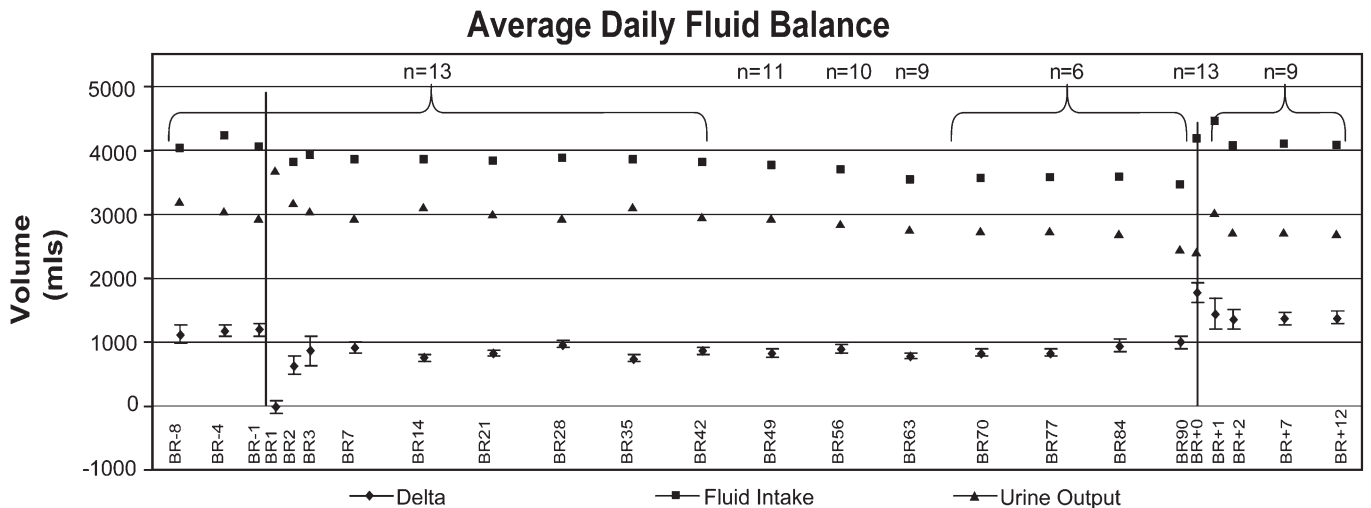
in women (significant gender difference,  $P < 0.01$ ). After an initial adjustment to the head-down position, during which diastolic pressure and heart rate decreased slightly, all three hemodynamic parameters stayed relatively constant until subjects resumed upright posture and ambulation.

*Fluid Balance*

Water intake (water content of food + liquid consumed) and urine output are presented in **Fig. 4**. Prior to bed rest, this delta was about 1100 ml  $\cdot$  d<sup>-1</sup>. On the first day of head-down bed rest (BR1) the delta was zero, but by day BR3, the delta stabilized between 750–1000 ml throughout head-down. On the first day of re-ambulation (BR+0) the delta was about 1700 ml, and then stabilized at about 1400 ml within 2 d.

*Symptoms and Medications*

Some subjects reported very few symptoms of discomfort during bed rest, while others reported symptoms almost daily. The most common complaint was headache, which most frequently occurred during the 3rd–5th d of head-down, but also sporadically throughout the bed rest protocol. Acetaminophen or ibuprofen was provided as an analgesic. About half of the subjects reported backache or back soreness, most frequently occurring from the 2nd–4th d of bed rest. Upon reambulation, about half of the subjects reported aches and pains during the first 48–72 h. Difficulty sleeping during at least one night during the study was reported by about half of the subjects, most commonly in the pre-bed rest phase and during the first week of bed rest. Subjects were given 5 mg zolpidem tartrate to help them fall



**Fig. 4.** Water balance (daily water intake minus the daily urine output) is summarized (mean  $\pm$  SE; *N* for each data point is indicated). In addition, fluid intake and urine output are plotted separately. At the beginning and end of head-down bed rest, each of the first 3 d is shown. Otherwise, data points represent weekly averages. As described in the text, subjects experienced different durations of bed rest. For illustrative purposes, BR+0 represents the first day out of bed, regardless of the duration of head-down bed rest.

asleep. About one quarter of the subjects reported at least one episode of dizziness while in the head-down position, but never severe enough to accept meclizine offered by the attending physician. Other medical issues included a toothache (treated with a topical oral anesthetic) and gastric reflux (treated with famotidine).

## DISCUSSION

The group of manuscripts presented here will describe the specific conditions and processes under which the NASA Flight Analogs Project at the Johnson Space Center conducts head-down bed rest studies. In addition, they will describe the multi-disciplinary responses to head-down bed rest and compare those responses to those during and after spaceflight. These control data will be used as the baseline from which spaceflight countermeasures will be evaluated in a standardized, multi-disciplinary manner. The results presented in this overview are meant to serve as a context in which to view the data presented in the discipline-specific manuscripts. The dietary support and behavioral health papers provide additional specific information regarding those aspects of implementing bed rest studies successfully.

### *Blood Pressure and Heart Rate*

Consistent with previous bed rest literature (4,10), resting heart rate and blood pressure recorded daily showed predictable transient responses at the onset and cessation of bed rest, but no trends of note during bed rest.

### *Fluid Balance*

Prior to bed rest, subject fluid intake was 1100 ml greater than their urine output. About 800 ml of this loss is known to be transdermal, respiratory, and fecal, all of which remain relatively stable in controlled environmental conditions. The additional loss is from sweat, which can change significantly during physical activity. Prior to bed rest, subjects were ambulatory and underwent testing protocols which were sometimes strenuous, causing sweating. During the first day of head-down, the urine output increased to equal intake. This reflects the diuresis associated with the increases in venous return and central volume, which stimulate cardiopulmonary baroreceptors. This diuresis was confirmed by plasma volume testing (6). By the third day of bed rest, fluid intake exceeded urine output by only 750–1000 ml, and remained relatively stable throughout head-down. While confined to bed, these control subjects performed no strenuous activity and were in a tightly controlled environment, so it is assumed that the difference in water balance from pre-bed rest was likely due to a decrease in fluid loss via sweating. When the subjects returned to ambulation, urine output decreased transiently, as fluid was retained to restore plasma volume and then returned to pre-bed rest levels, as confirmed through plasma volume testing (6).

The intent of this collection of papers is to compare bed rest responses to spaceflight responses. The limited data presented in this overview serve only to show that

these subjects were in a steady state fluid and hemodynamic condition across the bed rest period. Daily fluid balance or hemodynamic parameters are not taken during spaceflight, so a direct comparison cannot be made. However, data presented by Platts et al. in the cardiovascular adaptations paper in this supplement (6) do provide comparisons between bed rest and spaceflight plasma volume changes.

### *Conclusion*

Bed rest is a critical analog to spaceflight, permitting multi-disciplinary investigations within controlled experimental conditions. The value of the bed rest model is that it reduces the effective orthonormal gravitation influence on the human body. The major strength of the current data set is that the protocols used in the FAP have been used for the medical testing of U.S. crewmembers since the first ISS expedition, allowing direct validation between responses to spaceflight and responses to head-down bed rest.

With control data from the 13 subjects presented in the papers within this issue, the FAP possesses the ability to assess candidate countermeasures by evaluating their effectiveness on the targeted systems as well as to elucidate any effects on non-targeted systems. Although we chose to report these data at this time, we will continue to collect standard measures for three purposes. First, these same data will be collected on every subject on whom we are testing a countermeasure. Second, we will continue to take these measures on additional control subjects to avoid the issue of having only historical controls. Third, we plan to increase the sample size sufficiently to evaluate the effects of gender on bed rest responses. NASA's planned exploration of the Moon and Mars will require spaceflights with combinations of exposure to gravitational fields of zero, 1/6, and 3/8 gravity during missions of up to 3 yr. The baseline data reported here is the beginning of the use of long-duration bed rest in the development of countermeasures for future exploration missions.

### ACKNOWLEDGEMENTS

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