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# Physiological Responses to Prolonged Bed Rest in Humans: A Compendium of Research (1981–1988)

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Phuong B. Luu, Vanessa Ortiz, Paul R. Barnes,  
and John E. Greenleaf

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# ABSTRACT

"Physiological Responses to Prolonged Bed Rest in Humans: A Compendium of Research (1981-1988)"

P.B. Luu, V. Ortiz, P.R. Barnes and J. E. Greenleaf

The purpose of this compendium is to summarize results from clinical observations and results from more basic studies that help to elucidate the physiological mechanisms of the adaptation of humans to prolonged bed rest.

If the authors' abstract or summary was appropriate, it was included. In some cases a more detailed annotation was provided under the subheadings: purpose, methods, results and conclusion.

This volume includes material published from 1981 through December, 1988, and is a continuation of two previously published bed rest volumes: Greenleaf, J.D., C.J. Greenleaf, D. Van Derveer, and K.J. Dorchak. Adaptation to Prolonged Bed Rest in Man: A Compendium of Research. NASA Technical Memorandum X-3307, 1976. 180 p., and Greenleaf, J.D., L. Silverstein, J. Bliss, V. Langenheim, H. Rossow, and C. Chao. Physiological Responses to Prolonged Bed Rest and Fluid Immersion in Man: A Compendium of Research (1974-1980). NAST Technical Memorandum 81324, 1982, 110 p.

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## SUMMARY

This compendium summarizes published results of clinical observations and of more basic studies that help to elucidate the physiological mechanisms of adaptation of humans to prolonged bed rest. If the authors' abstract or summary was appropriate, it was included. In some cases a more detailed synopsis is provided, under the subheadings Purpose, Methods, Results, and Conclusions. This volume includes material published from 1981 through 1988.



## INTRODUCTION

The purpose of this compendium is to summarize clinical observations and results from more basic studies that help to elucidate the physiological mechanisms of the adaptation of humans to prolonged bed rest. If the authors' abstract or summary was appropriate, it was included. In some cases a more detailed synopsis was provided under the subheadings Purpose, Methods, Results, and Conclusions.

This volume includes material published from 1981 through 1988 and is a continuation of two previously published volumes on bed rest (refs. 1 and 2): Greenleaf, J. E., C. J. Greenleaf, D. Van Derveer, and K. J. Dorchak, *Adaptation to Prolonged Bedrest in Man: A Compendium of Research*, NASA Technical Memorandum X-3307, 1976, 180 p., and Greenleaf, J. E., L. Silverstein, J. Bliss, V. Langenheim, H. Rossow, and C. Chao, *Physiological Responses to Prolonged Bed Rest and Fluid Immersion in Man: A Compendium of Research (1974-1980)*, NASA Technical Memorandum 81324, 1982, 110 p.

The abstracts and synopses are in alphabetical order by first author and are numbered serially. Subject and author indexes are provided. Note that numbers shown with the index entries are abstract numbers, not page numbers.

We thank our many colleagues who sent reprints of their work, and we apologize to those whose studies we have inadvertently overlooked.



## SYNOPSIS AND ABSTRACTS

1. **Abildgaard, U., J. Aldershvile, H. Ring-Larsen, J. Falk, N. J. Christensen, J. Giese, M. Hammer, and J. H. Henriksen:**  
Bed rest and increased diuretic treatment in chronic congestive heart failure.  
*European Heart Journal* 6:1040-1046, 1985.

### Authors' abstract

To elucidate the effect of bed rest used as an adjunct to increased diuretic treatment, twelve patients with chronic congestive heart failure (CHF) had a 50% increase in loop diuretic dosage and were allocated to either continuous bed rest or bed rest during nights only. The 24-hour bed rest group reduced their weight significantly (mean±SEM:2.00±0.79 kg,  $P<0.001$ ), whereas the night bed rest group had no significant weight reduction (1.10±0.37 kg,  $0.1<P<0.2$ ) during three days of observation. Furthermore, the 24-hour bed rest group had a significantly increased diuresis ( $P<0.05$ ) during the first day of the study and a tendency towards increased natriuresis. The cumulated diureses for the two groups (24-hour bed rest versus night bed rest) during the three days of study were 7773±700 ml and 5861±909 ml ( $0.05<P<0.1$ ), respectively. Plasma concentrations of adrenaline, noradrenaline, renin and aldosterone were increased, as measured in the supine position. No significant differences were found between the two groups. Plasma concentrations of antidiuretic hormone were within normal limits. In conclusion, continuous bed rest is a reasonable adjunct to diuretic treatment in patients with CHF.

2. **Alexander, G. J. M., C. Hortas, and P. A. Bacon:**  
Bed rest, activity and the inflammation of rheumatoid arthritis.  
*British Journal of Rheumatology* 22:134-140, 1983.

### Synopsis

**Purpose.** To assess the relative contributions of bed rest and planned activity on the observed improvement in arthritis during hospitalization.

**Methods.** Two groups of patients who were diagnosed as having definite or classical rheumatoid arthritis were studied.

Group 1: one week of bed rest after a preliminary clinical assessment of five parameters.

Group 2: nonsteroidal anti-inflammatory drugs were given and subjects were randomly allocated to receive (a) bed rest for one week followed by planned activity for one week, or (b) planned activity for 1 week, followed by bed rest for one week.

The full clinical assessment was repeated after one week for both groups. An evaluation index for each group was calculated from alterations in grip strength, morning stiffness, articular index, line pain analogue, and the compound thermographic index.

### Results.

1. Using the overall evaluation index for Group 1, only 11 patients showed substantial improvement, 11 patients showed a small improvement, and 14 had deteriorated.

2. For Group 2, the effect of bed rest was more pronounced. More patients showed improvement than showed deterioration, in every parameter. A similar but less pronounced effect was seen with activity, and there was no difference between pre-rest and post-rest activity.

3. For both groups, the best response was seen in those patients with the most abnormal assessment results prior to bed rest. Patients who deteriorated on bed rest and who showed the most improvement with activity were those with pre-treatment results closest to normal.

**Conclusions.** Bed rest as an anti-inflammatory measure is only marginally superior to activity in a large group of patients. Careful selection of individuals with the more abnormal indices of synovitis, both on clinical assessment and sample laboratory tests, could double the percentage of patients responding to rest. The converse was also true; those with normal indices of synovitis show a good response to activity and a poor response to rest. A more critical approach to the prescription of bed rest will increase the number of patients who respond to treatment.

3. **Annat, G., A. Güell, G. Gauquelin, M. Vincent, J. L. Bascands, G. Geelen, A. Sassolas, and C. Gharib:**

Plasma renin activity during 5-hour antiorthostatic hypodynamia.

*The Physiologist* 27:S49-S50, 1984.

**Synopsis**

**Purpose.** To investigate the short-term variations of renin secretion in the early stages of bed rest (BR) and to compare in this respect horizontal and head-down BR.

**Methods.** Six normal male adult volunteers (age 22-27 yr) participated in the following three postural tests:

First test (day 1): 7 hr sitting.

Second test (day 2): 1 hr sitting, then 5 hr horizontal supine, finally 1 hr sitting.

Third test (day 3): 1 hr sitting, then 5 hr head-down bed rest ( $-10^{\circ}$ ), finally 1 hr sitting.

The order of the postural tests was randomized for each subject. Serial blood samples were obtained from each subject to measure the following parameters: plasma sodium, potassium, creatinine and osmolality, hematocrit, and plasma renin activity (PRA) using radioimmunoassay of angiotensin I generation.

**Results.**

1. During the course of the 3 postural tests, there were no significant variations in heart rate, blood pressure, hematocrit, or plasma sodium and potassium. The control PRA values, measured at 0900, were of the same magnitude:  $152 \pm 27.9$  ng/l/min (postural test 1),  $140 \pm 25.6$  ng/l/min (postural test 2), and  $177 \pm 22.7$  ng/l/min (postural test 3).

2. Test 1: PRA remained unchanged throughout 7 hr spent in the seated position.

3. Test 2: PRA decreased significantly from the second hour (47% of the control value). After resuming the seated position (1 hr), PRA returned to its control value.

4. Test 3: 5-hr head-down tilt resulted in a progressive decline of PRA, significant from the first hour, and tended to be more important (35% of the control value.) After the last hour in the seated position, PRA rose, but did not return to its control value.

**Conclusions.** The kinetics of the renin response to head-down BR is similar to that observed during a head-out water immersion of the same duration.

4. **Annat, G., A. Güell, G. Gauquelin, M. Vincent, M. H. Mayet, C. A. Bizollon, J. J. Legros, J. M. Pottier, and C. Gharib:**  
Plasma vasopressin, neurophysin, renin and aldosterone during a 4-day head-down bed rest with and without exercise.  
*European Journal of Applied Physiology* 55:59-63, 1986.

(Same as Annat, G., E. Jarsaillon, G. Gauquelin, M. Vincent, A. Güell, A. Sassolas, J. M. Pottier, and C. Gharib. Plasma vasopressin, renin activity and aldosterone during a 4-day head-down bed rest with and without exercise. In: *Proceedings of the 35th Congress of the International Astronautical Federation*, Lausanne, Switzerland, October 7-13, 1984. p.1-5.)

### Synopsis

**Purpose.** To define the kinetics of hormonal adaptations in subjects submitted to  $-6^\circ$  head-down tilt (HDT) and to examine the effect of performing a muscular exercise twice daily.

**Methods.** Eight male subjects (age  $24.1 \pm 0.4$  yr) participated in this study:

1. 24-hr control period in horizontal position (day 0).  $-6^\circ$  HDT period (day 1 to 4): four randomly chosen subjects were submitted to two 1-hr periods of supine exercise performed at  $50\% \dot{V}O_{2\max}$  (10-11 h; 15-16 h) except on day 1 (only one exercise: 15-16 h). Subjects returned to horizontal position at 9 h (day 5).
2. Serial blood samples were taken for hormonal assays: day 1—at 9 h (before tilting) and then 30 min, 1 h, 3 h, 6 h, and 10 h (after tilting); day 2 to day 4—9 h and 19 h; and day 5—before and 1 h after returning to the horizontal position.
3. Conventional laboratory methods were used to measure plasma and urine sodium (Na), potassium (K), osmolality, and creatinine. Specific radioimmunoassay (RIA) as used to measure plasma renin activity (PRA), aldosterone (PA), antidiuretic hormone (ADH), and immunoreactive neurophysin-I (NpI) linked to vasopressin.

### Results.

1. Short term effects of HDT (day 1): PRA, PA, ADH, and NpI levels were not significantly altered at any time.
2. Long-term effects of HDT (from day 1 to day 5):
  - a) Body weight decreased in both groups: mean weight losses were  $2.0 \pm 0.3$  kg in non-exercising subjects and  $2.3 \pm 0.5$  kg in exercising subjects.
  - b) Plasma electrolytes, osmolality, and creatinine clearance remained unchanged.
  - c) Throughout the HDT period, urinary output remained stable but lower than in the control period (day 0), but the urinary Na/K ratio decreased. There were no significant differences between exercising and nonexercising subjects.
  - d) At the hormonal level, PRA and PA increases were more pronounced in the group with exercise.

- e) On day 5, just before subjects resumed the horizontal position, PRA and PA were about three times higher than on day 1.
- f) Plasma ADH and NpI were not significantly affected by prolonged HDT.

**Conclusions.** A 4-day HDT results in (1) no apparent changes in neurophysin secretory activity, and (2) a progressive secondary hypoaldosteronism.

5. **Artamonova, N. P., T. S. Zakharova, B. V. Morukov, G. S. Arzamazov, and V. Y. Semenov:** Bioelectrical activity of the heart and blood electrolytes in essentially healthy subjects submitted to antiorthostatic hypokinesia for 120 days.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 20:24-27, 1986.

**Authors' abstract**

Electrocardiographic parameters and serum concentrations of potassium, sodium, calcium (total and ionized) and magnesium in 6 essentially healthy men, aged 30-45 years, were measured before, during and after 120-day head-down tilt at  $-4.5^\circ$ . A close correlation was demonstrated between T-wave depression and serum concentrations of potassium (direct correlation) and calcium and magnesium (inverse correlation). No consistent changes in the sodium content during the 120-day test were seen. In spite of electrolyte changes in blood induced by head-down tilt, ECG variations showed minor hypokaliemia that was not followed by any clinical symptoms. These data can be used to evaluate the status of healthy people exposed to prolonged hypokinesia and to develop adequate prophylactic measures.

6. **Aust, G., H. Denz, and F. Baisch:** Inner ear characteristics during 7 day antiorthostatic bedrest ( $6^\circ$  head-down tilt).  
In: *Proceedings of the 2nd European Symposium on Life Sciences Research in Space*, Porz Wahn, Germany, 4-6 June, 1984. p.251-255. (ESA Special Publication 212, 1984).

**Authors' abstract**

The responses to bithermal monaural caloric stimulation with water of  $30^\circ\text{C}$  and  $44^\circ\text{C}$ , as well as the pure tone hearing threshold were measured in male volunteers before, during and after 0-g simulation by  $6^\circ$  head-down tilt (HDT). Nystagmus frequency and slow phase velocity were lower than at control level after 20 hours in HDT position. From there on they increased and reached an average value above control at the end of the HDT period; 30 hours later they were still elevated, but were normal again 4 days after termination of HDT. Hearing thresholds improved 20 hours after beginning of HDT. However, they were above control on day 3 during and at the end of the HDT period. Similar values were measured 30 hours later.



**7. Aust, G., A. Putzka, and F. Baisch:**

Effects of head-down tilt (HDT) fluid volume shift on cerebral sensory responses.

In: *Proceedings of the 35th Congress of the International Astronautical Federation*, Lausanne, Switzerland, October 7-13, 1984. p.1-5.

**Authors' abstract**

Fluid volume shift from caudal to thoracic and cranial occur in changes from 1-g environment to microgravity. Vestibular and cochlear functions were studied in healthy volunteers pre, during, and post microgravity simulation by 6° HDT using bithermal monaural caloric testing, vestibular-spinal testing and pure tone threshold audiometry. Nystagmus frequency and slow phase velocity decreased during the first 3 days of HDT, followed by an increase. After termination of HDT the mean values remained on the same level as shown on the last day of HDT, but on day HDT+5 the means reached the initial level again. In comparison to the responses during the control period, after termination of HDT, the pattern of the head and body movements demonstrated ataxia, widening of the lateral sways and a tendency of moving to the left. At the beginning of HDT the hearing thresholds improved slightly. On day HDT 3 there was a decrease of the thresholds and on day HDT 7 a normalization up to the initial levels. There are three possible causes for the changes in the inner ear functions: 1) fluid volume shift with a venous stasis in the cerebrum, 2) pressure changes in the inner ear fluids, and 3) variation in the autonomic nervous tone.

**8. Baisch, F., and L. Beck:**

Left heart ventricular function during a 7 day 0-g simulation (6° head down tilt).

In: *Proceedings of the 2nd European Symposium on Life Sciences Research in Space*, Porz Wahn, Germany, 4-6 June 1984. pp.125-132. (ESA Special Publication 212, 1984).

**Authors' abstract**

Ultrasound measurements of cardiac dimensions were performed on 12 volunteers during a 7-day -6° head-down tilt (HDT) 0-g simulation. From the uniform increase in left ventricle (LV) dimensions in the remobilization phase, it follows that a shift in the contractile state of the LV takes place during the HDT period. To non-invasively quantify this contractile change we propose to utilize systolic time interval (STI) response curves (ventricular function curves) obtained by reducing preload by a lower body negative pressure (LBNP) maneuver. The high correlation coefficient between pre-ejection period (PEP)/dp/dt max and between left ventricular ejection time/stroke volume (LVET/SV) obtained in animal experiments under different contractile states validate this proposal.

**9. Baisch, F., L. Beck, E. W. Muller, and A. Samel:**

Cardiocirculatory adjustment during a 7 day microgravity simulation (6° head-down tilt, HDT).

In: *Proceedings of the 35th Congress of the International Astronautical Federation*, Lausanne, Switzerland, October 7-13, 1984. p.1-5.

**Synopsis**

*Purpose.* To define, under control conditions, early adaptive response to microgravity.

**Methods.** Two groups of six healthy male volunteers (age  $22.9 \pm 2.5$  yr, body weight (BW) =  $75.4 \pm 5.6$  kg) participated in this study. Seven of the volunteers were highly endurance trained athletes. Orthostatic tolerance time was measured by a stepwise lower body negative pressure (LBNP) protocol before and after microgravity simulation. In both groups four-chamber-view and ultrasound M-mode recordings were performed by sector scanning and time motion equipment. Body core temperature and heart rate were recorded continuously on minitapes at 24-hr intervals over the whole period of the experiment. In addition, 24-hr urine samples were collected for the determination of adrenaline, noradrenaline, and 17-hydroxycorticosteroid levels.

**Results.**

1. Blood volume was reduced by 14%, red cell volume was reduced by 10%, and orthostatic tolerance was reduced by 37% at the end of the 7.5-day HDT period.
2. During 40 torr LBNP, reduction of compliance became more pronounced during the first two days of HDT. The average reduction was 18%, and in some cases it was as high as 50%.
3. The average heart rate during the first 24 hr of HDT was significantly decreased (14%). Later, it increased again, and approached control value toward the end of the simulation period.
4. When plasma volume reached the control value in the post-simulation period, the left ventricular diastolic diameter (LVDD) values were always higher than control.

**Conclusions.**

1. Ultrasound did not reveal an increase of left ventricular size during 0-g simulation. It indicates, rather, that heart rate may be reduced.
2. No significant changes in tissue stiffness of the lower extremities were observed. Thus a shift of the autonomic tone has to be taken into account besides the reduction of blood volume and the cardiovascular dysfunction to explain the decrease of orthostatic tolerance.

10. **Bascands, J. L., G. Gauquelin, G. Annat, J. P. Pequinot, C. Gharib, and A. Güell:**  
Effect of muscular exercise during 4 days simulated weightlessness on orthostatic tolerance.  
*The Physiologist* 27:S63-S64, 1984.

**Authors' abstract**

In this study, the effectiveness of muscular exercise to prevent orthostatic intolerance (OI), was investigated during a 4 days head-down tilt (HDT) at  $-6^\circ$  in two groups of four young males, one control and one submitted twice a day to one hour of bicycle exercise. To evaluate orthostatic tolerance two tilt tests were performed, one before the HDT and one after the HDT. Plasma renin activity (PRA), plasma arginine vasopressin and plasma catecholamines were measured. Heart rate (HR) and blood pressure (BP) were recorded every minute all through the test. In both groups, the two tilt tests have produced an increase in HR. After the HDT, the tilting at  $+85^\circ$  has induced an increase in PRA in both groups, but no difference was observed between the two groups. During the second tilt test, OI was only demonstrated by the exercise group. These results suggest that under our experimental conditions, physical exercise is ineffective to prevent OI.

11. **Bascands, J. L., J. P. Girolami, G. Gauquelin, G. Annat, J. M. Suc, C. Gharib, and A. Güell:**  
Effect of different resting position on urinary kallikrein activity in normal man.  
*The Physiologist* 27:S61-S62, 1984.

**Authors' abstract**

Renal kallikrein is an enzyme which could be involved in several putative functions: sodium and water balance, renal blood flow regulation... In this study we report the results of 3 normal subjects which have been submitted to three different protocols: day 1 seven hours in the sitting position, day 2 five hours in the supine position, day 3 head-down tilt (HDT) at  $-8^{\circ}$  for five hours. In day 2 and 3 one hour control in the sitting position was observed before and after the experiment. For the three subjects the results show the same pattern of evolution. In day 1 no significant change in diuresis and in kallikrein activity was observed, in day 2 and 3 change in position either supine or HDT provide effective stimuli to increase kallikrein excretion. Since kallikrein activity remained steady only in the sitting position, this position could appear suitable for determination of baseline value.

12. **Beck, L., and F. Baisch:**  
Non-invasive assessment of heart contractility changes during a 7 day  $6^{\circ}$  HDT 0-G simulation.  
*The Physiologist* 27:S57-S58, 1984.

**Authors' abstract**

Decreasing venous return to the heart by means of lower body negative pressure (LBNP) suction can be used to dynamically test heart function. Systolic time intervals (STI) are used to assess cardiac performance. Linking these two non-invasive methods we evaluated contractility changes on 6 male volunteers during a 7 day  $6^{\circ}$  HDT 0-G simulation. Left ventricular ejection time (LVET) and pre-ejection period (PEP) values were plotted as a function of preload. PEP curves obtained at the end of the HDT period were shifted upwards in comparison to the ones obtained under control conditions. LVET curves shifted in the opposite direction signaling the same trend of contractility change. From our results, and taking into account changes of heart size and heart rate, we conclude that a depression of the contractile state of the heart must be discussed as a part of the mechanisms involved in the cardiovascular adaptation to 0-G simulation.

13. **Beckett, W. S., N. B. Vroman, D. Nigro, S. Thompson-Gorman, J. E. Wilkerson, and S. M. Fortney:**  
Effect of prolonged bed rest on lung volume in normal individuals.  
*Journal of Applied Physiology* 61:919-925, 1986.

**Authors' abstract**

Pulmonary function was assessed in supine subjects before, during, and after three separate bed-rest studies of 11 and 12 days duration. Forced vital capacity (FVC) increased during bed rest in each subject. Total lung capacity (TLC) was measured by helium dilution in one bed-rest study and increased in each subject, while residual volume and functional residual capacity of the respiratory system did not change. No change in FVC was found in an ambulatory control group using identical measurement

techniques. Maintaining base-line plasma volume during one bed rest by the use of exogenous estrogen did not prevent an increase in FVC, and decreasing plasma volume with diuretics in ambulatory subjects to the same degree as seen in the bed rests did not cause an increase in FVC. We conclude that prolonged bed rest results in a small significant increase in TLC and that this change is not dependent on alterations in plasma volume.

**14. Benzoni, D., A. Güell, G. Gauquelin, M. Vincent, A. Sassolas, N. Gallo-Bona, A. Bes, and C. Gharib:**

Effects of a four day head-down tilt on the urinary excretion of prostaglandins.

In: *Space Physiology*, edited by J. Garcia, M. Guerin, and C. Laverlochere. Toulouse, France: Cepadues-Editions, 1983. p.431-437.

**Authors' abstract**

In order to study the effect of a body fluid redistribution on the renal biosynthesis of prostaglandins (PGs), the urinary excretion of PGE and PGF(alpha) was followed during a four day head-down tilt in 4 adult subjects. Head-down tilt which induced marked changes in the salt and water excretion failed to affect the urinary excretion of PGE and PGF(alpha). Similar results were also obtained in 4 additional subjects submitted to the same procedure but associated with a regular physical exercise (50%  $\dot{V}O_{2\max}$ ). These findings suggest that a prolonged head-down tilt does not markedly influence the renal biosynthesis of PGs.

**15. Blamick, C. A., D. J. Goldwater, and V. A. Convertino:**

Leg vascular responsiveness during acute orthostasis following simulated weightlessness.

*Aviation, Space, and Environmental Medicine* 59:40-43, 1988.

**Authors' abstract**

Ten men (35-49 years old) underwent lower body negative pressure (LBNP) exposures before and after 10 d of continuous 6° head-down bedrest in order to predict the effect of weightlessness on the responsiveness of leg vasculature to an orthostatic stress. Heart rate (HR), mean arterial blood pressure (MAP), and impedance rheographic indices of arterial pulse volume (APV) of the legs were measured during rest and at 1 min of -30 mm Hg LBNP. Bedrest-induced deconditioning was manifested by decreases ( $P<0.05$ ) in plasma volume (17%), peak oxygen uptake (16%), and LBNP tolerance (17%). Resting HR was unchanged after bedrest, but HR was higher ( $P<0.05$ ) at 1 min of -30 mm Hg LBNP after, compared with before, bedrest. Responses of MAP to -30 mm Hg LBNP were not altered by bedrest. Resting APV was decreased ( $P<0.05$ ) by simulated weightlessness. However, APV was reduced ( $P<0.05$ ) from rest to 1 min -30 mm Hg LBNP by the same relative magnitude before and after bedrest ( $-21.4\pm 3.4\%$  and  $-20.5\pm 2.7\%$ , respectively). We conclude that peripheral arterial vasoconstriction, as indicated by reductions in APV during LBNP, was not affected by bedrest. These results suggest that there was no apparent alteration in responsiveness of the leg vasculature following simulated weightlessness. Therefore, it appears unlikely that control mechanisms of peripheral resistance contribute significantly to reduced tolerance following spaceflight.

16. **Blomqvist, C. G., F. A. Gaffney, and J. V. Nixon:**  
Cardiovascular responses to head-down tilt in young and middle-aged men.  
*The Physiologist* 26:S81-S82, 1983.

**Synopsis**

*Purpose.* To compare the effects of a 24-hr period of head-down tilt (HDT) at  $-5^\circ$  in middle-aged and young men and show that age-related differences exist since many aspects of cardiovascular function show significant age trends.

*Methods.* Five men aged 41 to 48 yr underwent a 24-hr HDT ( $-5^\circ$ ) period. The results were compared to data from previous studies in 10 young men (22-30 yr). Time course and magnitude of the central fluid shift were evaluated by measurements of leg volume. The basic characteristics of the subjects were age, height, weight, maximum oxygen uptake ( $\dot{V}O_{2\max}$ ), total blood volume, and mean arterial pressure (MAP). Plasma renin activity (PRA), central venous pressure (CVP), left ventricular end-diastolic (LVED) diameter, stroke volume (SV), and urinary production rates were measured.

*Results.*

1. The decrease in total blood volume after 24 hr of tilt was non-significantly larger among older men (0.51 compared to 0.35 liters).
2. PRA was reduced in both groups, from a control level of  $1.2 \pm 0.2$  to  $0.5 \pm 0.2$  at 6 hr in the young and from  $0.65 \pm 0.2$  to  $0.17 \pm 0.02$  in the middle-aged men.
3. Urine production rates were increased during the initial 8 hr of tilt compared with the subsequent 16 hr in both groups.
4. CVP increased in both groups, but the increase was larger and more sustained in the older men.
5. An increase in LVED diameter also occurred in both groups, but the older group had a larger diameter in the control state.
6. SV increased initially in both the young and middle-aged groups but returned to baseline levels within 6 hr.
7. Younger men had compensatory bradycardia with a decrease from  $75 \pm 4$  to  $64 \pm 2$  beats/min during the initial 1.5 hr, whereas the middle-aged men had no significant heart rate changes.
8. Exercise response tended to alter less in the middle-aged men, and the reverse was true for the lower body negative pressure (LBNP) response.

*Conclusions.* The overall pattern of adaptation to a 24-hr period of head-down tilt was similar in young and middle-aged men. However, further studies are required to evaluate a trend suggesting a greater effect on exercise performance in young men and on LBNP response in middle-aged men.

**17. Blomqvist, C. G., J. V. Nixon, R. L. Johnson, and J. H. Mitchell:**

Early cardiovascular adaptation to zero gravity simulated by heart-down tilt.

*Acta Astronautica* 7:543-553, 1980.

(Also in: *ESA Cardiovascular Adaptation to Zero Gravity*. ESA Special Publication 1033, 1981. p.6-7).

**Authors' abstract**

The early cardiovascular adaptation to zero gravity, simulated by head-down tilt at  $-5^{\circ}$ , was studied in a series of 10 normal young men. The validity of the model was confirmed by comparing the results with data from Apollo and Skylab flights. Tilt produced a significant central fluid shift with a transient increase in central venous pressure, later followed by an increase in left ventricular size without changes in cardiac output, arterial pressure, or contractile state. The hemodynamic changes were transient with a nearly complete return to the control state within 6 hr. The adaptation included a diuresis and a decrease in blood volume, associated with anti-diuretic hormone (ADH), renin and aldosterone inhibition.

**18. Bonde-Petersen, F., A. Güell, K. Skagen, and O. Henriksen:**

The effect of clonidine on peripheral vasomotor reactions during simulated zero gravity.

*The Physiologist* 24:S89-S99, 1981.

**Synopsis**

*Purpose.* To study the influence of long-term bed rest (BR) upon the venous compliance (VC) and the vasoconstrictor response in the arterioles during local increases in hydrostatic pressure and during tilt.

*Methods.* Three normal subjects were treated with clonidine (Cl) and three served as controls during a 7-day BR study.

1) Skin blood flow was studied by local  $^{133}\text{Xe}$  clearance, and its relationship to control skin vascular resistance was calculated.

2) Resistance changes during  $45^{\circ}$  head-up tilt and the lowering of an arm and leg during horizontal BR were compared with horizontal controls to evaluate the local veno-arteriolar constrictor reflex, and the combination of this reflex with increased sympathetic nervous activity (SNA).

3) Forearm blood flow (FBF), leg blood flow (LBF), and VC were measured by venous occlusion plethysmography.

**Results.**

1) The arteriolar constrictor reflex activated during increased local hydrostatic pressure decreased in arms and legs during BR, but increased by a factor of 2.9 and 1.7, respectively, during BR+Cl. After BR, the reflex was back to normal in the control group but somewhat weakened in the group treated with Cl.

2) During BR and BR+Cl, FBF and LBF did not change. However, 48 hr after the medication was discontinued and 36 hr after termination of BR, resting FBF and LBF doubled in the group treated with Cl.

3) Forearm VC (decreased by Cl compared to controls) adapted slowly during BR to the control values, which were also slightly increasing. The opposite effect was seen in the legs, where VC (decreased due to Cl) did not adapt, whereas a steady decrease was observed in the controls.

**Conclusions.** These results add to the understanding of the peripheral effects of Cl, which acts as a peripheral alpha-stimulator.

- 19. Bonen, A., G. W. Ness, A. N. Belcastro, and R. L. Kirby:**  
Mild exercise impedes glycogen repletion in muscle.  
*Journal of Applied Physiology* **58**:1622-1629, 1985.

**Authors' abstract**

Bicycle ergometric exercise was used to deplete glycogen by either 80 or 35% in the vastus lateralis of both legs. Thereafter, subjects from each group rested or maintained single-leg exercise [20% of maximal O<sub>2</sub> consumption ( $\dot{V}O_{2\max}$ )] for 4 h. All subjects ingested glucose (1.5 gm/kg wt; 20% solution) at min 10-12 and min 130-132 of the 4-h period. With bed rest, significant glycogen increases occurred after exhaustive (+36%; P<0.05) and nonexhaustive exercise (+13%; P<0.05). With single-leg exercise, 1) a diminished glycogen repletion occurred in exercising (+11%; P<0.05) and nonexercising (+15%; P<0.05) muscle after exhaustive exercise, or 2) further glycogen loss occurred in exercising (-26%; P<0.05) and nonexercising muscle (-19%; P<0.05) after nonexhaustive exercise. Within both groups, glycogen concentrations did not differ between exercising and nonexercising muscles (P>0.05). Single-leg exercise, not preceded by exercise, provoked differences in glycogen loss in exercising (-47%) and nonexercising (-24%) muscle (P<0.05). These experiments demonstrate that mild exercise 1) impedes glycogen resynthesis or 2) provokes glycogen loss in both exercising and nonexercising muscle. These findings cannot be ascribed to circulating glucose and insulin concentrations in these studies.

- 20. Brand, S. N.:**  
Space-flight simulations of calcium metabolism using a mathematical model of calcium regulation.  
NASA Contractor Report 171883, 1985. p.1-31.

**Author's abstract**

This report presents the results of a series of simulation studies of calcium metabolic changes which have been recorded during human exposure to bed rest and space flight. Space-flight and bed-rest data demonstrate losses of total body calcium during exposure to hypogravic environments. These losses are evidenced by higher than normal rates of urine calcium excretion and by negative calcium balances. In addition, intestinal adsorption rates and bone mineral content are assumed to decrease. The bed-rest and space-flight simulations were executed in a mathematical model of the calcium metabolic system.

21. **Burkovskaya, T. Y., A. V. Ilyukhin, V. I. Lobachik, and V. V. Zhidkov:**  
Erythrocyte balance during 182-day hypokinesia.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 14:50-54, 1980.

*Purpose.* To investigate the effect of prolonged antiorthostatic hypokinesia (AOH) on circulation blood volume and some parameters of kinetics of erythroid elements.

**Authors' abstract**

A prolonged head-down tilt (HDT) resulted by the end of the second month in a significant decrease in the circulating blood volume at the expense of plasma and erythrocyte volumes. One of the factors that caused a reduction in the erythrocyte volume was their survival time shortening. The fact that during the remaining four hypokinetic months there was no further decline in the erythrocyte count was attributed to adaptive developments: increase of bone marrow production and rate of differentiation of erythroid elements. Exercises used as a countermeasure could slightly counteract the adverse effects of HDT.

22. **Bychkov, V. P., I. I. Borodulina, and T. F. Vlasova:**  
Amino acid metabolism during prolonged intake of dehydrated foods and simulation of some space flight factors.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 15:21-23, 1981.

**Authors' abstract**

Forty-two healthy volunteers, aged 19 to 49, participated in three bed rest studies of 69 to 180 days in duration. The test subjects were kept on the diet consisting of dehydrated foods: fresh, stored for up to 2 years, and exposed to proton irradiation at a dose of 24,000 rad. Metabolism of amino acids was investigated under these conditions. It was concluded that during prolonged storage and irradiation proteins of dehydrated foods retained their biological value. This allows their use in long-term space flights.

23. **Bystrov, V. V., A. F. Zhernavkov, and A. A. Savilov:**  
Human heart function in early hours and days of head-down tilt (echocardiographic data.)  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 20:42-46, 1986.

**Synopsis**

*Purpose.* To conduct comprehensive studies of the changes in intracardiac hemodynamics, pumping, and contractile function of the left ventricle during 7-day antiorthostatic hypokinesia ( $-10^\circ$ ).

*Methods.* Six healthy men (19-24 yr) were exposed to  $-10^\circ$  head-down tilt (HDT) for 7 days. Echocardiogram (ECG), heart rate (HR), end diastolic and end systolic size of the left ventricle, diameter of the left atrium and of the lumen of the aorta root, thickness of the left ventricle posterior wall (PWL) and interventricular septum (IVS) in systole and diastole, excursion of PWL, IVS and mitral valve movement, and ejection period for blood from the left ventricle (LV) were determined. Also, end-diastolic volume (EDV) and end-systolic volume (ESV) of the LV, stroke volume (SV) and minute



volume of circulation (CV), ejection fraction, fraction of shortening of the anteroposterior size of the LV and rate of circulatory shortening of myocardial fibers were calculated.

*Results.*

1. Throughout the HDT period, HR was significantly slower than in the baseline period, with the most marked decline found on day 2 and a tendency toward normalization on subsequent days.
2. Starting in the first 2 hr of HDT, there were significant increases in EDV and SV by an average of 6% and 10%, respectively, and these parameters declined to values slightly lower than baseline from the third hour to the end of the first day. In subsequent days, the mean EDV and SV gradually returned to almost baseline values.
3. The dynamics of mean CV were the same in direction as EDV and SV. However, in spite of the increase in EDV and SV, absolute CV did not differ appreciably or was 10-15% lower than the baseline.

*Conclusions.* The study findings confirm the concept of adaptation of the human circulatory system to real and simulated weightlessness as an undulant process that undergoes specific stages of development.

- 24. Cardus, D., W. G. McTaggart, and E. Domingo:**  
Cardiovascular changes with head-down ankle suspension.  
*The Physiologist* 27:S45-S46, 1984.

**Authors' abstract**

The purpose of the work reported here was to study the effects of head-down inversion on central and peripheral circulation. Ten healthy men, aged 21-30 years, participated in the study. The basic experimental design consisted of measurements taken in three phases: vertical head-up, horizontal supine and vertical head-down. Blood flow changes were assessed through measurements of electric impedance. Blood pressure changes were measured noninvasively. In relation to the standing position head-down suspension resulted in a non-significant lowering of the heart rate, a significant increase in mean blood pressure in the arms, an increase in stroke volume and cardiac output (which became the same as in the horizontal position) and a decrease in leg blood pressure. In assuming the head-down position there was a shift of fluids from the legs to the thorax suggested by impedance changes. The peripheral vascular resistance in the lower extremities markedly decreased, this resulting in an apparent increase in leg blood flow. The increase in blood pressure in the cephalad portion of the body is a potential risk for those practicing head-down suspension.

25. Chernukh, A. M., O. G. Gizenko, B. M. Fedorov, T. N. Krupina, P. N. Aleksandrov, D. I. Shagal, N. Y. Panferova, and T. M. Proskurina:  
Effect of hypokinesia on blood microcirculation.  
*Patologicheskaya Fiziologiya I Eksperimental' naya Terapiya* 9:10-13, 1979.

**Authors' abstract**

Blood microcirculation in the region of the scleral, bulbar conjunctiva and the nail folds on the fingers and toes was studied in 18 practically healthy men during 182 day antiorthostatic hypokinesia and 30 day rehabilitation period. Marked changes in microcirculation in the sclera and feet and less evident changes on the hands were revealed. A complex of special prophylactic physical exercises had a distinctly favorable effect on circulation in the hands.

26. Chestukhin, V. V., V. Y. Katkov, A. A. Seid-Guseynov, B. I. Shal'nev, V. S. Georgiyevskiy, O. K. Zybin, V. M. Mikhaylov, and V. N. Utkin:  
Activity of the right cardiac ventricle and metabolism in healthy persons during an orthostatic test after short-term immobilization.  
*Patologicheskaya Fiziologiya Eksperimental' noy Terapiya* 2:36-40, 1979.

**Authors' abstract**

A 15-minute orthostatic test was performed on healthy male volunteers under conditions of catheterization of the right ventricle of the heart and the radial (or brachial) artery before and after 5-day bedrest in an antiorthostatic position of the body (with the foot of the bed raised 4.5 degrees). The change to a vertical position after immobilization was attended by a more marked increase in the rate of cardiac contractions, an increase of max dp/dt pressure in the right ventricle, and a decrease of cardiac and stroke indices. The decrease of the cardiac index was compensated for, to a certain measure, by a further increase in the extraction and utilization of O<sub>2</sub> by the tissues. The arterial blood pH did not change essentially, while the decrease in pCO<sub>2</sub> and content of standard bicarbonate was more marked.

27. Convertino, V. A.:  
Exercise responses after inactivity.  
In: *Inactivity: Physiological Effects*, edited by H. Sandler and J. Vernikos-Danellis. N.Y.: Academic Press, Inc., 1986. p.149-191, (Chapter 7).

**Author's abstract**

The exercise response after bed rest inactivity is a reduction in the physical work capacity and is manifested by significant decreases in oxygen uptake. The magnitude of decrease in maximal oxygen uptake ( $\dot{V}O_{2\max}$ ) is related to the duration of confinement and the pre-bed-rest level of aerobic fitness; these relationships are relatively independent of age or gender. The reduced exercise performance and  $\dot{V}O_{2\max}$  following bed rest are associated with various physiological adaptations including reductions in blood volume, submaximal and maximal stroke volume, maximal cardiac output, skeletal muscle tone and strength, and aerobic enzyme capacities, as well as increases in venous compliance and submaximal and maximal heart rate. This reduction in physiological capacity can be partially restored by specific

countermeasures that provide regular muscular activity or orthostatic stress or both during the bed rest exposure. The understanding of these physiological and physical responses to exercise following bed rest inactivity has important implications for the solution to safety and health problems that arise in clinical medicine, aerospace medicine, sedentary living, and aging.

**28. Convertino, V. A.:**

Potential benefits of maximal exercise just prior to return from weightlessness.  
*Aviation, Space, and Environmental Medicine* 58:568-572, 1987.

**Author's abstract**

The purpose of this study was to determine whether performance of a single maximal bout of exercise during weightlessness within hours of return to earth would enhance recovery of aerobic fitness and physical work capacities under a 1G environment. Ten healthy men (36-51 yr) underwent maximal supine exercise followed by upright maximal exercise before and after a 10-d bedrest period in the 6° head-down position. A graded maximal supine cycle ergometer test was performed before and at the end of the bedrest to simulate exercise during weightlessness. Following 3 h of resumption of the upright posture from the supine exercise test, a second maximal exercise test was performed on a treadmill to measure work capacity under conditions of 1G. Compared to before bedrest, peak oxygen uptake ( $\dot{V}O_2$ ) decreased ( $p < 0.05$ ) by 8.7% and peak heart rate (HR) increased ( $p < 0.05$ ) by 5.6% in the supine cycle test at the end of bed rest. However, there were no significant changes in peak  $\dot{V}O_2$  and peak HR in the upright treadmill test following bed rest. These data, based on a simulation, suggest that one bout of maximal leg exercise prior to return from 10 d of weightlessness may be adequate to restore preflight aerobic fitness and physical work capacity.

**29. Convertino, V. A., B. A. Benjamin, L. C. Keil, and H. Sandler:**

Role of cardiac volume receptors in the control of ADH release during acute simulated weightlessness in man.  
*The Physiologist* 27:S51-S52, 1984.

**Authors' abstract**

Hemodynamic responses and antidiuretic hormone (ADH) were measured during body position changes designed to induce central blood volume shifts in ten cardiac and one heart-lung transplant recipients to assess the contribution of cardiac volume receptors in the control of ADH release during the initial acute phase of exposure to weightlessness. Each subject underwent 15 min of a sitting-control period (C) followed by 30 min of -6° head-down tilt (T) and 30 min of resumed sitting (S). Venous blood samples and cardiac dimensions were taken at 0 and 15 min of C; 5, 15, and 30 min of T; and, 5, 15, and 30 min of S. Blood samples were analyzed for hematocrit, plasma osmolality, plasma renin activity (PRA), and ADH. Heart rate (HR) and blood pressure (BP) were recorded every two min. Plasma osmolality was not altered by postural changes. Mean left ventricular end-diastolic volume increased ( $p < 0.05$ ) from 90 ml in C to 106 ml in T and returned to 87 ml in S. Plasma ADH was reduced by 20% ( $p < 0.05$ ) with T and returned to control levels with S. These responses were similar in six normal cardiac-innervated control

subjects. These data may suggest that cardiac volume receptors are not the primary mechanism for the control of ADH release during acute central volume shifts in man.

- 30. Convertino, V. A., R. Bisson, R. Bates, D. Goldwater, and H. Sandler:**  
Role of orthostatic factors in the mechanism of cardiorespiratory deconditioning following bed rest.  
*Aerospace Medical Association Preprints*, 1980. p.26-27.

### **Synopsis**

**Purpose.** To determine the orthostatic effects of gravity on exercise performance by a) comparing the cardiorespiratory responses during supine exercise of subjects exposed to horizontal bed rest (BR) to those of subjects exposed to antiorthostatic BR; and b) comparing the physiologic responses of supine against upright exercise following horizontal BR.

### **Methods.**

1. Ten adult volunteers, aged 35-40 yr, participated in this study:
  - (a) Five subjects in horizontal ( $0^\circ$ ) BR for 7 days.
  - (b) Five subjects in head-down ( $-6^\circ$ ) BR for 7 days.
2. Two days pre-BR and post-BR, each subject underwent body fat determination and performed a submaximal bicycle exercise ( $E_x$ ) test in the supine position (5 min rest, 5 min  $E_x$  at 700 kg/min [115 W] and 10 min recovery.)
3. After each subject's heart rate (HR) had returned to within 10 beats/min of the pre- $E_x$  value, the submaximal test was repeated in the upright position for the  $0^\circ$  subjects.
4. Oxygen uptake ( $\dot{V}O_2$ ), HR, steady-state  $E_x$  ventilation volume ( $\dot{V}_E$ ), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured at set times during the tests.

### **Results.**

1. Mean body weight decreased significantly ( $p < 0.05$ ) in both the  $0^\circ$  ( $-1.5$  kg;  $-2.2\%$ ) and  $-6^\circ$  ( $-2.1$  kg;  $-2.9\%$ ) subjects following BR.
2. BR resulted in a general decrease of exercise tolerance in both groups.
3. The  $-6^\circ$  head-down treatment appeared to cause greater cardiovascular deconditioning, evident during supine exercise, compared to  $0^\circ$  BR.
4. Exercise and recovery were more stressful in the upright position judging from  $\dot{V}_E$ ,  $\dot{V}O_2$ , HR and heart rate pressure product (RPP) changes compared to the supine test.

**Conclusions.** The data support the hypothesis that there is an orthostatic component to the deconditioning effects of BR separate from the effects caused by decreased physical activity.

31. **Convertino, V. A., R. Bisson, R. Bates, D. Goldwater, and H. Sandler:**  
Effects of antiorthostatic bedrest on the cardiorespiratory responses to exercise.  
*Aviation, Space, and Environmental Medicine* 52:251-255, 1981.

**Authors' abstract**

During this study, exercise performance was compared before and after bedrest (BR) in the horizontal and antiorthostatic ( $-6^\circ$ ) body positions. Subject groups (aged 35-40 years) were matched with respect to maximum oxygen uptake ( $\dot{V}O_{2\max}$ ), age, height, weight, percent body fat, and lean body mass. Five subjects were assigned to 7 d of horizontal ( $0^\circ$ ) BR, and five subjects underwent 7 d BR in a head-down ( $-6^\circ$ ) position. Two days prior to BR (pre-BR) each subject underwent body fat determination and performed a submaximal exercise test in the supine position consisting of 5 min rest, 5 min exercises at 700 kg[+].[+]m/min, and 10 min of recovery from exercise. Systolic (SBP) and diastolic (DBP) blood pressures, heart rate (HR), maximum oxygen uptake ( $\dot{V}O_{2\max}$ ), and ventilation volume ( $\dot{V}_E$ ) were measured during each 30 s of all exercise tests. Body composition and the submaximal test were repeated on the day following BR (post-BR). Mean body weight decreased in the  $0^\circ$  ( $-1.5$  kg,  $p<0.05$ ) and  $-6^\circ$  ( $-2.1$  kg,  $p<0.05$ ) groups following BR. These changes were due to significant decreases in lean body weight. Both groups showed significant ( $p<0.05$ ) increases in  $\dot{V}_E$  during exercise and recovery from exercise following BR. During the rest and exercise,  $\dot{V}O_2$  at post-BR was the same as pre-BR values for both groups. Recovery  $\dot{V}O_2$  following BR was greater than the pre-BR value in the  $-6^\circ$  group ( $+10.3\%$ ,  $p<0.05$ ) but the  $0^\circ$  group did not change. During exercise and recovery, mean HR of the  $0^\circ$  group increased  $+3.8\%$  and  $+5.9\%$ , respectively, ( $p<0.05$ ) following BR, while exercise and recovery HR increased to a greater degree ( $p<0.05$ ) in the  $-6^\circ$  group ( $+13.4\%$  and  $+17.6\%$ , respectively;  $p<0.05$ ) at post-BR. The mean heart-rate-pressure product (RPP) followed the same pattern as HR with greater ( $p<0.05$ ) increases during exercises and recovery following  $-6^\circ$  BR compared to  $0^\circ$  BR. These results suggest that: 1) BR resulted in a general decrease of exercise tolerance in both groups; 2) the  $-6^\circ$  head-down treatment caused greater cardiorespiratory changes during exercise and recovery compared to  $0^\circ$  BR; and 3)  $-6^\circ$  BR appeared to simulate the effects of weightlessness more effectively than horizontal BR when comparable space flight data were presented.

32. **Convertino, V. A., D. J. Goldwater, and H. Sandler:**  
Cardiorespiratory responses to exercise after bed rest in 55 to 65 year old men.  
*Aerospace Medical Association Preprints*, 1981. p.59-60.

**Synopsis**

**Purpose.** To measure cardiorespiratory responses of middle-aged men to submaximal and maximal workloads before and after 10 days of continuous bed rest (BR) and compare data to the results obtained from previously tested younger individuals.

**Methods.**

1. Eight healthy men (mean age  $60\pm 1$  yr) participated in 9 days of ambulation control followed by 10 days BR, and a 5-day ambulatory recovery period.
2. During BR, prior to exercise testing, the subjects were exposed to  $+1.5$ ,  $+2.0$ , and  $+3.0$   $G_z$  on days 7, 8, and 9, respectively, and lower body negative pressure on day 10.

3. Subjects performed a maximal exercise tolerance test 4 days before BR and at the end of the BR period (day 11) on a Collins cycle ergometer in the supine position.

4. Parameters measured include echocardiogram (ECG), oxygen uptake ( $\dot{V}O_2$ ), heart rate (HR), expired gas volume and composition, body weight, body composition, plasma volume, and hematocrit (blood volume and red cell volume).

#### *Results.*

1. Mean body weight and body fat did not change following BR.

2. Plasma volume changed from  $3214 \pm 166$  ml to  $3094 \pm 142$  ml ( $-3.7\%$ , NS) following BR. Change in PV produced proportionate changes in blood volume ( $r=+0.93$ ), and red cell volume did not change.

3. Ventilation volume at maximal exercise decreased but mean reduction was not significant. During submaximal work levels following BR, ventilation volume was unchanged while  $\dot{V}O_2$  was unchanged.

4.  $\dot{V}O_{2\max}$  decreased from 2.98 to 2.58 liters/min ( $-13.4\%$ ,  $p<0.05$ ) following BR, and the magnitude of  $\dot{V}O_{2\max}$  reduction was related to the initial  $\dot{V}O_{2\max}$  ( $r=-0.7$ ,  $p<0.05$ ).

5. Maximal HR increased significantly by 7 beats/min ( $p<0.05$ ) and maximal  $O_2$  pulse decreased  $17.3\%$  ( $p<0.05$ ) after BR.

6. Average maximal workload was  $-8.0\%$  (NS) and test duration decreased by  $10.5\%$  ( $p<0.05$ ).

7. Respiratory exchange ratio (R) did not change during submaximal and maximal exercise following BR.

#### *Conclusions.* The findings from this study suggest that

1. The magnitude of BR deconditioning observed in older subjects is similar to that measured in previously tested younger individuals.

2. Individuals with initially high work capacities and  $\dot{V}O_{2\max}$  will experience larger BR deconditioning.

#### **33. Convertino, V. A., D. J. Goldwater, and H. Sandler:**

Effect of orthostatic stress on exercise performance after bedrest.

*Aviation, Space, and Environmental Medicine* 53:652-657, 1982.

#### **Authors' abstract**

In this study, the cardiorespiratory responses to supine against upright exercise were compared to determine the orthostatic effects of gravity on exercise performance following bedrest (BR). Five healthy male subjects underwent 7 days of continuous BR. Two days prior to BR (pre-BR) each subject performed a submaximal exercise test in the supine position consisting of 5 min rest, 5 min exercise at 700 kgm/min and with 10 min of recovery from exercise. After the subject's heart rate (HR) returned to within 5 bpm of the pre-exercise value, the submaximal test was repeated in the upright position. Systolic (SBP) and diastolic (DBP) blood pressures, HR, oxygen uptake ( $\dot{V}O_2$ ), and ventilation volume ( $\dot{V}_E$ ) were measured during each 30 s of all exercise tests. Supine and upright submaximal exercise tests were repeated on the day following BR (post-BR). The subjects showed significant increases ( $p<0.05$ ) in post-BR  $\dot{V}_E$  during supine and upright exercise and recovery from exercise. During rest and exercise, post-BR  $\dot{V}O_2$  was not different from the pre-BR values for both tests. However, recovery  $\dot{V}O_2$

following post-BR upright exercise was greater than the pre-BR value (+8.1%,  $p < 0.05$ ) while supine recovery  $\dot{V}O_2$  did not change. Compared to pre-BR, upright resting HR was elevated ( $p < 0.05$ ) following BR. During supine exercise and recovery, mean HR increased by 3.8% and 5.9%, respectively ( $p < 0.05$ ) post-BR while exercise and recovery HR increased to a greater degree ( $p < 0.05$ ) in the upright position. Compared to pre-BR values, post-BR heart rate-pressure-product (RPP) increased more ( $p < 0.05$ ) during upright rest, exercise and recovery compared to corresponding supine values. During the post-BR upright test, pulse pressure (PP) and  $O_2$  pulse decreased in both tests compared to pre-BR values, with consistently larger changes observed in the upright position. The data suggest that there is an orthostatic effect on work performance following BR deconditioning in addition to the effects caused by decreased physical activity.

**34. Convertino, V. A., D. J. Goldwater, and H. Sandler:**

$\dot{V}O_2$  kinetics of constant-load exercise following bed-rest-induced deconditioning.  
*Journal of Applied Physiology* 57:1545-1550, 1984.

**Authors' abstract**

The purpose of this study was to determine the effects of bed-rest-induced deconditioning on changes in  $O_2$  uptake ( $\dot{V}O_2$ ) kinetics,  $O_2$  deficit, steady-state  $\dot{V}O_2$ , and recovery  $\dot{V}O_2$  during the performance of constant-load exercise. Five male subjects (36-40 yr) underwent 7 days of continuous bed rest (BR) in the head-down ( $-6^\circ$ ) position. Two days before (pre) and the day after (post) BR each subject performed one submaximal exercise test in the supine and one in the upright position consisting of 5 min of rest, 5 min of cycle ergometer exercise at 700 kg · m/min, and 10 min of recovery from exercise.  $\dot{V}O_2$  was measured continuously in all tests from 2-liter aliquot gas samples collected every 30 s. Following BR steady-state  $\dot{V}O_2$  was unchanged in supine and upright exercise. In the supine position BR did not change total exercise  $\dot{V}O_2$ ,  $O_2$  deficit, or total recovery  $\dot{V}O_2$ . However, compared with pre-BR, total exercise  $\dot{V}O_2$  decreased ( $P < 0.05$ ) from  $7.41 \pm 0.11$  to  $7.23 \pm 0.17$  liters,  $O_2$  deficit increased ( $P < 0.05$ ) from  $1.15 \pm 0.05$  to  $1.41 \pm 0.07$  liters, and total recovery  $\dot{V}O_2$  increased ( $P < 0.05$ ) from  $5.17 \pm 0.11$  to  $5.47 \pm 0.17$  liters during the post-BR upright test. Despite the ability to attain similar steady-state  $\dot{V}O_2$  within 5 min, bed-rest-induced deconditioning resulted in a reduction of total  $\dot{V}O_2$  capacity and an increase in the  $O_2$  deficit during submaximal constant-load exercise. This change in  $\dot{V}O_2$  kinetics is found only with exercise in the upright rather than supine position implicating orthostatic mechanisms in the delayed response to submaximal exercise.

**35. Convertino, V. A., D. J. Goldwater, and H. Sandler:**

Bedrest-induced peak  $\dot{V}O_2$  reduction associated with age, gender, and aerobic capacity.  
*Aviation, Space, and Environmental Medicine* 57:17-22, 1986.

**Authors' abstract**

To compare the factors of age and gender on aerobic work capacity following bedrest-induced deconditioning, peak oxygen uptake ( $\dot{V}O_2$ ), peak heart rate (HR), and exercise tolerance time were measured in 15 middle-aged men ( $55 \pm 2$  yr) and 17 middle-aged women ( $55 \pm 1$  yr) before and after 10 d of continuous bedrest (BR). The average body weight following BR was unchanged in both men and women.

Following BR, peak  $\dot{V}O_2$  decreased from  $35.6 \pm 2.0$  to  $32.6 \pm 1.1$  ml  $\cdot$  kg<sup>-1</sup>  $\cdot$  min<sup>-1</sup> (-8.4%, p<0.05) in the men and from  $26.5 \pm 1.4$  to  $24.7 \pm 1.3$  ml  $\cdot$  kg<sup>-1</sup>  $\cdot$  min<sup>-1</sup> (-6.8%, p<0.05) in the women, while total exercise tolerance time was reduced by 8.1% (p<0.05) and 7.3% (p<0.05) in the men and women, respectively. The peak HR was elevated by BR from  $158 \pm 4$  to  $165 \pm 4$  bpm (+4.4%, p<0.05) in the men and from  $157 \pm 4$  to  $159 \pm 4$  bpm (+1.3%, NS) in the women. The percent changes in peak  $\dot{V}O_2$ , peak HR, and exercise tolerance time measured in the men were not significantly different compared to those of the women. The reduction in peak  $\dot{V}O_2$  in the middle-aged men and women in the present study were comparable to the reductions of 9.3% and 7.8% observed in our earlier studies with 15 young men ( $21 \pm 1$  yr) and 8 young women ( $28 \pm 2$  yr), respectively. The correlations between initial peak  $\dot{V}O_2$  and percent change in peak  $\dot{V}O_2$  following BR were -0.78 (p<0.05) for young men, -0.84 (p<0.05) for middle-aged men, -0.38 (NS) for young women, and -0.25 (NS) for middle-aged women with regression line slopes of -1.72, -1.14, -0.88, and -0.26, respectively. These results suggest that: (a) bedrest-induced aerobic deconditioning is essentially independent of age since the relative reduction in peak  $\dot{V}O_2$  measured in older subjects following BR was similar to that observed in younger individuals; (b) the relative decrease in peak  $\dot{V}O_2$  following BR is similar in men and women; and (c) the relative change in peak  $\dot{V}O_2$  following BR appears to be dependent upon the initial peak  $\dot{V}O_2$  in men, but not necessarily in women.

**36. Convertino, V. A., J. Hung, D. Goldwater, and R. F. DeBusk:**

Cardiovascular responses to exercise in middle-aged men after 10 days of bedrest.

*Circulation* 65:134-140, 1982.

**Authors' abstract**

The cardiorespiratory response to 10 days of continuous recumbency was assessed in 12 healthy men, age  $50 \pm 4$  years, who underwent supine and upright graded maximal exercise testing before and after bedrest. The decrease in peak oxygen uptake after bedrest was greater during upright exercise (15.1%, p<0.05) than during supine exercise (6.1%, NS): from  $25.8 \pm 5.2$  to  $21.9 \pm 4.5$  ml/kg/min and from  $24.6 \pm 5.2$  to  $23.1 \pm 4.8$  ml/kg/min. The decrease in submaximal work was also greater in the upright than in the supine position (p<0.05). Ventilation volume was significantly elevated (p<0.05) after bedrest during maximal and submaximal effort in both the supine and upright positions. After bedrest, peak heart rate increased 5.7% and 5.9% during supine and upright testing, respectively (p<0.05). The increases in rate-pressure product after bedrest were significantly larger (p<0.05) during upright than during supine exercise. These results indicate that orthostatic stress is the most important factor limiting exercise tolerance after bedrest in normal middle-aged men. This mechanism also increases the myocardial oxygen demands during submaximal effort after bedrest. Intermittent exposure to gravitational stress during the bedrest stage of hospital convalescence may obviate much of the deterioration in cardiovascular performance that follows myocardial infarction.



37. **Convertino, V. A., G. M. Karst, C. R. Kirby, and D. J. Goldwater:**  
Effect of simulated weightlessness on exercised-induced anaerobic threshold.  
*Aviation, Space, and Environmental Medicine* 57:325-331, 1986.

**Authors' abstract**

Ventilation ( $\dot{V}_E$ ), CO<sub>2</sub> output ( $\dot{V}CO_2$ ), oxygen uptake ( $\dot{V}O_2$ ), respiratory exchange ratio (R), and the ventilatory equivalents for VO<sub>2</sub> and VCO<sub>2</sub> were measured during graded exercise before and after 10 d of continuous bed rest (BR) in the -6° headdown position to determine the effect of deconditioning on the anaerobic threshold (AT), i.e., the highest workrate of  $\dot{V}O_2$  which was achieved without evidence of lactic acidosis, as judged from the profile of ventilatory and gas exchange responses. Ten healthy male subjects performed a supine graded cycle ergometer test before (pre) and after (post) BR which consisted of 4 min of unloaded pedaling at 60 rpm followed by an increased workrate of 15 W · min<sup>-1</sup> until volitional fatigue (max).  $\dot{V}_E$ ,  $\dot{V}CO_2$ ,  $\dot{V}O_2$ , R,  $\dot{V}_E/\dot{V}O_2$  and  $\dot{V}_E/\dot{V}CO_2$  were measured every 30 s and used collectively to identify the AT. Plasma (PV) and blood (BV) volumes were measured pre- and post-BR by T-1824. Following BR,  $\dot{V}O_{2\max}$  decreased from 2.42±0.17 to 2.25±0.13 L · min<sup>-1</sup> (7.0%, p<0.05). BR significantly (p<0.05) reduced the AT from 1.26±0.09 to 0.95±0.05 L · min<sup>-1</sup>  $\dot{V}O_2$ ; from 52.2±2.0 to 42.6±1.6%  $\dot{V}O_{2\max}$ ; and from 93±9 to 65±6 W. A correlation coefficient (r) of -0.11 (NS) was found between the change in  $\dot{V}O_{2\max}$  and change in AT. A decrease in BV of 8.8% (p<0.05) was due to the 11.0% reduction in PV; red cell volume remained constant. The change in AT following BR was significantly (p<0.05) correlated with the changes in BV and PV (r=+0.73 and +0.80, respectively). These data suggest that: (a) the reduction in AT induced by BR deconditioning cannot be completely explained by the reduction in  $\dot{V}O_{2\max}$ ; (b) the change in AT following BR is manifested by a decrease in both absolute and relative workrate; and (c) the decrease in AT is associated with the reduction in intravascular fluid volume.

38. **Convertino, V. A., C. R. Kirby, G. M. Karst, and D. J. Goldwater:**  
Response to muscular exercise following repeated simulated weightlessness.  
*Aviation, Space, and Environmental Medicine* 56:540-546, 1985.

**Authors' abstract**

The effect of repeated weightlessness exposures on maximal aerobic capacity was determined when seven healthy men (36-48 yr) underwent two 10-d bedrest (BR) periods in the -6° head-down position, which were separated by a 14-d recovery period. No prescribed exercise was performed by the subjects during the course of the experiment. A graded supine cycle ergometer test consisting of 4 min of unloaded pedaling at 60 rpm followed by increased work rate of 15 W · min<sup>-1</sup> until volitional fatigue (max) was performed before (pre) and after (post) the first and second BR periods, i.e., BR1 and BR2, and again 14 d after BR2 (REC). During exercise, submaximal and maximal oxygen uptake  $\dot{V}O_2$ , ventilation (VE), heart rate (HR), systolic (SBP) and diastolic (DBP) blood pressures were measured and the gas exchange anaerobic threshold (AT) was determined. Plasma volume (V<sub>p</sub>, T-1824) and body composition were measured pre- and post-BR1 and BR2 and following REC. Compared to the respective pre-BR control values,  $\dot{V}O_{2\max}$  decreased (p<0.05) by 8.7% after BR1 and 5.2% after BR2 but returned to pre-BR values following 14 d REC. Submaximal and maximal HR increased (p<0.05) post-BR1 and BR2 but returned to pre-BR levels after REC. The AT and V<sub>p</sub> decreased (p<0.05) post-BR1 and BR2 but returned to pre-BR levels after REC. Body weight increased (p<0.05) gradually during the

experiment and did not return to control values. With regard to muscle work performance, these data suggest that 2 weeks of minimal activity are adequate for complete recovery from simulated weightlessness and that repeated exposure can be safely tolerated.

**39. Convertino, V. A., and H. Sandler:**

$\dot{V}O_2$  kinetics during submaximal exercise following simulated weightlessness.  
*The Physiologist* 25:S159-S160, 1982.

**Synopsis**

**Purpose.** To determine the effects of deconditioning following 7 days of continuous head-down ( $-6^\circ$ ) bed rest on changes in steady-state  $\dot{V}O_2$ ,  $O_2$  deficit, and recovery  $\dot{V}O_2$  during the performance of constant-load exercise.

**Methods.** Five healthy male subjects (mean age  $38 \pm 1$  yr, mean height  $174 \pm 4$  cm, mean weight  $69.7 \pm 3.0$  kg) participated in this study.

1. The experimental protocol consisted of a 14-day ambulatory control period followed by 7 days of continuous bed rest (BR) in the head-down ( $-6^\circ$ ) position and 10 days of recovery after BR.
2. On days 13 pre-BR and 2 post-BR, each subject performed submaximal exercise tests in both supine and upright positions on an electronic cycle ergometer. The exercise test consisted of a 5-min rest period followed by 5 min of exercise at 700 kg/min (115 W) with 10 min of recovery from exercise.
3. Oxygen uptakes (total  $\dot{V}O_2$ , steady-state  $\dot{V}O_2$  and recovery  $\dot{V}O_2$ ) were measured during all exercise tests to compute oxygen deficits and half times ( $t_{1/2}$ ).

**Results.**

1. Constant-load exercise intensity of 700 kg/min produced a steady-state  $\dot{V}O_2$  of 1.71 liters/min in pre-BR supine exercise and 1.70 liters/min in pre-BR upright exercise (approximately 65% of the subjects' supine  $\dot{V}O_{2\max}$ ).
2. Following BR, steady-state  $\dot{V}O_2$  was unchanged in supine and upright exercise.
3. In the supine position, BR did not change total exercise  $\dot{V}O_2$ ,  $O_2$  deficit, or recovery  $\dot{V}O_2$ .
4. In the upright exercise, total exercise  $\dot{V}O_2$  decreased,  $O_2$  deficit increased, and recovery  $\dot{V}O_2$  increased significantly.
5. The half-time for  $\dot{V}O_2$  during exercise in the supine position was not changed following BR, but there was a significant increase in the upright position resulting in the elevation of  $O_2$  deficit.

**Conclusions.** The restoration of some  $\dot{V}O_2$  kinetics is induced by re-exposure of the cardiovascular system to the  $+1G_z$  (upright) environment.

40. **Convertino, V. A., H. Sandler, P. Webb, and J. F. Annis:**  
Induced venous pooling and cardiorespiratory responses to exercise after bed rest.  
*Journal of Applied Physiology* 52:1343-1348, 1982.

**Authors' abstract**

The purpose of this study was to deliberately induce venous pooling in the lower extremities of bed-rested subjects to determine whether such distention may reverse the reduction in maximal O<sub>2</sub> uptake that has regularly been observed. Bed-rest deconditioning was assessed in eight healthy male subjects by measuring submaximal and maximal O<sub>2</sub> uptake ( $\dot{V}O_{2\max}$ ), ventilation, and heart rate (HR<sub>max</sub>) before and after 15 days of bed rest. During bed rest, four subjects in the experimental group received daily treatments of venous pooling for 210 min/day with a reverse gradient garment (RGG), whereas the four subjects in the control group received no treatment. Compared with prebed-rest values,  $\dot{V}O_{2\max}$  was reduced by 14.0 (P<0.05), HR<sub>max</sub> was increased by 4.2 (P<0.05), and endurance time for the exercise test was decreased by 9.2% (P<0.05) in the control group. In the RGG group,  $\dot{V}O_{2\max}$ , HR<sub>max</sub>, and endurance time were essentially unchanged after bed rest. The plasma volume (PV) of the control group decreased by 16.7 (P<0.05) after bed rest compared with a 10.3% (not significant) reduction in the RGG group. The percent  $\Delta$ PV was related to the percent  $\Delta\dot{V}O_{2\max}$  (r=0.75, P<0.05) and percent  $\Delta$ HR<sub>max</sub> (r=-0.65, P<0.05). The data support the hypothesis that the lack of venous pooling and associated fluid shifts contribute to the decrement in  $\dot{V}O_{2\max}$  associated with bed-rest deconditioning.

41. **Davydova, N. A., S. K. Shishkina, N. V. Korneyeva, Y. V. Suprunova, and A. S. Ushakov:**  
Biochemical aspects of some neurohumoral system functions during long-term antiorthostatic hypokinesia.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 20:91-95, 1986.

**Synopsis**

**Purpose.** To investigate human sympathoadrenal (SAS) and cholinergic (CS) activity during long-term antiorthostatic [head-down tilt] hypokinesia.

**Methods.** Six healthy men 25 to 40 yr of age were submitted to -4.5° head-down tilt (HDT) for 120 days.

1. Samples of venous blood were drawn and 24-h urine specimens were collected at the baseline period, HDT, and recovery period.

2. Blood cholinergic activity was examined according to parameters of activity of acetylcholinesterase (ACE) of erythrocytes, nonspecific cholinesterase (NCE) of blood plasma, and concentration of acetylcholine (AC) in whole blood.

3. Sympathoadrenal activity was assessed on the basis of blood epinephrine (E), norepinephrine (NE) levels, and urine E, NE, dopamine (DA), metanephrine (MN), and normetanephrine (NMN) levels.

**Results.** During the test stages of HDT:

1. AC and E levels in blood were elevated as compared to baseline values.

2. NE concentration was below the baseline level during the entire HDT period.

3. Erythrocyte ACE and plasma NCE activities increased only in two sampled days of HDT. At the same time, E, MN, vanillylmandelic acid (VMA), and homovanillic acid (HVA) excretions in urine increased significantly.

4. There was significant decline in activity of transmitter elements of SAS. NE, DA, and NMN excretions in urine decreased progressively with increased duration of hypokinesia.

During the recovery period:

1. Returning the subjects to normal physical activity elicited significant elevation of blood E, NE, AC, ACE, and NCE levels, as well as urine E, NE, DA, dopa, MN, NMN, HVA, and VMA.

2. There was an increase in relative activity of metabolic processes, indicative of considerable strain on the tested systems.

By the end of the rest period, SAS activity reverted to the baseline level, while blood CS activity remained high, probably due to decline of adaptability of the CNS caused by long-term HDT.

**Conclusions.** Long-term exposure of man to HDT is associated with marked functional changes in SAS and CS, which form the body's adaptive reactions. The successive changes in activity of both systems are instrumental in preserving homeostasis of the body.

42. **DeBusk, R. F., V. A. Convertino, J. Hung, and D. Goldwater:**  
Exercise conditioning in middle-aged men after 10 days of bed rest.  
*Circulation* 68:245-250, 1983.

**Authors' abstract**

Of 12 healthy men with a mean age  $50 \pm 4$  years who had been at bed rest for 10 days, six were randomly assigned to perform individually prescribed physical exercise daily for 60 days after bed rest (exercise group) and six simply resumed their customary activities (control group). Exercise group subjects were significantly more active than control subjects during this interval ( $p < 0.05$ ). Two classic training effects observed in the 60 days after bed rest were significantly larger among exercise than among control group subjects; compared with value immediately after bed rest, heart rate at a constant submaximal workload declined by  $36 \pm 11$  beats/min in the exercise group vs  $16 \pm 8$  beats/min in the control group and peak oxygen consumption increased by  $4.8 \pm 4.2$  vs  $2.2 \pm 5.0$  ml/kg/min (both  $p < 0.05$ ). Despite these differences in the cardiovascular response to exercise, peak oxygen consumption in both groups returned to before bed rest levels by 30 days after bed rest, and this was accompanied by significant ( $p < 0.05$ ) and similar increases in resting left ventricular end-diastolic and stroke volumes in both groups. Simple resumption of usual physical activities after bed rest was as effective as formal exercise conditioning in restoring functional capacity to before-bed rest levels.

- 43. Dela, F., K. J. Mikines, H. Galbo, and E. A. Richter:**  
Effects of insulin and bedrest on haemodynamic parameters.  
*Acta Physiologica Scandinavica* 129:A49, 1987.

**Synopsis**

**Purpose.** To investigate the influence of insulin on haemodynamic parameters in man and whether a decreased level of physical activity (bed rest) influences these parameters.

**Methods.** Six healthy male subjects participated in this study.

1. Euglycemic insulin clamp technique was used to measure haemodynamic parameters.
2. Insulin was infused sequentially at 0.2, 0.7, and 5.0 mU/min/kg before control and after 7 days of bed rest.
3. Insulin concentrations were 10, 19, 39, and 365  $\mu$ U/ml.
4. Blood flow in one leg was measured by the thermodilution technique.
5. Blood pressure (BP) was measured by indirect cuff method in the brachial artery.
6. Plasma glucose was maintained at an euglycemic level throughout the clamp.

**Results.**

1. With increasing insulin concentrations, heart rate and systolic BR increased, while mean arterial BP was unchanged.
2. Both before and after BR, leg blood flow was increased at the highest insulin concentration (significantly different from values at basal insulin).
3. After BR, leg blood flow was lower than before BR, at each insulin concentration.

**Conclusions.** Since mean arterial BP was unchanged by insulin, the insulin-induced increase in leg blood flow must be due to leg vasodilatation.

- 44. Dikshit, M. B., and J. M. Patrick:**  
Vital capacity and airflow measured from partial flow-volume curves during 5° head-down tilt.  
*Aviation, Space, and Environmental Medicine* 58:343-346, 1987.

**Authors' abstract**

Ten healthy young males were subjected to 7 min of 5° head-down tilt, during which their forced vital capacity, peak flow rate (from complete flow-volume curves), and MEF 40% and 25% (airflows when 40% and 25% of the vital capacity remains in the lungs) from the partial curves were measured. The values of these variables and the heart rate and blood pressure were not significantly different from the values obtained in the supine position. In view of these findings it is concluded that the increase in the intra-thoracic blood volume, known to occur with 5° head-down tilt used as a model for simulating weightlessness, does not embarrass respiratory mechanics.

45. **Draeger, J., K. Hanke, R. Berger, and E. Rumberger:**  
Intraocular fluid dynamics in micro gravity.  
In: *Proceedings of the 2nd European Symposium on Life Sciences Research in Space*, Porz Wahn, Germany, 4-6 June, 1984. p. 175-177. (ESA Special Publication 212, 1984.)

**Authors' abstract**

Specific alterations in systemic circulation due to fluid shift in micro gravity may lead to a rise in intraocular pressure (IOP). This situation can be simulated by head-down tilt (HDT). Several series of tonometry were performed using a handheld applanation tonometer: 1) Short time postural change up to  $-90^\circ$  head-down and back. 2) Tonometry in  $-10^\circ$  HDT over a period of 2 hours. 3) Repetition of series 2 after dehydration of the patients. 4) Two 7-day bedrest studies in  $-6^\circ$  HDT. 5) Tonometry during lower body negative pressure (LBNP). 6) Tonometry during Valsalva-manuever. Immediately on tilting, the IOP changes with hydrostatic pressure. After 1 h the raised IOP returns to normal again. IOP seems to change parallel to venous pressure. Further experiments are planned for space lab missions.

46. **Dunn, C. D. R., R. D. Lange, S. L. Kimzey, P. C. Johnson, and C. S. Leach:**  
Serum erythropoietin titers during prolonged bedrest; relevance to the "anaemia" of space flight.  
*European Journal of Applied Physiology* 52:178-182, 1984.

**Authors' abstract**

The overall objective of these studies was to test the hypothesis that the suppression of erythropoiesis, which occurs during both spaceflight and bedrest (BR), was mediated by reduction in circulating levels of erythropoietin. In each of two 7-day studies, groups of subjects were exposed to either horizontal or  $6^\circ$  head-down tilt BR and no evidence was obtained to suggest that the erythropoietic effects were dependent on the angle of recumbency. An additional study involved six men who were exposed to horizontal BR for 28 days. Serum erythropoietin titers were not significantly depressed in any of the subjects but total red cell volume was decreased. Absolute increases in red cell numbers and reductions in plasma volume both elevate the hematocrit, but our data suggest that the mechanism of erythrosuppression in these two instances may be different.

47. **Ernst, E., E. Schmidt-Pauly, P. Muhlig, and A. Matrai:**  
Blood viscosity in patients with bone fractures and long-term bed rest.  
*British Journal of Surgery* 74:301-302, 1987.

**Synopsis**

**Purpose.** To study the hemorheological effects of bone fractures and those of prolonged immobilization and to examine the hypothesis that a lack of physical activity, an accepted cardiovascular risk factor, might induce a worsening of blood fluidity.

**Methods.** Six men and 11 women [age  $63 \pm 24$  yr] were confined to bed for at least 30 days (hospitalization due to fractures of the spine, pelvis, and femur). The control group consisted of 17 healthy individuals (criteria as above) matched for age and sex.

1. Heparinization with calcium heparin was routinely measured.
2. Blood rheology was tested on admission, and 15 and 30 days after the start of the immobilization.
3. The variables tested were: blood viscosity at 3 shear rates (hematocrits), plasma viscosity, blood filterability, red cell aggregation, and colloid oncotic pressure.

**Results.** At entry, patients had higher blood and plasma viscosities than controls. There was no significant intra-individual change of any parameter after 15 days bedrest (BR). After 30 days, however, a significant fall in hematocrit and in native blood viscosities at all shear rates could be detected. Plasma viscosity tended to decrease and blood cell filterability to increase, but not significantly. All other parameters remained constant during BR. The cross-sectional comparison of patients after 30 days immobilization with controls showed that, in patients, hematocrit standardized blood viscosities were still higher, while the hematocrit was lower than in controls.

**Conclusions.** The results neither support nor refute the hypothesis, as 30 days of immobilization is too short a period to give an answer to this particular question.

**48. Fortney, S. M:**

Thermoregulatory adaptations to inactivity.

In: *Adaptive Physiology to Stressful Environments*, edited by S. Samueloff and M.K. Yousef. Boca Raton, Florida: CRC Press, 1987. p.75-83. (Chapter 10).

**Author's abstract**

Exercise conditioning is usually accompanied by increases in blood volume and improvements in heat tolerance. Deconditioning, on the other hand, especially when produced by extended periods of bedrest, is accompanied by a decrease of blood volume. In this study, the effects of bedrest deconditioning on exercise thermoregulatory responses were studied, both with and without an accompanying reduction in plasma volume. Two groups of women underwent identical 12-day bedrest protocols. Group 1 (n=12) was administered no hormonal treatment, and their plasma volumes were significantly reduced (19.9%) at the end of the bedrest. Group 2 (n=7) received daily estrogen supplementation (1.25 mg premarin) during bedrest, and they did not suffer a significant reduction in plasma volume during the last days of bedrest. Both groups, however, had impaired thermoregulatory responses after bedrest. Therefore, deconditioning, even if unaccompanied by a reduction in plasma volume, results in an impairment of thermoregulatory function.

49. Fortney, S. M., W. S. Beckett, A. J. Carpenter, J. Davis, H. Drew, N. D. LaFrance, J. A. Rock, G. Tankersley, and N. B. Vroman:  
Changes in plasma volume during bed rest: Effects of menstrual cycle and estrogen administration.  
*Journal of Applied Physiology* 65:525-533, 1988.

**Authors' abstract**

Bed rest (BR) is associated with a decrease in plasma volume (PV), which may contribute to the impaired orthostatic and exercise tolerances seen immediately after bed rest. The purpose of this study was to determine whether increases in blood estrogen concentration, either during normal menstrual cycles or during exogenous estrogen administration, would attenuate this loss of PV. Nineteen healthy women (21-39 yr of age) completed the study. Twelve women underwent duplicated 11-day BR without estrogen supplementation. PV decreased significantly ( $P < 0.01$ ) during both BR's, from  $2532 \pm 113$  to  $2027 \pm 102$  ml during BR<sub>1</sub> and from  $2445 \pm 115$  to  $2244 \pm 96$  ml during BR<sub>2</sub>. The women who began BR in the periovulatory stage of the menstrual cycle ( $n=3$ ), a time of elevated endogenous estrogens, had a transient delay in loss of PV during the first 5 days of BR. Women who began BR during other stages of the menstrual cycle ( $n=17$ ) showed the established trend to decrease PV primarily during the first few days of BR. Seven additional women underwent a single 12-day BR while taking estrogen supplementation (1.25 mg/day premarin). PV decreased during the first 4-5 days of BR, then returned toward the pre-BR level during the remainder of the BR (pre-BR PV,  $2525 \pm 149$  ml; post-BR PV,  $2519 \pm 162$  ml). Thus menstrual fluctuations in endogenous estrogens appear to have only small transient effects on the loss of PV during BR, whereas exogenous estrogen supplementation significantly attenuates PV loss.

50. Gaffney, F. A., J. V. Nixon, E. S. Karlsson, W. Campbell, A. B. C. Dowdey, and C. G. Blomqvist:  
Cardiovascular deconditioning produced by 20 hours of bedrest with head-down tilt ( $-5^\circ$ ) in middle-aged healthy men.  
*American Journal of Cardiology* 56:634-638, 1985.

**Authors' abstract**

Cardiovascular deconditioning after prolonged bedrest has been attributed to inactivity. To examine the role of the altered distribution of body fluids, 5 healthy men, aged 41 to 48 years, were studied before, during and after a 20-hour period of bedrest with head-down tilt ( $-5^\circ$ ). This intervention produces a marked central shift of intravascular and interstitial fluid, but the short duration minimizes the effects of inactivity. Central venous pressure, cardiac output and stroke volume all increased significantly ( $p < 0.05$ ) from supine baseline mean values; central venous pressure from 8.6 to 12.6 cm H<sub>2</sub>O, cardiac output from 6.9 to 7.9 liters/min, and stroke volume from 104 to 113 ml after 15 minutes of tilt, but all values returned to baseline within 20 hours. Supine central venous pressure after tilt was 7.4 cm H<sub>2</sub>O, cardiac output 5.7 liters/min and stroke volume 84 ml. Blood volume decreased 0.51 liters. After tilt, orthostatic stress produced a higher heart rate ( $90 \pm 18$  vs  $68 \pm 12$  beats/min). Maximal oxygen consumption decreased ( $2.36 \pm 0.41$  vs  $2.62 \pm 0.48$  liters/min), mainly owing to reduced stroke volume ( $87 \pm 22$  vs  $107 \pm 18$  ml,  $p < 0.05$ ). Thus, tilt produced a transient increase in central venous pressure, stroke volume and cardiac output, but supine mean values were below baseline levels after 20 hours. The post-tilt state was qualitatively and quantitatively similar to that seen after 2 to 3 weeks of bedrest or several days of



spaceflight. These results are also similar to those from a previously studied group of ten 20- to 30-year-old normal men. However, the increase in central venous pressure tended to be larger and of longer duration in the middle-aged group. Furthermore, in the young men the initial increase in stroke volume produced relative bradycardia, with no change in cardiac output and arterial pressure. Cardiac output increased in the middle-aged group, but arterial pressure was controlled by vasodilatation. Heart rate did not change. The results support the concept that cardiovascular deconditioning after bedrest is primarily an adaptation to a postural fluid shift rather than to inactivity. Age-related differences in hemodynamic responses to central fluid shifts appear to be present.

- 51. Gauquelin, G., A. Güell, J. L. Mauroux, G. Geelen, G. Annat, M. Vincent, A. M. Allevard, A. Sassolas, C. A. Bizollon, and C. Gharib:**  
Volume regulating hormones during a 5-hour head-down tilt at  $-10^\circ$ : II-Plasma renin activity and aldosterone.  
In: *Proceedings of the 2nd International Conference on Space Physiology*, Toulouse, France, 20-22 November, 1985. p. 191-193. (ESA Special Publication 237, 1986).

**Authors' abstract**

Head-down tilt experiments are conducted to simulate the cardiovascular and hormonal modifications occurring during space flight. The purpose of this study was to observe the short term effects of weightlessness simulations on the hormones controlling volume homeostasis. Ten young healthy volunteers were submitted to the 3 following postural tests:

Day 1: 7 hours sitting;

Day 2: 1 hour sitting, then 5 hours horizontal supine, and 1 hour sitting;

Day 3: 1 hour sitting, then 5 hours of  $-10^\circ$  head-down tilt, and 1 hour sitting.

The results showed that a 5 hour horizontal bed rest or head-down tilt  $-10^\circ$  induce an early and progressive decline of PRA and aldosterone which is comparable to that observed during immersion. This study showed also that the subject's posture during the control period is critical.

- 52. Gauquelin, G., B. Roussel, J.-O. Fortrat, G. Geelen, P. Arbeille, L. Pourcelot, A. Güell, J. Gutkowska, M. Cantin, and C. Gharib:**  
Is ANF implied in the night attenuated renal response to central hypervolemia?  
In: *Proceedings of the 3rd European Symposium on Life Sciences Research in Space*, Graz, Austria, 14-18 September, 1987. p. 269-272.

**Authors' abstract**

Plasma levels of atrial natriuretic factor (ANF) were measured during a 4 hr head-down tilt at  $-6^\circ$  in 5 healthy male volunteers (aged 20-22 yrs). Experiments took place from 08.00h to 14.00 h (day), and from 22.00 h to 07.00 h (night). The control period was 1 hr in a seated position (08.00 h to 09.00 h for day and 22.00 h to 23.00 h for night). Blood samples were collected at 09.00 h and 23.00 h and every 20 minutes during the first hour, and every hour thereafter. Electroencephalograms were continuously

recorded during night. Our results showed a similar significant increase in ANF under both experimental conditions. During night there was no correlation between ANF and sleep stages.

Finally the differences observed in renal responsiveness to central volume expansion during day or night could not be explained by a difference in renin, aldosterone, vasopressin (previously demonstrated in several studies) or ANF secretion.

53. **Gazenko, O. G., V. I. Shumakov, L. I. Kakurin, V. E. Katkov, V. V. Chestukhin, V. M. Mikhailov, A. Z. Troshin, and V. N. Nesvetov:**  
Central circulation and metabolism of healthy man during postural exposures and arm exercise in head-down position.  
*Aviation, Space, and Environmental Medicine* 51:113-120, 1980.

**Authors' abstract**

The effect of postural exposures and arm exercise in the head-down position on central circulation and metabolism was studied in seven test subjects. Their left ventricle, pulmonary and femoral arteries were catheterized. The tilt test at +70° for 15 min was accompanied by a decrease of systolic pressure in those compartments, a drop of the end-diastolic pressure in the left ventricle, and an increase in its distensibility. At the same time, contractile parameters remained essentially unchanged and the transpulmonary gradient of the intravascular pressure (mean pressure in the pulmonary artery minus end-diastolic pressure in the left ventricle) increased. Some 10-15 min after the transition from the head-up to the head-down (at -30°) position, a drastic increase in the pulmonary artery pressure and left ventricular end-diastolic pressure and a decline of the left ventricular distensibility and contractility (Veraguth's index) occurred. During the last 45-60 min of the head-down tilt, contractility indices returned to the pretest level and other parameters remained unaltered. Arm workload (100 kg/min for 7 min), performed at the end of the head-down tilt, resulted in an increase of the systolic pressure in the left ventricle and femoral artery without any changes in the pulmonary artery. Contractile indices of the left ventricle, cardiac index, and heart rate increased significantly. Compensated metabolic acidosis with hyperventilation developed in the arterial blood.

54. **Genin, A. M., V. M. Baranov, V. G. Shabel'nikov, N. M. Asyamolova, A. N. Kotov, M. Y. Volkov, K. S. Yurova, and A. T. Poleshchuk:**  
Effect of short-term antiorthostatic hypokinesia on dynamics of cardiorespiratory parameters during graded physical exercise.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 19:43-46, 1985.

**Authors' abstract**

Seven healthy volunteers were exposed to head-down tilt at -15° for 5 h. Before and after exposure they exercised on a bicycle ergometer in the supine and seated positions. During the study their respiration function, gas exchange and arterialized blood parameters were measured. It was found that after exposure the physical aerobic performance diminished. The changes detected suggest that a lower exercise

tolerance can be caused not only by a decreased circulating blood volume but also by increased energy expenditures of the cardiorespiratory system itself.

**55. Gharib, C., G. Gauquelin, G. Geelen, M. Cantin, J. Gutkovska, J. L. Mauroux, and A. Güell:**

Volume regulating hormones (renin, aldosterone, vasopressin and natriuretic factor) during simulated weightlessness.

*The Physiologist* 28:S30-S33, 1985.

**Authors' abstract**

The decrease of hydrostatic pressure during space flights (microgravity state) or simulations of weightlessness (by immersion, bed rest or head-down tilt) results in a body fluid shift and an engorgement of the central circulation where mechanoreceptors involved in plasma volume regulation are located. Their activation induces the initial (first hours) hormonal response with a decrease in plasma vasopressin, renin and aldosterone and an increase of natriuretic factor (Gauer reflex).

The long term effects of weightlessness are linked to electrolyte disturbances, mainly a sodium loss which induces an increase in plasma renin and aldosterone and an amplification of the circadian rhythm of plasma renin activity. The discrepancies between the results of different studies could be explained by several factors (training level of subjects, diet, the subjects posture during the control period).

**56. Gharib, C., G. Gauquelin, G. Geelen, M. Vincent, F. Ghaemmaghami, C. Grange, M. Cantin, J. Gutkovska, and A. Güell:**

Levels of plasma atrial natriuretic factor (Alpha hANF) during acute simulated weightlessness.

In: *Proceedings of the 2nd International Conference on Space Physiology*, Toulouse, France, 20-22 November, 1985. p.173-176. (ESA Special Publication 237, 1986).

**Synopsis**

*Purpose.* To determine the variations of plasma levels of Alpha hANF during two experimental procedures known to increase central venous pressure: head-down tilt ( $-9^{\circ}$ ) and water immersion.

*Methods.* Two protocols were carried out:

1. Three healthy male subjects were seated for 30 min (control), followed by 3 hr of  $-9^{\circ}$  head-down tilt (HDT), followed by an additional 30 min of sitting upright. Blood samples were taken, and hematocrit, hANF, plasma renin activity (PRA), electrolytes, proteins, and osmolality were measured.

2. Two healthy male volunteers were subjected to 2-hr head-out water immersion, and blood samples were taken and analyzed for alpha hANF, plasma renin activity, plasma vasopressin (AVP), electrolytes, proteins, and osmolality. No statistical analysis was done, because of the small number of subjects.

**Results.**

1. HDT resulted in no variation in plasma sodium and potassium, while plasma osmolality, hematocrit, and plasma proteins decreased. PRA decreased continuously and reached 50% of control value 2 hr after tilting. Plasma hANF levels showed a rapid elevation which reached a maximum in 30 min, and by 1 hr returned to pre-tilt levels.

2. As in the tilt experiment, there was very little variation in sodium and potassium but the osmolality, hematocrit, and proteins decreased. Plasma AVP and PRA decreased, and hANF increased during immersion.

**Conclusions.** The decrease in hematocrit plasma proteins and osmolality could be interpreted as a translocation of fluid of interstitial origin. The decrease in PRA in both protocols, and in plasma AVP levels in the immersion study, is widely attributed to the translocation of blood to the thorax and the subsequent increase of atrial pressure. Knowledge of the main actions of ANF on the kidney—direct and indirect inhibition of aldosterone secretion, increase in glomerular filtration rate (GFR) with an increase in sodium load, decrease in vascular tone, and increase in filtration fraction—could explain many of the findings in this study. A future study with a more detailed protocol and more subjects is needed to confirm these findings.

57. **Gharib, C., G. Gauquelin, J. M. Pequinot, G. Geelen, C. Bizollon, and A. Güell:**  
Early hormonal effects of head-down tilt ( $-10^\circ$ ) in humans.  
*Aviation, Space, and Environmental Medicine* 59:624-629, 1988.

**Authors' abstract**

The aim of this study was to determine the effects of a 5-h weightlessness simulation (using supine bed rest or head-down tilt at  $-10^\circ$ =HDT) on plasma renin activity (PRA), aldosterone (PA), and catecholamines (epinephrine-E, norepinephrine-NE, and dopamine-DA) and to compare the results with those obtained with horizontal bed rest (BR), which is often taken as a control situation for simulation studies. Ten healthy young volunteers submitted to the three following postural tests: 7 h sitting; 1 h sitting, 5 h supine, and 1 h sitting; 1 h sitting, 5 h HDT, and 1 h sitting. Our results showed that a 5-h HDT or BR induced a significant progressive increase in plasma volume (14.5% for HDT and 7% for BR) and a decrease in diastolic blood pressure (18% for HDT and 17% for BR) compared to the sitting position. E decreased only in HDT, and DA was unchanged. We concluded that the main part of the cephalad shift is achieved by bed rest as reflected by changes in hematocrit and plasma protein concentration. The decrease in diastolic blood pressure, and the inhibition of the renin-angiotensin aldosterone system (in part explained by a decrease in NE) are similar in BR and HDT. We demonstrate that the use of a relevant body position as control is a major concern when investigating the hormonal effects of HDT. If recumbency is chosen as the control situation in HDT studies, it is not surprising to observe only few changes when HDT is applied.

**58. Gogolev, K. I., E. A. Aleksandrova, and E. B. Shul'zhenko.**

Comparative assessment of changes during antiorthostatic hypokinesia and immersion in man.  
*Fiziologiya Cheloveka* 6:978-983, 1980.

**Synopsis**

*Purpose.* To compare changes arising as a result of a model of antiorthostatic hypokinesia (AOH) and immersion.

*Methods.* Twenty men served as subjects in this study. After background investigation for 6 days of unrestricted motor activity in the room in which the experiments were to be carried out, they were divided into two groups: Seven subjects were kept under conditions of AOH for 7 days tilted  $-6^\circ$ , and 13 subjects were subjected to immersion for 7 days by the method of unsupported "dry" immersion. At all stages the hematocrit index and the concentrations of total protein and protein fractions (albumins and globulins) in the blood plasma were determined. The compliance of the soft tissues of the lower limbs and changes in the volume of the limb under the influence of occlusion were studied using limb compression technique and elastic capsule, respectively.

*Results.*

1. Water balance: There was a negative water balance for the subjects during the first day of AOH, but this returned to background level. Urine output during the first day of immersion was considerably greater than  $H_2O$  intake.

2. Hematocrit index increased during the first 3 days of AOH and remained unchanged thereafter. For immersion there was a greater increase after the first day and a tendency to increase thereafter.

3. Circulating plasma volume was reduced significantly at the end of the first day in both AOH and immersion. In subsequent days the AOH subjects showed some recovery, whereas the immersion subjects showed further reduction.

4. Changes in concentration of the blood proteins in AOH and immersion were qualitatively and quantitatively similar and were represented by a virtually unchanged albumin concentration and considerable hyperglobulinemia.

5. Soft tissues compliance dynamics: There was no significant change after the first and third days of AOH as compared to the background data. However, immersion for 24 hr led to a significantly greater increase in the volume of the limb in response to occlusion.

*Conclusions.*

1. The use of AOH ( $-6^\circ$ ) and immersion as methods of simulating certain physiological effects of weightlessness at ground level confirmed the reproducibility of changes in water metabolism, hematocrit index, and circulating plasma volume characteristic of the acute period of adaptation to circulatory disorders connected with the intravascular redistribution of blood.

2. A comparative analysis of the results confirms that immersion, with a stronger effect on the human body, causes an increase in changes in the parameters studied which continued for a longer period.

3. Immersion led to a considerable increase in compliance of the soft tissues during the occlusion test, evidence of changes in regulation of the regional circulation in the lower limbs. A phenomenon of this type that can be simulated in investigations at ground level enabled the physiological effects of exposure of man to an acute period of weightlessness to be simulated most completely.

59. **Goldsmith, S. R., G. S. Francis, and J. N. Cohn:**  
Effect of head-down tilt on basal plasma norepinephrine and renin activity in humans.  
*Journal of Applied Physiology* 59:1068-1071, 1985.

**Authors' abstract**

The effects of loading cardiopulmonary baroreceptors on basal norepinephrine and renin activity were studied in six normal human subjects. Loading of cardiopulmonary baroreceptors was accomplished by a 60-min 30° head-down tilt with small supplemental saline infusions. Central venous pressure was measured continuously by intrathoracic catheter; arterial pressure was measured indirectly by cuff. During the tilt, central venous pressure increased from  $5.1 \pm 1.3$  to  $8.9 \pm 1.7$  mmHg ( $P < 0.001$ ), whereas arterial pressure was unchanged. Plasma norepinephrine ( $185 \pm 85$  pg/ml) and plasma renin activity ( $3.9 \pm 5.7$  ng · ml<sup>-1</sup> · h<sup>-1</sup>) did not change. Moderate sustained loading of cardiopulmonary baroreceptors is therefore without effect on unstressed plasma norepinephrine and renin activity in normal humans, suggesting that the tonic inhibitory effects of these receptors on these neurohumoral control systems are not readily increased in the basal state.

60. **Goldwater, D. J., M. DeLada, A. Polese, L. Keil, and J. A. Luetscher:**  
Effect of athletic conditioning on orthostatic tolerance after prolonged bedrest.  
*Circulation* 62:287, 1980.

**Synopsis**

**Purpose.** To study the mechanisms responsible for orthostatic tolerance after bedrest (BR).

**Methods.** Twelve healthy 45- to 55-yr-old normotensive men underwent 10 days of BR.

1. Pre-BR maximal exercise tests were performed to reveal the range of athletic conditioning.
2. Serial plasma aldosterone, cortisol, vasopressin, and renin activity levels were sampled during supine rest and lower body negative pressure.
3. Blood pressure was also measured during supine rest and lower body negative pressure (LBNP).

**Results.**

1. High athletic conditioning predicted a large drop in post-BR LBNP tolerance which was associated with low pre-BR supine resting and peak LBNP plasma renin activity (PRA).
2. Sedentary men had higher post-BR resting and peak LBNP PRA, and lower post-BR upright maximal exercise  $\dot{V}O_{2\max}$ .
3. Blood pressures (BP) were similar for the resting, low R, peak PRA, and normal PRA groups at supine rest; however, the low R group became hypotensive more rapidly during LBNP.

**Conclusions.** These results suggest a relationship of AC to PRA and BP regulation which may predispose to orthostatic intolerance.

- 61. Goldwater, D. J., D. B. O'Hara, and H. Sandler:**  
Increased hematuria following hypergravic exposure in middle-aged women.  
*The Physiologist* 25:S167-S169, 1982.

**Synopsis**

*Purpose.* To determine the relationship of microscopic hematuria with hypergravic and orthostatic stress.

*Methods.*

1. Nine post-menopausal female subjects underwent testing during a 9-day control period consisting of +1.5 G<sub>z</sub>, +2 G<sub>z</sub> and +3 G<sub>z</sub> exposures, in addition to lower body negative pressure (LBNP). All were fed a high-grade protein diet.
2. The +1.5 G<sub>z</sub> exposure was repeated on bed rest (BR) day 7, +2 G<sub>z</sub> on BR day 8, and +3 G<sub>z</sub> on BR day 9. All G levels were run with and without inflation of an anti-G suit.
3. Maximal bicycle ergometer tests were performed before and after BR.
4. Mid-stream clean catch urines were tested using Labstix for hemoglobinuria, and microscopic exam of well-mixed sediment was performed if the dipstick screen was positive.

*Results.* Three subjects developed hematuria after entry into the study. In two of these subjects LBNP increased hematuria. Horizontal bed rest did not affect hematuria. Individual serum creatinine and BUN indicated no change in renal function. During and after episodes of hematuria, subjects reported no symptoms usually associated with traumatic injury. Lab analysis revealed negative cultures and no pyuria or other abnormalities. These three subjects had a low total urine creatinine concentration from 20 mg/dL to 44 mg/dL (normal 80 to 170) before bed rest, on the day following maximal exercise testing.

*Conclusions.*

1. Increased microscopic hematuria following orthostatic or acceleration stress may be similar to the "Stress Hematuria Syndrome" occurring with heavy exertion.
2. The sporadic occurrence of this phenomenon suggests a multifactorial etiology in predisposed individuals. Mechanisms which contribute to this phenomenon probably include mechanical trauma (upper or lower urinary tract), and alterations in glomerular permeability due to renal hemodynamic changes and circulating neurohormonal factors.
3. Bed rest or weightlessness simulation per se does not appear to significantly alter renal function, but may decrease microscopic hematuria with an orthostatic component.
4. The use of a dipstick hematest may underestimate the frequency of microscopic hematuria.
5. Clinical evaluation (e.g., urography and cystoscopy) is recommended if hematuria persists longer than 72 hr following exertional or hypergravic stress.

**62. Goldwater, D., A. Polese, L. Montgomery, L. London, P. Johnson, D. Yuster, and H. Sandler:**

Comparison of orthostatic intolerance following horizontal or  $-6^\circ$  head-down bed rest simulation of weightlessness.

*Aerospace Medical Association Preprints*, 1980. p.28-29.

**Synopsis**

**Purpose.** To determine the most effective way to simulate physiological effects of weightlessness.

**Methods.** Ten healthy 35- to 40-yr-old men underwent orthostatic tolerance tests using lower body negative pressure (LBNP): five men in a horizontal ( $0^\circ$ ) group and five men in head-down ( $-6^\circ$ ) bed rest.

1. Cardiovascular responses during LBNP were determined using echocardiography, automated heart rate (HR) and blood pressure (BP) recordings, doppler temporal artery flow velocity, systolic time intervals (STI), and impedance plethysmography.
2. Impedance plethysmography was used to measure pelvic and leg blood volumes during LBNP and the associated 5-min control and recovery periods.
3. LBNP testing occurred on days 2 and 13 of the ambulatory 14-day control period, following 7 days of bed rest (R+0), and on recovery days 5 and 10 (R+5 and R+10).
4. Plasma volumes (PV) were done using  $^{125}\text{I}$  serum albumin and red blood cell (RBC) mass determined with  $^{51}\text{Cr}$ .

**Results.**

1. Both  $0^\circ$  and  $-6^\circ$  subjects showed significant orthostatic intolerance after 7 days BR.
2. Peak LBNP stress ( $-50$  mmHg) decreased left ventricle ejection time (LVET) and increased pre-ejection time (PEP) in both  $0^\circ$  and  $-6^\circ$  subjects.
3. LBNP recovery period values were similar to those during control.
4. No significant changes were found for  $\text{QS}_2\text{I}$ ,  $\text{QS}_1$ , and isovolumic contraction time (ICV) throughout the tests.
5. LBNP significantly increased blood volume pooling in the leg and pelvic areas for both  $0^\circ$  and  $-6^\circ$  subjects according to impedance data.
6. After 7 days of BR, plasma volume and red blood cell mass decreased in all subjects compared to pre-BR, with no significant differences between  $0^\circ$  and  $-6^\circ$  subjects.
7. Peak LBNP stress caused a significantly greater HR increase than pre-BR LBNP.
8. Post-BR cardiac output for  $-6^\circ$  subjects fell to a greater degree during LBNP compared to  $0^\circ$  subjects.
9. There was a larger post-BR LBNP-induced fall in end diastolic volume for  $-6^\circ$  subjects compared to subjects who underwent horizontal BR.
10. Stroke volume decreases during LBNP were correspondingly lower in  $-6^\circ$  subjects than in  $0^\circ$  subjects immediately post-BR.
11. Both groups showed persistent orthostatic intolerance on R+10.

**Conclusions.** From the data, the  $-6^\circ$  BR appears to produce greater orthostatic intolerance immediately post-BR than horizontal BR.



**63. Goldwater, D. J. and H. Sandler:**

Orthostatic and acceleration tolerance in 55 to 65 year old men and women after weightlessness simulation.

*Aerospace Medicine Association Preprints*, 1982, p. 202-203.

**Synopsis**

**Purpose.** To evaluate the physiological responses of older individuals to simulated weightlessness and to the stresses of Shuttle reentry and "postflight" orthostasis.

**Methods.** Nine healthy women and eight men (aged 55 to 65 yr) underwent 10 days horizontal bed rest (BR) to simulate a period of weightlessness comparable to early flights.

1. Subjects underwent duplicate testing during a 9-day control period consisting of +1.5 G<sub>z</sub>, +2 G<sub>z</sub> and +3 G<sub>z</sub> exposures, plus LBNP as a test of orthostatic tolerance.
2. Subjects underwent each +G<sub>z</sub> level first without G-suit protection, and then with an Air Force cutaway G-suit inflated to 1 psia/G. [The +3 G<sub>z</sub> run was used as a physiological acceleration tolerance test.]
3. The +1.5 G<sub>z</sub> exposures were repeated on BR day 7, +2 G<sub>z</sub> on BR day 8, and +3 G<sub>z</sub> on BR day 9.
4. Supine LBNP exposures (-50 mmHg suction × 15 min) were repeated on BR day 10.

**Results.**

1. There were no statistically significant differences in the +1.5, +2.0 and +3 G<sub>z</sub> tolerance times between the men and the women, although at +2.0 and +3 G<sub>z</sub>, the men had consistently longer tolerance times. At +3 G<sub>z</sub> the mean pre-BR tolerance of the women was 541 ± 111 (SE) seconds compared to 725 ± 83 sec for men.

2. Post-BR unprotected +3 G<sub>z</sub> time decreased significantly (p < 0.05) to 214 ± 80 sec or 59% for the women, and 377 ± 91 sec or 50% for the men. In addition, after BR, anti-G suit inflation significantly improved +3 G<sub>z</sub> tolerance by an average of 494 sec for women and 498 sec for men.

3. The women's orthostatic tolerance times were not significantly lower than the men's times prior to BR. However, after BR the mean time of the women was greatly different (p < 0.01) than the men's.

4. There were large (p < 0.05) bed-rest-induced plasma volume losses in the older women (10.9%), but only 3.3% loss (NS) for the older men.

5. Post-BR resting and peak LBNP systolic blood pressure (BP) and diastolic BP were significantly lower (p < 0.05 to p < 0.01) in women than in men.

6. After BR, heart rate increased to a consistently greater degree (p < 0.05) in response to LBNP in men than in women.

**Conclusions.** The results suggest a need for alternative countermeasures or more rigorous selection criteria prior to flight.

64. Golikov, A. P., V. Y. Vorob'yev, V. R. Abdrakhmanov, L. L. Stazhadze, V. V. Bogomolov, and S. G. Voronina:  
External respiration and acid-base balance of human blood during long-term antiorthostatic hypokinesia and in the recovery period.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 1:42-46, 1980.

**Authors' abstract**

The study of external respiration and acid-base equilibrium of blood of 35 test subjects exposed to 49-day head-down ( $-4^\circ$ ) tilting (HDT) and of 6 test subjects exposed to 182-day ( $-4^\circ$ ) HDT demonstrated a trend for a decrease in the respiration rate, lung ventilation, oxygen consumption, and a relative increase in the exhalation time. With respect to the arterialized blood gases, a significant decrease in  $\text{PaO}_2$ , an increase in  $\text{PaCO}_2$  and in the  $\text{O}_2$  alveolar-arterial difference were seen during the 49-day HDT. During the 182-day HDT a further increase in the  $\text{CO}_2$  arterio-alveolar difference was noted. These changes suggest shifts of the ventilation-perfusion ratio in the lungs and, probably, disturbances of central regulation of respiration induced by HDT. During the recovery period the above changes diminished gradually and disappeared by the 14th and 30th day after the 49- and 182-day HDT, respectively.

65. Greenleaf, J. E.:

Bed-rest studies: Fluid and electrolyte responses.

In: *Space Physiology*, edited by J. Garcia, M. Guerin, and C. Laverlochere. Toulouse, France: Cepadues-Editions, 1983. p.335-348.

**Author's abstract**

Acute and chronic changes in hydrostatic and osmotic pressures have a major influence on body fluid-electrolyte composition and distribution in humans. Acute changes in body position (e.g., standing) result in a decrease in plasma volume (PV), and subsequent assumption of the horizontal position restores the depleted PV. Long-term confinement in the horizontal position for 2-3 weeks results in a chronic decrease in PV, increased interstitial fluid volume, and unchanged or slightly increased extracellular fluid volume. Concentrations of blood electrolytes, glucose, and nitrogenous constituents remain within normal limits of variability when maintenance levels of isometric or isotonic exercise are performed for 1 hr/day. Hematocrit and plasma osmolality can be elevated significantly throughout bed rest (BR). Significant diuresis occurs on the first day, and increases in urine sodium [Na] and calcium [Ca] continue throughout BR, although voluntary fluid intake is unchanged. Urine Na and potassium [K] are elevated during the second week of BR in spite of stabilization of PV and extracellular volume. The initial diuresis probably arises from the extracellular fluid while subsequent urine loss above control levels must come from the intracellular fluid. Preservation of the extracellular volume takes precedence over maintenance of the intracellular fluid volume. These findings suggest the functioning of a natriuretic factor (hormone) to account for the continued increased loss of Na in the urine.

**66. Greenleaf, J. E.:**

Physiological responses to prolonged bed rest and fluid immersion in man.  
*Journal of Applied Physiology* 57:619-633, 1984.

**Author's abstract**

Rest in bed and immersion in water have been used for centuries by physicians and healers in treating injury and disease. The qualitative similarity of acute and chronic responses to bed rest, immersion, and weightlessness has sparked renewed interest in and a resultant greater understanding of the mechanisms of disuse deconditioning. Some combination of changes in hydrostatic pressure, reduced total metabolism (exercise), compression force on weight-bearing bones, as well as psychological factors associated with prolonged confinement in a new environment probably comprise the major input stimuli for the adaptive responses. Virtually every physiological system is affected. Early responses involve the fluid, electrolyte, and blood pressure control systems with significant muscular atrophy and decreases in bone density occurring over weeks and months. Much effort has been expended to describe the various responses to bed rest and immersion with understandably less effort devoted to research during weightlessness. Future research should be directed mainly toward an understanding of the mechanisms of these adaptive responses. Additional work is especially needed to elucidate the effects of deconditioning on drug metabolism, functioning of the immune system, carbohydrate metabolism, protein and peptide metabolism in muscle, and calcium metabolism as it affects integrity of bone.

**67. Greenleaf, J. E.:**

Physiology of fluid and electrolyte responses during inactivity: Water immersion and bed rest.  
*Medicine and Science in Sports and Exercise* 16:20-25, 1984.

**Author's abstract**

This manuscript emphasized the physiology of fluid-electrolyte-hormonal responses during the prolonged inactivity of bed rest and water immersion. An understanding of the total mechanism of adaptation (deconditioning) should provide more insights into the conditioning process. Findings that need to be confirmed during bed rest and immersion are: 1) the volume and tissues of origin of fluid shifted to the thorax and head; 2) interstitial fluid pressure changes in muscle and subcutaneous tissue, particularly during immersion; and 3) the composition of the incoming presumably interstitial fluid that contributes to the early hypervolemia. Better resolution of the time course and source of the diuretic fluid is needed. Important data will be forthcoming when hypotheses are tested involving the probable action of the emerging diuretic and natriuretic hormones, between themselves and among vasopressin and aldosterone, on diuresis and blood pressure control.

68. **Greenleaf, J. E., L. T. Juhos, and H. L. Young:**  
Plasma lactic dehydrogenase activities in men during bed rest with exercise training.  
*Aviation, Space, and Environmental Medicine* 56:193-198, 1985.

**Authors' abstract**

Peak oxygen uptake (peak  $\dot{V}O_2$ ) and basal total activity of lactic dehydrogenase (LDH-T) and its five isoenzymes were measured in seven men, 19-21 years old, before, during, and after three 2-week bed rest (BR) periods, each separated by 3-week recovery periods. For 1 h · d<sup>-1</sup> during BR, they performed isometric (250 kcal · d<sup>-1</sup>) leg exercise, or no exercise. LDH-T was reduced (p<0.05) with all three regimens by day 10 of BR, but the decrease occurred at different rates. The earliest significant (p<0.05) reduction in LDH-T with the no-exercise regimen was associated with the greatest decrease in peak  $\dot{V}O_2$  of 12.3%; isotonic exercise was next with a peak  $\dot{V}O_2$  decrease of 9.2%; finally, isometric exercise had the least decrease in peak  $\dot{V}O_2$  at 4.8%. Irrespective of the exercise regimen during BR, the increases in isoenzyme activities occurred mainly in LDH-1 and LDH-2 (heart subunits). Isometric (aerobic) muscular strength training appears to maintain skeletal muscle integrity and, perhaps, oxygen uptake capacity better during bed rest than isotonic exercise training. Reduced hydrostatic pressure during bed rest, however, ultimately overrides effects of both moderate isometric and isotonic exercise training (metabolism) in the resulting decrease in LDH-T.

69. **Greenleaf, J. E., and S. Kozlowski:**  
Reduction in peak oxygen uptake after prolonged bed rest.  
*Medicine and Science in Sports and Exercise* 14:477-480, 1982.

**Authors' abstract**

The purpose was to test the hypothesis that the magnitude of the reduction in peak oxygen uptake ( $\dot{V}O_2$ ) after bed rest is directly proportional to the level of pre-bed rest peak  $\dot{V}O_2$ . Complete pre- and post-bed rest working capacity and body weight data were available from three studies involving 24 men (19-24 yr; peak  $\dot{V}O_2$ , 2.39-4.80 l · min<sup>-1</sup>) and 8 women (23-34 yr; peak  $\dot{V}O_2$  1.47-2.58 l · min<sup>-1</sup>), who underwent bed rest for 14-20 d with no remedial treatments. Regression analysis of percent change in post-bed rest peak  $\dot{V}O_2$  on pre-bed rest peak  $\dot{V}O_2$  with 32 subjects resulted in correlation coefficients (r) of -0.03 (NS) for data expressed in l · min<sup>-1</sup> and -0.17 (NS) for data expressed in ml · min<sup>-1</sup> · kg<sup>-1</sup>. Significant correlations were found that supported the hypothesis only when peak  $\dot{V}O_2$  data were analyzed separately from studies that utilized the cycle ergometer, particularly with subjects in the supine position, as opposed to data obtained from treadmill peak  $\dot{V}O_2$  tests. We conclude that orthostatic factors, associated with the upright body position and relatively high levels of physical fitness from endurance training, appear to increase variability of pre- and particularly post-bed rest peak  $\dot{V}O_2$  data, which would lead to rejection of the hypothesis.

- 70. Greenleaf, J. E., and R. D. Reese:**  
Exercise thermoregulation after 14 days of bed rest.  
*Journal of Applied Physiology* **48**:72-78, 1980.

**Authors' abstract**

Rectal ( $T_{re}$ ) and mean skin ( $\bar{T}_{sk}$ ) temperatures and sweating responses were measured during 70-min submaximal supine exercise (relative  $\dot{V}O_2$  43-48%) in seven men (19-22 yr) during an ambulatory-control (AC) period and after three 2-wk bed-rest (BR) periods separated by 3-wk ambulatory recovery periods. During each of the three BR periods they performed isometric exercises (IME) or isotonic exercises (ITE) for 1 h/day or no prescribed exercise (NOE). Mean basal oral temperature decreased from 36.0 to 35.7°C in the last 10 days of the control-recovery periods, but it varied between 35.7 and 35.9°C during BR. In the exercise-temperature test the equilibrium level of  $T_{re}$  for the IME (37.92°C) and NOE (37.75°C) regimens were higher ( $P < 0.05$ ) than the AC level of 37.51°C. Mean skin temperatures with the IME and ITE regimens increased by only 0.4°C during exercise, and both equilibrium  $\bar{T}_{sk}$  values, 31.98°C and 31.87°C, respectively, were lower ( $P < 0.05$ ) than the AC values of 32.71°C. There were no significant differences between any of the sweat rates (range, 438-565 g/h) in the four experiments, but calculated skin heat conductances ( $H_{sk}$ ) correlated +0.86 with equilibrium levels of  $\bar{T}_{sk}$ . It was concluded that the excessive increase in  $T_{re}$  during submaximal exercise following BR deconditioning could be influenced by changes in  $H_{sk}$ , but inhibition of sweating may also be a factor.

- 71. Greenleaf, J. E., W. Van Beaumont, V. A. Convertino, and J. C. Starr:**  
Handgrip and general muscular strength and endurance during prolonged bedrest with isometric and isotonic leg exercise training.  
*Aviation, Space, and Environmental Medicine* **54**:696-700, 1983.

**Authors' abstract**

Maximal grip strength and endurance at 40% max strength were measured in 7 men 19-21 years old, 1-2 d before and on the first recovery day during three 2-week bedrest (BR) periods, each separated by a 3-week ambulatory recovery period. In the three BR periods, they performed isometric exercise (IME) for 1 h/d (250 kcal/h), isotonic exercise (ITE) for 1 h/d (780 kcal/h), or no exercise (NOE) at 90 kcal/h. Mean maximal grip strength was unchanged after all three BR periods. Mean  $\pm$  S.E. grip endurance was unchanged after IME ( $147 \pm 7$  to  $136 \pm 8$  s, -7.5%, N.S.) and ITE ( $138 \pm 8$  to  $143 \pm 15$  s, +3.6%, N.S.) training, but was reduced from  $148 \pm 7$  to  $119 \pm 10$  s (-19.6%,  $p < 0.05$ ) after NOE. Results from the present study and from a review of the literature indicate that: (i) IME and ITE training during BR do not increase or decrease maximal grip strength, but they prevent loss of grip endurance; (ii) maximal strength of all other major muscle groups decreases in proportion to the length of BR to 70 d; (iii) maximal strength reduction of the large muscle groups (trunk, thigh, and leg) is about twice that of the small muscle groups (hand, forearm, and arm) during BR; (iv) isotonic leg exercise training during BR greatly reduces loss of strength in all major muscle groups; (v) remedial exercise training during BR can counteract the debilitating effect of hypovolemia and dehydration upon handgrip muscular endurance; and (vi) changes in maximal strength after spaceflight, BR, or water immersion deconditioning cannot be predicted from changes in submaximal or maximal oxygen uptake values.

72. **Grigoriev, A. I., and B. R. Dorokhova:**  
Fluid-electrolyte metabolism in space flights of varying duration.  
In: *Space Physiology*, edited by J. Garcia, M. Guerin, and C. Laverlochere. Toulouse, France: Cepadues-Editions, 1983. p. 353-360.

**Authors' abstract**

Forty-three cosmonauts, who performed 60 space flights aboard Soyuz spacecraft and Salyut orbital stations whose duration varied from 2 to 185 days and over 60 test subjects who were exposed to bed rest of up to 182 days, were examined. After space flights they showed changes in the osmoregulatory renal function including a decreased capacity of kidneys for both urine dilution (after short-term flights) and urine concentration (after longer-term flights). The renal excretion of potassium and calcium increased in prolonged space flights and simulation studies. During the load tests with potassium and calcium salt, excretion after longer-duration flights was much higher than preflight. Modified function of hormonal systems is the secondary process aimed at maintaining the blood concentration of electrolytes at a constant level. The most probable cause of the negative ion balance in weightlessness is the reduced capacity of tissues to retain electrolytes due to the decreased ion pool capacity.

73. **Grigoriev, A. I., V. S. Oganov, A. S. Rakhmanov, B. V. Morukov, H. A. Janson, V. V. Dzenis, and V. E. Zaichick:**  
Bone examination by noninvasive techniques in a 120-day head-down tilt test.  
In: *Proceedings of the 2nd International Conference on Space Physiology*, Toulouse, France, 20-22 November, 1985. p.99-103. (ESA Special Publication 237, 1986).

**Authors' abstract**

The effect of 120-day head-down tilt ( $-5^\circ$ ) on different bones was investigated using noninvasive methods: gamma-photon absorptiometry, ultrasonic introscopy and neutron-activation analyses. The study was carried out on 15 test subjects who were divided into a control group and 3 groups that used various countermeasures (drugs, exercises or a combination of drugs and exercises). No strict correlation was established between the negative calcium balance and the variation of photon absorptiometry and neutron-activation data. The mineral content of leg bones was found to be best in the drug groups. The noninvasive methods of mineral measurement and mechanical properties of bones are compared from the point of view of their diagnostic and prognostic significance.

74. **Grigoryev, A. I., B. R. Dorokhova, G. I. Kozyrevskaya, Y. V. Namochin, G. S. Arzamazov, and V. B. Noskov:**  
Water-salt metabolism and the functional state of the kidneys during bedrest of varying duration.  
*Fiziologiy Cheloveka* 5:660-669, 1979.

**Authors' abstract**

The functional capability of the kidneys does not suffer under prolonged bedrest. Apparently the antiorthostatic position, in comparison with the horizontal and particularly the orthostatic, accelerates hemodynamic changes. Basic changes in the electrolyte composition of the blood are apparent in the low

hypokalemia and hypercalcemia. Functional load samples make it possible to discover the condition of separate systems for ion regulations when their minimum shifts occur. Hypokinesia causes a change in tissue metabolism accompanied by a loss of electrolytes, which are not retained in the tissue; the addition of electrolytes can be only a symptomatic therapy for these conditions.

75. Güell, A., L. Braak, J. Bousquet, M. Barrere, and A. Bes:  
Orthostatic tolerance and exercise response before and after 7 days simulated weightlessness.  
*The Physiologist* 23:S151-S152, 1980.

**Authors' abstract**

Four volunteers underwent orthostatic tests before and after a 7 days period of prolonged bedrest in antiorthostatic position ( $-4^\circ$ ). A  $+85^\circ$  tilt test (head up) during 20 minutes and a squat-stand test were performed. Tests on an ergometric bicycle were also performed. Concerning orthostatic tolerance after the simulation, we noted a greatly increased intolerance among 2 of the volunteers, that can be translated as a presyncopal state with severe arterial hypotension, whereas the other 2 volunteers showed a paradoxical reaction with a hypertensive spike. The exercise response was also perturbed after bed rest, especially for one of the volunteers for whom the test had to be stopped. We feel that these results confirm the value of such a position where one intends to simulate the cardiovascular changes that occur during weightlessness.

76. Güell, A., P. Dupui, M. Barrere, G. Fanjaud, A. Bes, and A. Kotowskaia:  
Changes in the loco-regional cerebral blood flow (r.C.B.F) during a simulation of weightlessness.  
*Acta Astronautica* 9:689-690, 1982.

**Authors' abstract**

Experiments of prolonged bedrest in antiorthostatic position are conducted in order to simulate cardio-circulatory modifications observed in weightlessness. Until now, no studies of r.C.B.F. have been effected in these conditions. Six young, healthy volunteers (average age 23.8) were placed in strict bedrest and in antiorthostatic position  $-4^\circ$  for 7 days. The r.C.B.F. measurements were studied by  $^{133}\text{Xe}$  inhalation method using a 32-detector system. Studies were made first in basal conditions, then between the 6th and 12th hr, and finally between the 72nd and the 78th hr after the beginning of the experiment. Three of the subjects received 0.450 mg of clonidine daily during the experiment. In the subjects having taken no clonidine, we observed a constant increase in r.C.B.F. (12, 17 and 16% respectively) in the first 12 hr; at the 72nd hour, all values had returned to basal state. This finding agrees with the well known notion of a rapid correction of hemodynamic disturbances observed in the first days of weightlessness. In the subjects treated with clonidine, the increase of r.C.B.F. did not occur. Several mechanisms of action are possible; the clonidine affecting either the heart by inhibiting volemic atrial receptors, or the brain by direct vasoconstriction.

77. **Güell, A., P. Dupui, G. Fanjaud, A. Bes, J. P. Moatti, and C. Gharib:**  
Hydroelectric and hormonal modifications related to prolonged bed rest in antiorthostatic position.  
*Acta Astronautica* 9:589-592, 1982.

**Author's abstract**

The effects of prolonged bedrest in antiorthostatic position ( $-4^{\circ}$  head down) on electrolyte balance were studied in 4 young volunteers. An increase was noted in sodium excretion during the first 4 days. Plasma renin activity and plasma aldosterone varied in parallel manner during the same period. Potassium balance and creatinine clearance were not significantly modified. In light of these data we feel that prolonged bedrest in antiorthostatic position constitutes an effective way to simulate on earth metabolic and hormonal modifications occurring in man under weightlessness conditions.

78. **Güell, A., G. Gauquelin, M. Vincent, G. Annat, A. M. Allevard, C. A. Bizollon, J. J. Legros, A. Bes, and C. Gharib:**  
Effects of a 7 day head-down tilt with and without clonidine on volume regulating hormones in normal human.  
In: *Space Physiology*, edited by J. Garcia, M. Guerin, and C. Laverlochere. Toulouse, France: Cepadues-Editions, 1983. p.415-425.

**Authors' abstract**

Head-down tilt experiments are conducted to simulate cardiovascular and hormonal modifications observed during space flight. In this study, 6 young healthy volunteers were observed during a 7 day head-down tilt (at  $-4^{\circ}$ ). Three of these subjects received 0.45 mg of clonidine/day as a countermeasure to prevent the humoral and hormonal modifications induced by head-down tilt. In both groups plasma renin (PRA) and aldosterone (Aldo) rose, but the increase was significantly less in the subjects receiving clonidine. In the latter group we also observed a smaller variation in hematocrit, plasma sodium and potassium, and the urinary excretion of AVP was significantly reduced. Clonidine appears therefore to be an effective countermeasure under these conditions (and in weightlessness), but our data suggest that head-down tilt increases central venous pressure for not longer than a few hours. This is in agreement with data of Nixon et al. and Katkov et al. who have demonstrated that central venous pressure decreases after the third hour of tilting.

79. **Güell, A., C. Gharib, G. Fanjaud, P. Dupui, and A. Bes:**  
Effects of antiorthostatic position at  $-4^{\circ}$  on hydromineral balance.  
*The Physiologist* 25:S71-S72, 1982.

**Authors' abstract**

Experiments of bedrest in antiorthostatic position are conducted to simulate cardio-circulatory, metabolic and hormonal modifications observed during space flight. Four young healthy volunteers were placed in strict bedrest and in antiorthostatic position at  $-4^{\circ}$  during 7 days. One day before, during and 2 days after the experiment, we took 2 samples daily of blood for the determination of the plasma concentration of  $\text{Na}^+$ ,  $\text{K}^+$ , creatinine, urea, renin activity, aldosterone; in the urines the same parameters



were studied. The haematocrit rose from  $43.5 \pm 1.5$  to  $46.8 \pm 0.9$  ( $p < 0.001$ ); the plasma sodium fell from  $138.1 \pm 0.5$  to  $136.3 \pm 0.7$  mmol ( $p < 0.01$ ); plasma renin activity and plasma aldosterone rose significantly after the 24th hour. We also noted increased diuresis, sodium depletion and aldosterone out flow; the volunteers presented with the classic clinical picture of cephalic congestion. Blood pressure was not significantly modified; heart rate decreased by 22% until the 4th day. These reactions were most striking during the first 3 or 4 days and result from a redistribution of the body's fluid volume toward the cardiac cavities and the head, away from the lower part of the body.

- 80. Güell, A., C. Gharib, G. Gauquelin, P. Montastruc, and A. Bes:**  
Clonidine as a counter measure for metabolic studies during weightlessness simulation.  
*The Physiologist* 25:S69-S70, 1982.

**Authors' abstract**

Montastruc et al. (1981) show that clonidine (C) inhibits the diuretic response elicited by left atrial distension in chloralose anesthetized dogs. Furthermore, the increase in the intrathoracic volume observed in man during space flight provokes a diuretic response. Our work involves the effects of C in man during a simulation of weightlessness.

Six young, healthy volunteers were placed in bedrest and in antiorthostatic position at  $-4^\circ$  during 7 days; 3 of these received 0.450 mg of C during the bedrest. Before, during and after the experiment we took blood and urine samples for the determination of the hormonal and metabolic indices involved in blood volume regulation. In the subjects without C, we noted increased diuresis, sodium depletion and aldosterone outflow; plasma renin and aldosterone rose after the 24th hour. In the subjects with C the diuresis was inhibited and the sodium depletion was stopped after the 2nd day; plasma renin and plasma aldosterone don't rise significantly: finally the ADH concentration in urine was reduced. We conclude that it's interesting to use C as a counter measure for metabolic and hormonal studies during the experiments of weightlessness simulation.

- 81. Güell, A., J. M. Pequinot, G. Gauquelin, J. L. Bascands, G. Geelen, A. M. Allevard, G. Annat, L. Pourcelot, L. Peyrin, A. Bes and C. Gharib:**  
Volume regulating hormones during a 5-hour head-down tilt at  $-10^\circ$ : I-Epinephrine, norepinephrine and dopamine.  
In: *Proceedings of the 2nd International Conference on Space Physiology*, Toulouse, France, 20-22 November, 1985. p.177-179. (ESA Special Publication 237, 1986).

**Authors' abstract**

The aim of the study was to determine the short term effects of a weightlessness simulation (head-down tilt at  $-10^\circ$ ) on plasma catecholamines (epinephrine [E], norepinephrine [NE] and dopamine [DA]) and to compare the results with the supine position which is often take as control for simulation studies. Ten young healthy volunteers were submitted to the 3 following postural tests:

Day 1: 7 hours sitting;

Day 2: 1 hour sitting, then 5 hours horizontal supine, and 1 hour sitting;

Day 3: 1 hour sitting, then 5 hours head-down tilt (HDT)  $-10^\circ$ , and 1 hour sitting.

The results showed that a 5-hr HDT ( $-10^\circ$ ) or supine bedrest induce an early decrease in NE compared to the seated position. E decreases in HDT only. We can conclude that during such maneuvers there is a decrease in the sympathoadrenal activity which could explain the decrease in plasma renin activity.

**82. Güell, A., L. Pourcelot, J. L. Mauroux, P. Dupui, and A. Bes:**

Interest of head down tilt to simulate the neurocirculatory modifications observed during space flight.

In: *Proceedings of the 35th Congress of the International Astronautical Federation*, Lausanne, Switzerland, October 7-13, 1984. p. 1-4.

**Synopsis**

*Purpose.* To study eventual circulatory modifications in the cephalic region caused by prolonged bedrest at  $-6^\circ$  and their consequences on the brain.

*Methods.* Three volunteers (mean age  $23.6 \pm 3.4$  yr) remained in an antiorthostatic position at  $-6^\circ$  for 7 days. The study of the neurocirculatory modifications was approached in five different and complementary ways:

1. Clinical study; three daily evaluations of the subjective and objective symptomatology in the volunteers.
2. Study of eye fundus; three photographs of the eye fundus were taken daily in each volunteer to detect the presence or absence of edema or microhemorrhages.
3. Electroencephalographic study; before, during, and after bed rest, two electroencephalograms were performed twice daily on all subjects.
4. Brain computerized tomography scan; three measurements were performed in each of the subjects.
5. Psychometric tests; two types of attention tests were performed before, during, and after the experiment.

*Results.*

1. Objective and subjective symptomatology; all three subjects reported feelings of head fullness, nasal congestion, buccal and gingival turgescence, facial edema, and palpebral edema. Only one reported headache and dizziness.
2. Study of eye fundus; all three subjects showed a significant increase in the caliber of veins in the eye fundus; this increase in diameter persisted during the first 3 days of the experiment. Two subjects developed retinal and peripapillary edema.
3. Electroencephalographic study; modifications in electrogenesis were noted particularly during the first 48 hr (microvoltage of tracings, strong tendency to sleepiness, and global disorganization of activity).
4. Brain CT Scans; three sections of the third ventricle were performed. A significant modification in brain tissue density was noted in the second set of sections.

5. Psychometric studies; during the first 24 hr of bedrest there was a decrease in perceptive speed and performance in the triple sign identification test. A period of progressive accommodation or recuperation was observed from the second day and a transitory effect on the quality of precision on the third day. Only on the fourth day did adaptation again become possible.

*Conclusions.* The hypothesis suggesting significant increase of intracranial pressure during the first phase of a stay in weightlessness is quite plausible according to the results obtained from this study.

**83. Güell, A., G. Victor, A. Bru, P. Montastruc, and A. Bes:**

Effects of prolonged bedrest in antiorthostatic position on rCBF measured by  $^{133}\text{Xe}$  inhalation technique: effects of clonidine.

*The Physiologist* 24:S19-S20, 1981.

**Authors' abstract**

Experiments of prolonged bedrest in antiorthostatic position are conducted in order to simulate cardio-circulatory modifications observed in weightlessness. Until now, no studies of rCBF have been effected in these conditions.

Six young, healthy volunteers were placed in strict bedrest and in antiorthostatic position  $-4^\circ$  for 7 days. The rCBF measurements were studied by  $^{133}\text{Xe}$  inhalation method using a 32 detector system. Studies were made in basal conditions, then between the 6th and the 12th hour, and finally between the 72nd and 78th hour after the beginning of the experiment. Three of the subjects received 0.450 mg of clonidine daily during the experiment. In the subjects having taken no clonidine, we observed a constant increase in rCBF in the first 12 hours; at the 72nd hour all values had returned to basal state. These findings agree with a well known notion of a rapid correction of hemodynamic disturbances observed in the first days of weightlessness. In the subjects treated with clonidine, the increase of rCBF did not occur. Several mechanisms of action are possible; the clonidine affecting either the heart, or the brain by direct vasoconstriction.

**84. Hargens, A. R.:**

Fluid shifts in vascular and extravascular spaces during and after simulated weightlessness.

*Medicine and Science in Sports and Exercise* 15:421-427, 1983.

**Authors' abstract**

To simulate weightlessness in a normal-gravity environment, eight male subjects were tilted  $5^\circ$  head-down for 8 h to determine vascular and extravascular shifts of fluid. Most of the initial loss of leg volume during head-down tilt represented a passive shift of venous blood toward the head. Facial edema, headache, nasal congestion, and a pronounced diuresis were associated with this redistribution of blood volume. As measured by the wick-catheter technique during head-down tilt, interstitial fluid pressure in lower-leg muscle and overlying subcutaneous tissues decreased by 7.4 and 4.4 mmHg, respectively. Interstitial fluid was shifted from the lower legs at a rate of  $12 \text{ ml} \cdot \text{hr}^{-1}$ . Dehydration of lower-leg tissues probably resulted from decreased capillary blood pressure within these tissues during tilt. Other

transcapillary pressures were unchanged. The abrupt alterations in local blood pressure upon changes in body posture were probably sufficient to explain all shifts of vascular and extravascular fluid. In this regard, countermeasures may be necessary to maintain precapillary-muscle tone during long space flights in order to prevent swelling of lower-leg tissues upon readjustment to Earth's gravity.

85. Hargens, A. R., C. M. Tipton, P. D. Gollnick, S. J. Mubarak, B. J. Tucker, and W. H. Akeson:  
Fluid shifts and muscle function in humans during acute simulated weightlessness.  
*Journal of Applied Physiology* 54:1003-1009, 1983.

**Authors' abstract**

Head-down tilt is considered an effective experimental model to simulate weightlessness. To determine the acute effects of simulated weightlessness on transcapillary fluid balance, tissue fluid shifts, muscle function, and triceps surae reflex time, eight supine subjects were tilted 5° head down for 8 h. A cephalic fluid shift from the legs was indicated by facial edema, nasal congestion, increased urine flow, decreased creatinine excretion, reduced calf girth, and decreased lower leg volume. As measured by wick catheters inserted under local anesthesia, interstitial fluid pressure in the tibialis anterior muscle ( $4.6 \pm 0.6$  mmHg) and subcutaneous tissue ( $0.6 \pm 0.5$  mmHg) of the lower leg fell significantly to  $-2.8 \pm 0.5$  and  $-3.8 \pm 0.4$  mmHg, respectively. Other transcapillary pressures (capillary and interstitial fluid colloid osmotic pressures) were relatively unchanged. Needle-biopsy specimens, obtained just before and after tilt, indicated that total water content of soleus muscle was unchanged during 8 h of head-down tilt. After head-down tilt, isometric strength and isokinetic strength of the plantar flexors were unchanged. Triceps surae reflex time associated with plantar flexion movement slowed slightly after the tilt maneuver. Collectively these results demonstrated a dehydration effect of head-down tilt on muscle and subcutaneous tissues of the lower leg that may affect muscle function.

86. Harrison, M. H., R. J. Edwards, L. A. Cochrane, and M. J. Graveney:  
Blood volume and protein responses to skin heating and cooling in resting subjects.  
*Journal of Applied Physiology* 54:515-523, 1983.

**Authors' abstract**

The effects of alterations in skin temperature on intravascular volume and protein content have been investigated in resting subjects. With a normal core temperature ( $T_{ac}$ ) both skin cooling and skin heating caused hemoconcentration, and heating was associated with an increased rate of protein loss from the intravascular space. Raising of the skin temperature after cooling, with  $T_{ac}$  depressed, and cooling of the skin after heating, with  $T_{ac}$  raised, were associated with an immediate reversal of the hemoconcentration, and gain of protein by the intravascular space. It is concluded that intravascular volume responses to thermal stress are dependent on the skin and core temperatures obtaining immediately prior to imposition of the stress and that, in particular, a low skin temperature predisposes toward hemodilution on subsequent exposure to heat; sweating per se does not necessarily result in hemoconcentration. The association of hemodilution with augmentation of intravascular protein, and the rapidity with which

extravascular protein can apparently gain entry to the intravascular space, is taken as indicating a possible direct return of protein through capillary walls.

- 87. Hoogstraten, M. C., A. Cats, and J. M. Minderhoud:**  
Bed rest and ACTH in the treatment of exacerbations in multiple sclerosis patients.  
*Acta Neurologica Scandinavica* 76:346-350, 1987.

### **Synopsis**

**Purpose.** To plan a prospective study and to perform a retrospective study to evaluate the results of treatment, consisting of bedrest (BR) and bedrest combined with adrenocorticotrophic hormone (ACTH), of multiple sclerosis (MS) patients suffering from an exacerbation.

**Methods.** Fifty-five multiple sclerosis patients who had suffered a total of 99 relapses participated in this study.

1. Treatment periods:
  - a) Two weeks absolute BR,
  - b) One week BR with toilet facilities, and
  - c) Two to three weeks gradual mobilization under supervision of a physiotherapist.
2. Bedrest in combination with ACTH (BA) was given 74 times and BR alone only 25 times.
3. Blood pressure, blood cell count, blood glucosis, serum electrolytes, and liver and renal function were checked regularly.

### **Results.**

1. There was improvement in 43.5% of the patients by 0.5-4.0 points and a deterioration in 1% of the patients with 0.5 point on the EDSS-scale; the remainder, 55.5%, were unchanged.
2. The outcome of BA treatment was not significantly different from the BR treatment, either with respect to the effect of treatment on the restoration of the handicap (EDSS score) or to the progression rate in the year following the treatment period.
3. EDSS was comparable within the groups, but significant differences were found between the groups (all in favor of the BR group).

**Conclusions.** Bedrest treatment alone of multiple sclerosis patients suffering from an exacerbation was found to be as effective as BR treatment combined with ACTH.

- 88. Hung, J., D. Goldwater, V. A. Convertino, J. H. McKillop, M. L. Goris, and R. F. DeBusk:**  
Mechanisms for decreased exercise capacity after bed rest in normal middle-aged men.  
*The American Journal of Cardiology* 51:344-348, 1983.

### **Authors' abstract**

The mechanisms responsible for the decrease in exercise capacity after bed rest were assessed in 12 apparently healthy men aged  $50 \pm 4$  years who underwent equilibrium gated blood pool scintigraphy during supine and upright multistage bicycle ergometry before and after 10 days of bed rest. After bed rest, echocardiographically measured supine resting left ventricular end-diastolic volume decreased by 16% ( $p < 0.05$ ). Peak oxygen uptake during *supine* effort after bed rest was diminished by 6% ( $p = \text{not}$

significant [NS]), whereas peak oxygen uptake during *upright* effort declined by 15% ( $p < 0.05$ ). After bed rest, increases in heart rate were also greater during exercise in the upright than in the supine position ( $p < 0.05$ ). Values of left ventricular ejection fraction increased normally during both supine and upright effort after bed rest and were higher than corresponding values before bed rest ( $p < 0.05$ ). After bed rest, increased left ventricular ejection fraction and heart rate largely compensated for the reduced cardiac volume during supine effort, but these mechanisms were insufficient to maintain oxygen transport capacity at levels during upright effort before bed rest. These results indicate that orthostatically induced cardiac underfilling, not physical deconditioning or left ventricular dysfunction, is the major cause of reduced effort tolerance after 10 days of bed rest in normal middle-aged men.

89. **Hwang, T. I. S., K. Hill, V. Schneider, and C. Y. C. Pak:**  
Effect of prolonged bedrest on the propensity for renal stone formation.  
*Journal of Clinical Endocrinology and Metabolism* 66:109-112, 1988.

**Authors' abstract**

The effect of prolonged bedrest immobilization on urinary risk factors for stone formation and on the propensity for the crystallization of calcium salts was examined in eight normal subjects. During 5 weeks of bedrest, the mean urinary calcium excretion rose during the first week and remained elevated (from 5.68 to 7.50 mmol/day). Mean urinary phosphorus excretion increased by the second week of bedrest and remained elevated (from 2.70 to 30.6 mmol/day). Urinary sodium and uric acid excretion rose slightly, as did urinary magnesium. Urinary pH, oxalate, and citrate changed slightly or not at all. Owing to these biochemical alterations, urinary saturation of calcium phosphate, calcium oxalate, and monosodium urate increased significantly during bedrest, but that of uric acid did not change. The inhibitor activity against the spontaneous nucleation of brushite ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ) and calcium oxalate was not altered significantly by bedrest. Thus, the propensity for the crystallization of stone-forming calcium salts was enhanced by bedrest, suggesting that immobilization may confer increased risk for the formation of calcium-containing renal stones.

90. **Iakovleva, I. I.:**  
Electromagnetic examination of the human gustatory analyser in health and on simulating zero gravity.  
*Vestnik Otorinolaringologii* Mar.-Apr. (2):15-17, 1982.

**Author's abstract**

Threshold sensitivity of the tongue taste receptors to electrostimulation, as well as parameters of the gastrolingual reflex were determined with the help of an electrogustometer-1 made in Poland. Under examination were 62 healthy men aged 25 to 45 years. The standards of the parameters examined were defined in 53, and 9 men were examined in conditions of strict bed rest during 5 days at the bed head end slope of  $8^\circ$ . This brought about statistically significant elevation of taste thresholds as well as the change of the gastrolingual reflex direction (7 men), and its inhibition (2 men). More manifest shifts were observed at the start of the body adaptation to new conditions. Possible response mechanisms are discussed.

**91. Jaspers, W. J. M., P. A. DeJong, A. W. Mulder:**

Decrease of angiotensin sensitivity after bed rest and strongly sodium-restricted diet in pregnancy. *American Journal of Obstetrics and Gynecology* 145:792-796, 1983.

**Authors' abstract**

Angiotensin II (A-II) sensitivity was determined in 23 nonmedicated nulliparas in the third trimester of pregnancy, before and after a 7- to 10-day period of bed rest and a strongly sodium-restricted diet (maximal 20 mmol Na<sup>+</sup>/24 hr). Seventeen nulliparous women had pregnancy-induced hypertension (PIH). The effective pressor dose (EPD), that is the minimal amount of A-II necessary for a 20 mm Hg elevation of the diastolic blood pressure, rose from a mean of 11.0 ± 5.0 to 17.9 ± 5.7 ng/kg/min. This is an increase of the mean of 63%. Six women were normotensive during the course of the pregnancy. They showed an increase of EPD from 12.6 ± 4.9 to 28.3 ± 10.9 ng/kg/min after sodium restriction and bed rest. This is a mean increase of 124%. It is concluded from this study that sodium not only is important in volume regulation but also seems to play a role in vessel wall reactivity. This effect of sodium on vascular reactivity could be the explanation for the favorable effect of a strongly sodium-restricted diet in lowering the incidence of eclampsia in women.

**92. Kas'yan, I. I., V. A. Talavrinov, V. I. Luk'yanchikov and Y. A. Kobzev:**

Effect of antiorthostatic hypokinesia and space flight factors on change in leg volume. *Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 14:51-55, 1980.

**Synopsis**

*Purpose.* To assess variations and level of fluid shift as well as atrophic changes in leg muscles as a result of prolonged bed rest.

*Methods.* Eighteen male subjects maintained 182 days of -4.5° head-down tilt. Leg volume of the subjects was determined on various days of the background, bed rest, and recovery period with a specially developed measuring device. The subjects were divided into three groups; Group 1 exercised during bed rest, Group 2 performed exercises for a lesser time and with less energy expended, and Group 3 was the control group for which no preventative measures were used. The leg volumes of two cosmonauts were measured concurrently in the background period and on various days of space flight for comparison purposes.

*Results.*

1. The overall changes in leg volume (LV) were the greatest in Group 3, which had a 12.3% decrease (267 cm<sup>3</sup>, P<0.05).
2. The overall change in LV for Group 2 was an 11.6% decrease (260 cm<sup>3</sup>).
3. For Group 1, the overall change in LV constituted 9.5% (226 cm<sup>3</sup>).
4. In the course of an actual flight, it was found that LV decreased most appreciably by the third week, dropping by 16% in the commander and 13% in the flight engineer.

*Conclusions.* The authors attribute the loss of volume of the lower extremities to fluid that shifted in a cranial direction (about 7% of leg fluid volume). The performance of exercise seems to prevent almost entirely the development of atrophic processes and aided in preserving the functional capacity of muscle

leg at a high level (Group 1). Conversely, less intense exercise or the lack of exercise allowed for impairment of the functional state of muscle tissue and for greater atrophy of leg muscles (Groups 2 and 3).

93. **Kates, R. E., S. R. Harapat, D. L. D. Keefe, D. Goldwater, and D. C. Harrison:**  
Influence of prolonged recumbency on drug disposition.  
*Clinical Pharmacology and Therapeutics* 28:624-628, 1980.

#### **Synopsis**

**Purpose.** To determine the effects of extended recumbency on drug disposition.

**Methods.** The disposition of lidocaine and penicillin was studied in 12 normal men between the ages of 45 and 55 yr before and after 7 days of total recumbency. Penicillin (1,000,000 u) and lidocaine (100 mg) were administered intravenously. Lidocaine protein binding was also followed. Total body clearance elimination half-life and volume distribution were calculated.

**Results.** There were no statistically significant differences in the disposition parameters before and after 7 days of recumbency. The binding of lidocaine also was not changed after bed rest.

**Conclusions.** The physiologic changes that occur during prolonged bed rest do not affect distribution or elimination of lidocaine or penicillin.

94. **Katkov, V. E., V. V. Chestukhin, and L. I. Kakurin:**  
Coronary circulation of the healthy man exposed to tilt tests, LBNP, and head-down tilt.  
*Aviation, Space, and Environmental Medicine* 56:741-747, 1985.

#### **Authors' abstract**

The effect of tilt (head-up and head-down) tests, LBNP tests, and 7-d head-down tilt (at  $-15^{\circ}$ ) on coronary circulation was investigated in healthy male volunteers. Catheters were implanted into the coronary sinus and brachial artery. The Ganz catheter in the coronary sinus was used to measure volume flow in the area (constant thermodilution), pressure, and to withdraw samples of outflowing blood for biochemical analysis (acid-base equilibrium and oxygenation).

Transfer from supine to upright body position, lower body negative pressure ( $-30$  mm Hg for 20 min), as well as  $15^{\circ}$  head-down (by day 5-6) produced similar changes in the basic parameters of coronary circulation—reduction of blood flow and oxygen consumption, decrease of pressure in the coronary sinus, and increase of coronary resistance. Transfer from head-up to head-down position caused opposite changes of the above parameters. The changes in coronary circulation were adequate for myocardial metabolic requirements since the biochemical composition of the outflowing blood remained essentially constant during the gravitational exposures described.



95. **Katkov, V. Y., V. V. Chestukhin, E. M. Nikolayenko, S. V. Gvozdev, V. V. Rummyantsev, T. M. Guseynova, and I. A. Yegorova:**  
Central circulation in healthy man during 7-day head-down hypokinesia.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 16:45-51, 1982.

**Authors' abstract**

The effect of 7-day head-down tilt ( $-15^{\circ}$ ) and lower body negative pressure on circulation and oxidative metabolism was investigated on 13 healthy male test subjects. For 7-10 days they had Swan-Ganz catheters implanted in the pulmonary artery and a special cannula in the radial artery. The most marked changes were seen in the pulmonary artery pressure (PAP) and central venous pressure (CVP) that varied in a phase-like manner. By the 7th hour of bed rest the PAP increased significantly; this was followed by increases in the total lung resistance and the right ventricle function, as well as by a slight decrease of renin and aldosterone. Beginning with bed rest days 2 or 3, the PAP and CVP declined and remained lowered, as compared to the pretest level, till the end of bed rest. The responses to LBNP tests changed by bed rest day 2. Possible mechanisms of the above changes at rest and during LBNP tests are discussed.

96. **Katkov, V. E., V. V. Chestukhin, E. M. Nikolayenko, V. V. Rummyantsev, and S. V. Gvozdev:**  
Central circulation of a normal man during 7-day head-down tilt and decompression of various body parts.  
*Aviation, Space, and Environmental Medicine* 54:524-530, 1983.

**Authors' abstract**

The effect of 7-d head-down tilt ( $-15^{\circ}$ ) and decompression of various body parts (lower body-LBNP, upper body in the area of the hydrostatically indifferent point-UBNP, and local negative pressure applied to both calves-LNP) on central circulation was investigated on eight healthy test subjects who, for 10 d, had catheters (Swan-Ganz) implanted into the pulmonary and radial arteries. It was shown that, when calculated by square centimeter of the decompression area, the effect of UBNP on central venous pressure (CVP) and pulmonary artery pressure (PAP) was 3-4 times greater than that of LBNP or LNP. This indicates a high sensitivity of this body part to the exposure. During the 7-d study, CVP and PAP showed the most distinct changes. By the 7th hour of the head-down tilt study, CVP remained unchanged and systolic PAP increased by 5.5 mm Hg (27%) ( $p < 0.05$ ). This was paralleled by a decrease of plasma aldosterone and renin. By the 2nd day of the study, CVP and PAP were close to the pretest level; on the 3rd day, they began to decline and remained about 3 mm Hg lower than the pretest values to the end of the study ( $p < 0.05$ ). During this same period, the contractility of the right heart (the mean rate of right ventricular pressure increment) decreased by 34% ( $p < 0.05$ ) and its work by 27% ( $p < 0.05$ ). By 24 h after the study (the recovery period), CVP and PAP were close to the pretest values, whereas heart rate, cardiac index and oxygen tension in the mixed venous blood were significantly higher than the pretest values ( $p < 0.05$ ). The factors responsible for these changes and the potential application of the catheterization technique in biomedical investigations during real space flight are discussed.

**97. Katkov, V. Y., V. V. Chestukhin, O. K. Zybin, S. S. Sukhotskiy, S. V. Abrosimov, and V. N Utkin:**

The effect of short-term antiorthostatic hypokinesia on central and intracardiac hemodynamics and metabolism of a healthy person.

NASA Technical Memorandum 76525, 1981. p. 1-17.

**Synopsis**

*Purpose.* To examine the effects of short-term bed rest on the central and intracardiac hemodynamics and metabolism of healthy people.

*Methods.* During the initial period, 10 male subjects underwent catheterization of the heart and main vessels. Six subjects then maintained 5 days of strict  $-4.5^\circ$  bed rest, after which catheterization was then repeated. The remaining 4 subjects served as a control group and did not undergo bed rest. After the 5-day period, hemodynamic indices (i.e., blood pressure, minute volume of the heart, contraction of the myocardium, total peripheral resistance, and volume of circulating blood) were measured, as well as biochemical and hematologic indices (gas composition of the blood, hemoglobin, lactic acid, insulin, glucose, and B-lipoprotein content of the blood) for each subject.

*Results.* Bed rest did not significantly affect the majority of the indices of the central blood circulation ( $P < 0.05$ ) with the exception of the indices characterizing the inotropic state of the myocardium, which changed significantly ( $P < 0.05$ ).

*Conclusions.* The significant changes in the indices of the inotropic state of the myocardium may be due to changes in the metabolism of the cardiac muscle itself, the biochemical and gas composition of the arterial blood, and the hemodynamic conditions.

**98. Katkovskiy, B. S., and V. P. Buzulina:**

Evaluation of the functional state of the human cardiovascular system during prolonged antiorthostatic hypokinesia, using different levels of physical exercise on a bicycle ergometer.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 14:86-87, 1980.

**Synopsis**

*Purpose.* To examine the functional state of the human cardiovascular system during prolonged bed rest.

*Methods.* Twelve healthy volunteers were divided into two groups. Group 1 performed a set of physical exercises twice a day during bed rest. Both groups maintained strict bed rest for 45 days, and on various days performed 5-min tests with increasing physical loads of 150, 300, 600 and 800 kg-m/min in a supine position. Pulse rate and endurance were analyzed.

*Results.*

1. Pulse reaction to physical loads changed insignificantly during bed rest for a majority of the subjects in the study.
2. Subjects in Group 2 showed a decreased physical endurance.

3. With a load of 800 kg-m/min, Group 2 showed an increase of 15-25/min in pulse rate, as compared to the background. With a load of 600 kg-m/min, an increased pulse reaction was demonstrated in five out of six subjects.

**Conclusions.** The authors concluded that small physical loads are not appropriate for evaluation of functional changes in the human cardiovascular system in studies simulating prolonged weightlessness. The functional state of crew members should be assessed with the use of physical loads of at least 800 kg-m/min.

- 99. Khapilov, N. V., V. S. Pachenko, N. N. Kotkov, and B. F. Asyamolov:**  
Effect of hypokinesia and +G<sub>z</sub> accelerations on transport function of human blood.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 19:31-33, 1985.

**Authors' abstract**

The results of 44 studies of circulation parameters and blood transport function of 14 test subjects exposed to 7-day bed rest (−10° head-down tilt) and acceleration of +4.5 G<sub>z</sub> have demonstrated that the blood transport carriers and their actively binding centers form working structures in the adaptive reactions. As compared to the pretest level, the distribution ratio of <sup>14</sup>C-adenine between two immiscible phases (plasma/oil, erythrocytes/oil) varies from −12 to +14% on bed rest day 3 to +32 to +40% on bed rest day 7; it increases by 145-150% after exposure to +4.5 G<sub>z</sub> acceleration. The parameters of the blood transport function give a quantitative description of its adaptive reactions to environmental effects.

- 100. Knapp, C. F., A. Bhattacharya, and E. P. McCutcheon:**  
Effects of whole-body oscillating acceleration on orthostatic response after head-down bed rest and water immersion. Part I: Effect of whole-body oscillating acceleration on orthostatic response after head-down BR.  
NASA Contractor Report 176884, 1978-1981. p. 1-22.

**Authors' abstract**

Whole-body oscillating acceleration (WBOA) was used to modify the decrease in orthostatic tolerance (OT) of six healthy adult males deconditioned by 6 hours of 5°, head-down, bed rest (BR). The subjects were exposed to a WBOA profile consisting of a half-sine wave table displacement, a table frequency of 1 Hz, and a peak table acceleration between +1G<sub>z</sub> and +1.6G<sub>z</sub> (subject restrained horizontally, acceleration along the spine). The protocol consisted of 1) a control OT test (OTT) using 70° head-up tilt for 20 min; 2) an OTT after BR; and 3) an OTT after BR plus an 18 min WBOA exposure. Biomechanical and physiological measurements included table acceleration, net force transmitted to the subject, heart rate (HR), and whole-body oxygen consumption. Four of the six subjects exhibited a decreased OT time following BR without WBOA; with WBOA, two subjects returned to control values and two exhibited partial recovery. Of the remaining two subjects who did not exhibit presyncopal episodes, one had a lower orthostatic HR response, and the other a higher HR response with the WBOA exposure.

- 101. Kotovskaya, A. R., L. N. Gavrileva, and R. R. Galle:**  
Effect of hypokinesia in head-down position on man's equilibrium function.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 15:26-29, 1981.

### **Synopsis**

**Purpose.** To examine the changes in postural equilibrium during prolonged bed rest and to determine the role of visual, proprioceptive and vestibular stimulation in these changes.

**Methods.** Six healthy male subjects (age 35-40) maintained 182 days of  $-4^{\circ}$  bed rest. Stabilography was used to evaluate the subjects' ability to maintain equilibrium in an upright position. Subjects were tested on various days of the background and bed rest periods. Additional functional tests, such as visual, change in sensation of support, and circular head movements were performed to assess their effect on the subjects' equilibrium.

### **Results.**

1. Background stabilography revealed that the test using a soft support had the most adverse effect on equilibrium, and the test with circular head movements had the least marked effect.
2. There was a progressive worsening of equilibrium function during the first 30-50 days of bed rest, with subsequent stabilization of vacillations of the general center of gravity. After 50 days, attenuation of equilibrium disturbances was observed with the subjects standing on firm and soft surfaces. With eyes shut, a tendency toward further increase in amplitude was observed.
3. The percentile correlations between stabilogram amplitude parameters during the various functional tests reflect the direct involvement of vision, proprioception and the vestibular system in holding an upright position. The role of vision in maintaining equilibrium increased in the second half of the bed rest period.

**Conclusions.** The authors conclude that functional changes and deconditioning of the vestibular system are some of the causes of impaired equilibrium during bed rest.

- 102. Kovalenko, Y. A., and N. N. Gurovskiy:**  
Hypokinesia.  
NASA Technical Memorandum 76395, 1980. p.1-319.

### **Authors' abstract**

This book highlights the physiological and pathophysiological mechanisms leading to disorders caused by hypokinesia. Particular attention is focused on energy, gas, and plastic metabolism during hypokinesia. It cites numerous data obtained in experiments on animals using modern research methods, as well as observations on short-term and prolonged hypokinesia in humans.

The book sets forth some questions concerning hypokinesia relevant to space and sports medicine and throws some light upon problems of recovery following prolonged hypokinesia. Ways and means of preventing and treating various disorders caused by hypokinesia are proposed.

**103. Kozlovskaya, I. B., L. S. Grigor'yeva, and G. I. Gevlich:**

Comparative analysis of effects of weightlessness and its models on velocity and strength properties and tone of human skeletal muscles.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 18:22-29, 1984.

**Authors' abstract**

The effect of various types of support elimination (actual zero-G, water immersion, and head-down tilt) on the strength-velocity properties and tone of leg muscle was investigated. With all the exposures used, there was a high correlation between the tone decrease and the strength potential of antigravitational muscles, as well as the degree of support elimination (immersion and bed rest). This suggests that the tonic changes associated with the decrease of the support in input are the major factor responsible for motor disorders during short-term exposures to zero-G.

**104. Krølner, B., and B. Toft:**

Vertebral bone loss: An unheeded side effect of therapeutic bed rest.

*Clinical Science* 64:537-540, 1983.

**Authors' abstract**

1. The skeletal effects of simple bed rest and re-ambulation were studied in a consecutive series of 34 patients (aged 18-60 years) hospitalized with low backache due to protrusion of a lumbar intervertebral disc. The bone mineral content of the second, third and fourth lumbar vertebrae was determined by dual-photon (<sup>153</sup>Gd) absorptiometry immediately after admission to the hospital, at the end of the bed-rest period (mean 27 days, range 11-61 days) and approximately 15 weeks later (range 11-24 weeks).

2. During recumbency a mean decrease in lumbar spine bone mineral content of 0.9% per week was observed.

3. Re-ambulation resulted in bone mineral gain, and restoration of lumbar spine bone mineral content was nearly complete after 4 months.

4. The findings suggest that the simple therapeutic bed-rest regimen leads to excessive vertebral bone loss. Recurrent bed-rest periods may predispose to spinal osteoporosis.

**105. Krotov, V. P.:**

Water metabolism regulating mechanisms in hypokinesia.

*Patologicheskaya Fiziologiya I Eksperimental' naya Terapiya* 10:15-18, 1980.

**Synopsis**

*Purpose.* To qualitatively assess the normal range of total fluid content in humans, and the effects of bed rest on this range.

*Methods.* Six healthy men maintained 49 days of strict bed rest. Water consumption was not limited. The range of fluctuations of the hydration status for each subject was evaluated by determining the water

metabolism regulation coefficient, an index proposed and defined by the authors as the relative measure of the fluctuation of the constant of tritium water elimination from the organism every 24 hr.

#### *Results.*

1. The value of the water metabolism regulation coefficient changed in a wavelike manner. There was a significant increase during the first week of bed rest ( $P < 0.01$ ) as compared to the background, no significant difference during the second and third weeks and, finally, a significant increase during days 43 to 49 of bed rest ( $P < 0.05$ ).

2. In the recovery period, during which motor activity was restored, the value of the coefficient increased to an even greater degree, and by the end of the period, it significantly exceeded the background level ( $P < 0.01$ ).

*Conclusions.* During bed rest, a deterioration of the functional condition of the central nervous system is noted, as well as the formation of two syndromes: vegetovascular dysfunction and marked neuro-psychic asthenization of the organism. These syndromes cause a reduction in the resources of adaptive mechanisms which control the interaction of the organism with its environment. This could explain the observed disturbance in the systems that regulate water metabolism in humans during bed rest.

- 106. Krupina, T. N., A. Y. Tizul, M. P. Kuz'min, and N. I. Tsyganova:**  
Clinicophysiological changes in man during long-term antiorthostatic hypokinesia.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 16:29-34, 1982.

#### **Synopsis**

*Purpose.* To study the clinicophysiological and biochemical changes in man resulting from 182 days of antiorthostatic hypokinesia (AOH).

*Methods.* Eighteen men, aged 31 to 42 yr underwent 182 days of strict bed rest in an antiorthostatic position ( $-4.5^\circ$ ).

The subjects were divided into three groups:

Group 1: Subjects performed graded exercise with energy expenditure of 700 kcal/day.

Group 2: Subjects performed graded exercise with energy expenditure of 350 kcal/day.

Group 3: Subjects served as controls; no exercise.[TO]

Traditional methods were used to determine biochemical parameters. Diastolic blood pressure (DBP) in the central retinal artery and intraocular pressure were also measured.

#### *Results.*

1. During the first few days of AOH there were sensations of blood rushing to the head, dull headaches, face and neck hyperemia, nasal congestion, puffiness of the face, and signs of physical and temperature discomfort. These signs of "acute" AOH adaptation disappeared almost entirely by the 8th to 10th day.

2. DBP in the central retinal artery was elevated during AOH, but returned to base level at the 8th day of the recovery period.

3. The parameters of lipid metabolism revealed a reliable increase in blood cholesterol esters, beta-lipoprotein, cholesterol, esterification index, and Kundel test; and a decline of lecithin-cholesterol index, free cholesterol, and lecithin.

4. (a) Throughout the test period, catecholamine (epinephrine and norepinephrine) content of blood was above the mean normal levels except during the interval between the 65th and 100th days.

(b) Acetylcholine level dropped at the end of the first month and was below normal to the 65th day, but it gradually increased to the normal range of fluctuation, and by the second half of the study was above the normal range.

5. The most distinct increase in severity of clinical disorders in most systems was demonstrated up to the 90th-100th day, after which there was relative stabilization of the developed changes.

**Conclusions.** The changes that arise at the early stages of AOH are a reflection of consistent processes of adaptation to redistribution of blood and change in excitability of the reflexogenic regions of the chest and head. At later stages of AOH, as a result of the prolonged strain of adaptive mechanisms, there is development of more complex changes in regulatory and effector systems, which could lead to disruption of the normal course of adaptive reactions, compensatory and defense mechanisms, as well as development of pathophysiological processes that require appropriate corrective measures in the recovery period.

**107. Krupina, T. N., K. K. Yarullin, and D. A. Alekseyev:**

Bioelectric activity of the human brain during and after 182-day antiorthostatic hypokinesia.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 14:49-54, 1980.

**Authors' abstract**

Cerebral bioelectric activity of 18 healthy test subjects, aged 31-40, was examined during and after their 182-day head-down tilting. The test subjects were divided into a group that performed countermeasures (exercise, muscle stimulation) against hypokinesia-induced disorders, and a control group. During the study EEG index decreased, slow wave frequency was reduced, whereas index of zonal differences and amplitude of fast and slow waves increased. Phasic changes in the central nervous system excitability in response to a flickering light of 6-25 cps were found. Typical changes in spontaneous EEG during a 3 min pulmonary hyperventilation test were enhanced. The study gives evidence that the dynamics of spontaneous EEG as well as cerebral bioelectric activity in response to flickering light and pulmonary hyperventilation are important indicators of the cerebral function, especially of the cortical activity decrease.

**108. LaRochelle, F., C. Leach, and J. Vernikos-Danellis:**

Effects of age and sex on hormonal responses to weightlessness simulation.

*The Physiologist* 25:S161-S162, 1982.

**Authors' abstract**

As the age of experienced astronauts increases and women become Shuttle crewmembers, the need to study effects of age and sex on physiologic responses to space flight is evident. We have examined

effects of horizontal bedrest on excretion of catecholamines, aldosterone, and cortisol by human subjects grouped by age and sex. Responses were assessed by assays of 24-hr urine samples collected throughout the studies. In 36-45-yr-olds the excretion of epinephrine increased, while it decreased in the 46-55- and 55-65-yr-old groups. Norepinephrine excretion decreased (5-27%) in all groups during bedrest. Aldosterone excretion increased in the younger two groups of both males (19 and 6%) and females (47 and 9%). A slight decrease was seen in 56-65-yr-old males (6%) while excretion in females was unchanged. Cortisol excretion increased in the youngest groups of both men (12%) and women (13%) but decreased in the 56-65-yr-old groups (6 and 5%). In the two groups of intermediate age (46-55 yr) excretion in females decreased (15%) while in males it increased (19%). Hormone measurement may be of value in explaining variations in stress tolerance due to age and/or sex during space flight.

**109. Leach, C. S., P. C. Johnson, and W. N. Suki:**

Current concepts of space flight induced changes in hormonal control of fluid and electrolyte metabolism.

*The Physiologist* 26:S24-S27, 1983.

**Synopsis**

*Purpose.* To study early adaptation to simulated weightlessness, a series of experiments to record early responses of renal function and fluid and electrolyte balance during 6° head-down bed rest was undertaken.

*Methods.* Twenty-eight healthy adult subjects (mean age 27) were fed a controlled diet (2000 kcal/day) and underwent a 3-day ambulatory control period, a 60-hr period of 6° head-down bed rest, and a 3-day recovery period. Renal function tests were initiated during the ambulatory control period and were repeated on each day of bed rest. Glomerular filtration rate (GFR), effective renal plasma flow (ERPF), central venous pressure (CVP) and plasma volume (PV) were determined. Blood samples were analyzed for Angiotensin I, aldosterone, epinephrine, and norepinephrine.

*Results.*

1. CVP and ERPF exhibited a biphasic pattern.
2. GFR was depressed at 2 hr and then returned to control levels by 8-9 hr.
3. Plasma aldosterone had decreased by 3 hr but was elevated above control levels by 9 hr. Angiotensin I (renin activity) decreased by 6 hr and then increased to exceed the pre-bed-rest level by 9 hr.
4. Plasma norepinephrine and epinephrine decreased.

*Conclusions.* There are several phases of response to the initial exposure to bed rest and, by analogy, exposure to microgravity:

1. Elevated CVP, decreased sympathetic activity, decreased GFR, and decreased plasma levels of hormones which affect the renal tubule (ADH and aldosterone).
2. By 4 hr into bedrest, CVP returns to baseline value while ERPF has decreased. Plasma ADH, angiotensin, and aldosterone remain decreased.
3. After 6 hr, CVP has decreased to below the control value, and plasma angiotensin and aldosterone levels are below control.



4. By 8 hr, renal blood flow has increased and GFR and plasma ADH and aldosterone are probably approaching baseline values.
5. By 9 hr, plasma aldosterone and angiotensin are elevated while other parameters are close to normal.

**110. Leach, C. S., J. Vernikos-Danellis, J. M. Krauhs, and H. Sandler:**

Endocrine and fluid metabolism in males and females of different ages after bedrest, acceleration and lower body negative pressure.  
NASA Technical Memorandum 58270, 1985. p.1-52.

**Authors' abstract**

Space Shuttle flight simulations were conducted to determine the effects of weightlessness, lower body negative pressure (LBNP), and the acceleration on fluid and electrolyte excretion and the hormones that control it. Measurements were made on male and female subjects of different ages before and after bedrest. After admission to a controlled environment, groups of 6 to 14 subjects in the age ranges 25 to 35, 35 to 45, 45 to 55, and 55 to 65 years were exposed to +3 G<sub>z</sub> for 15 minutes (G1) and to LBNP (LBNP1) on different days. On 3 days during this pre-bedrest period, no tests were conducted. Six days of bedrest followed, and the G<sub>z</sub> (G2) and LBNP (LBNP2) tests were run again. Hormones, electrolytes, and other parameters were measured in 24-hour urine pools throughout the experiment. During bedrest, cortisol and aldosterone excretion increased. Urine volume decreased, and specific gravity and osmolality increased. Urinary electrolytes were statistically unchanged from levels during the non-stress control period. During G2, cortisol increased significantly over its control and bedrest levels. Urine volume, sodium, and chloride were significantly lower; specific gravity and osmolality were higher during G2 than during the control period or bedrest. During LBNP2, volume was lower than during the non-stress control period, and specific gravity and osmolality were higher than during control or bedrest periods. The retention of fluids and electrolytes after +G<sub>z</sub> may at least partially explain decreased urine volume and increased osmolality observed during bedrest in this study. There were some statistically significant differences between the sexes and age groups. Results of the study indicated that space flight would not affect the fluid and electrolyte metabolism of females or older males any more severely than it has affected that of male or female astronauts.

**111. LeBlanc, A., H. Evans, E. Schonfeld, J. Ford, V. Schneider, S. Jhingran, and P. Johnson:**

Changes in nuclear magnetic resonance (T<sub>2</sub>) relaxation of limb tissue with bed rest.  
*Magnetic Resonance in Medicine* 4:487-492, 1987.

**Authors' abstract**

Bed rest is used to simulate the effects of weightlessness on human physiology. A spinecho procedure was used to image the lower leg of 15 normal male volunteers before and after 5 weeks of horizontal bedrest. In addition to noninvasively measuring muscle size changes, accurate T<sub>2</sub> images were produced to investigate possible relaxation time changes immediately (2-4 h) and 1-2 days after bed rest. Subcutaneous fat showed no change in T<sub>2</sub>, bone marrow showed a decrease, and muscle showed no change immediately after bed rest but increased 1-2 days following reambulation.

- 112. LeBlanc, A., P. Gogia, V. Schneider, J. Krebs, E. Schonfeld, and H. Evans:**  
Calf muscle area and strength changes after five weeks of horizontal bed rest.  
*The American Journal of Sports Medicine* 16:624-629, 1988.

**Authors' abstract**

Nine male volunteers participated in a 10 week metabolic study in which subjects underwent 5 weeks of ambulatory control and 5 weeks of complete horizontal bed rest. Bed rest is a model commonly used to simulate space flight. The changes in muscle area and strength of the calf dorsiflexors and plantar flexors were measured before and after bed rest using magnetic resonance imaging (MRI) and a Cybex II dynamometer. The muscle area of the plantar flexors (gastrocnemius and soleus) decreased 12%, whereas the muscle area of the dorsiflexors was not significantly decreased. The maximal muscle strength of the plantar flexors decreased 26%; the muscle strength of the dorsiflexors was not significantly decreased. These results, which demonstrate differential muscle atrophy and a larger loss in strength relative to muscle area, have important implications in the development of exercise countermeasures to be implemented during space flight. The results also have implications for patients who have severe orthopaedic disorders and must be bed rested for long periods of time, and for persons who are voluntarily inactive (a large number of the elderly).

- 113. LeBlanc, A., V. Schneider, J. Krebs, H. Evans, S. Jhingran, and P. Johnson:**  
Spinal bone mineral after 5 weeks of bed rest.  
*Calcified Tissue International* 41:259-261, 1987.

**Authors' abstract**

Patients put at bed rest for medical reasons lose 1-2% of spinal bone mineral per week. Losses of this magnitude during even short-term space flights of a few months would pose a serious limitation and require countermeasures. The spinal bone mineral (L2-L4) was determined in 6 healthy males (precision=2%) before and after 5 weeks of complete bed rest. Only one individual had a significant loss (3%) and the -0.9% mean change for the 6 was not significant (P=0.06). The average negative calcium balance during the 5 weeks was 4g or 0.36% of total body calcium, similar to that reported in other bed-rest studies. Spinal bone loss, however, in healthy bed-rested males is significantly less than reported for bedrested patients, suggesting that a large loss of spinal bone mineral does not occur during space flight missions lasting 5 weeks or less.

- 114. Leonard, J. I.:**  
Analysis of head-down tilt as an analog of weightlessness using a mathematical simulation model.  
NASA Contractor Report 171870, 1984. p.1-86.

**Author's abstract**

Antiorthostasis or head-down tilt of a moderate degree has been used as a ground-based analog of weightlessness space flight to study headward fluid shifts, decreased plasma volume, orthostatic intolerance and muscular skeletal degradation. In the present study, a mathematical model was used to help interpret these observations. The model which proved most valuable for these studies was originally

developed by Guyton as a description of the major circulatory, fluid and electrolyte control systems. Two different experimental studies were employed in this paper to validate the model. The first is a 24-hour head-down tilt study and the second is a 7-day head-down bed-rest study. The major issues which were addressed included the reduction in plasma volume, the dynamic changes of venous pressure and cardiac output, the extent of central hypervolemia during long-term zero-g exposure, the renal-regulating hormones during the short-term and long-term periods, the significance of potassium loss on the other zero-g responses, and the role of transcapillary filtration in adjusting fluid shifts. This study illustrates the use of mathematical models as an interpretive and analysis technique for experimental research for space life science.

**115. Leonard, J. I.:**

Mathematical modeling of fluid-electrolyte alterations during weightlessness.  
NASA Contractor Report 171881, 1984. p.1-56.

**Author's abstract**

This report summarizes a number of separate studies of fluid-electrolyte metabolism and renal-endocrine control as it pertained to adaptation to weightlessness. The report discussed the mathematical models that have been particularly useful. However, the focus of the report is on the physiological meaning of the computer studies. A discussion of the major ground-based analogs of weightlessness are included; for example, head-down tilt, water immersion, and bed rest, as well as a comparison of findings from those studies with space flight. Several important zero-g phenomena are described in detail, including acute fluid volume regulation, blood volume regulation, circulatory changes, longer-term fluid-electrolyte adaptations, hormonal regulation, and body composition changes. Hypotheses are offered to explain the major findings in each area and these are integrated into a larger hypothesis of space-flight adaptation.

This report provided a conceptual foundation for the contractual tasks concerning fluid-electrolyte metabolism, blood volume regulation, and cardiovascular regulation.

**116. Leonard, J. I.:**

A systems analysis of the erythropoietic responses to weightlessness: Vol. I. Mathematical model simulations of the erythropoietic responses to weightlessness.  
NASA Contractor Report 171890, 1985. p.1-160.

**Author's abstract**

This document summarizes a number of theoretical studies conducted during the period 1974-1980 concerning the hematological responses to weightlessness. The studies include development and validation of a model of erythropoiesis regulation, analysis of the behavior of erythropoiesis under a variety of conditions, simulations of bed rest and space flight, and an evaluation of ground-based animal studies which were conducted as analogs of zero-g. This document contains a review of all relevant space-flight findings and a set of testable hypotheses which attempt to explain how red cell mass decreases in space

flight. An additional document describes details of the mathematical model used in these studies (Vol. II, Description of the Model of Erythropoiesis Regulation, TIR-2114-Med-5004).

**117. Lkhagva, L.:**

Circadian rhythm of human body temperature in antiorthostatic position.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 14:59-61, 1980.

**Synopsis**

*Purpose.* To study perturbations of the circadian rhythm of human body temperature in an antiorthostatic [head-down] position, which simulates weightlessness to some extent.

*Methods.* Three healthy male subjects maintained bed rest for 7 days in an  $-8^\circ$  head-down position. Body temperature was measured at 2-hr intervals during waking hours with an oral mercury thermometer and once during the sleeping period. An ambulatory control period of 3 days preceded bed rest and control measurements were taken, as described above, while the patients were upright. The daily average amplitude was determined by calculating the difference between maximum and minimum body temperatures and averaging the control and bed rest values for each subject.

*Results.*

1. The daily temperature minimums were higher ( $P < 0.05$ ) in all subjects during bed rest when compared to ambulatory control values.
2. The daily temperature maximums were less sensitive to the antiorthostatic position and failed to show a consistent difference between the period of bed rest and control.
3. In the antiorthostatic position, the amplitude of daily temperatures decreased in all subjects by a mean of  $0.20^\circ$ .

*Conclusions.* There were changes in some of the initial characteristics of the circadian rhythm of body temperature that were associated with spending 7 days in the antiorthostatic position ( $-8^\circ$  angle of inclination): increase in the values of minimums, decrease in amplitude and, in one subject, elevation of temperature during the day. If we consider that the head-down position at an angle of  $-8^\circ$  reproduces, at least in part, the effect of the redistribution of blood in weightlessness, perhaps such redistribution during a space flight could be associated with analogous changes in circadian rhythms of body temperature.

**118. Llagwa, L.:**

Circadian rhythm of human heart rate during antiorthostatic tests.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 18:60-63, 1984.

**Synopsis**

*Purpose.* To study the circadian rhythm of heart rate in subjects during bed rest for varying lengths of time.

**Methods.** Two series of observations of seven healthy subjects were conducted:

1. The first series lasted 18 days; the subjects sustained  $-8^\circ$  bed rest for the first 7 days.
2. The second series lasted 32 days, 12 days of which the subjects maintained a  $-8^\circ$  head-down tilt position.

Heart rate was measured from the EKG at various hours of the day during the waking and sleep periods.

**Results.**

1. Heart rate may decrease in the morning and during the day as early as the first day of bed rest.
2. The nocturnal period was characterized by an increase in heart rate.

**Conclusions.** Head-down position alters man's circadian heart rate rhythm.

**119. Loeppky, J. A., E. R. Fletcher, L. G. Myhre, and U. C. Luft:**

Validation and application of single breath cardiac output determinations in man.

*Aviation, Space, and Environmental Medicine* 57:759-768, 1986.

**Authors' abstract**

Cardiac outputs by single breath ( $\dot{Q}_{SB}$ ) and Fick ( $\dot{Q}_F$ ) procedures were compared in five healthy males during supine rest and exercise with  $\dot{Q}_F$  ranging from 6-19 L · min<sup>-1</sup>. The prolonged exhalation (SB) was not controlled. The  $\dot{Q}_{SB}$  calculations incorporated an equation of the CO<sub>2</sub> dissociation curve and a "moving spline" sequential curve-fitting technique to calculate the instantaneous R from points on the original expirogram. The resulting linear regression equation for all 38 comparisons obtained ( $r = +0.76$ ,  $p < 0.001$ , mean difference  $\pm$  S.D. =  $2.93 \pm 2.72$  L · min<sup>-1</sup>) indicated a 24% underestimation of  $\dot{Q}_F$ . A substantial portion of the variability during exercise ( $n=28$ ) was due to a difference in alveolar ventilation between the time of the mixed expired ( $\bar{E}$ ) gas collection and the SB maneuver. When  $\dot{Q}_{SB}$  was corrected ( $\dot{Q}'_{SB}$ ) by a linear regression based on the difference between  $\bar{R}_E$  and  $R_{SB}$  during exercise and by adding 2.44 L · min<sup>-1</sup> at rest (the mean difference), the relationship was greatly improved ( $\dot{Q}'_{SB} = 0.14 + 0.99 \dot{Q}_F$ ,  $r = +0.93$ , mean difference  $\pm$  S.D. =  $0 \pm 1.47$  L · min<sup>-1</sup>). A subsequent study during upright rest and exercise to 80% of  $\dot{V}O_{2\max}$  in 6 subjects indicated a close linear relationship between  $\dot{Q}'_{SB}$  and  $\dot{V}O_2$  for all 95 values obtained ( $r = +0.94$ ), with slope and intercept close to published studies utilizing invasive cardiac output measurements. Considerations of measured blood gases in relation to estimated values suggested that underestimates of  $\dot{Q}_F$  arose, at least in part, from arterial desaturation during SB maneuver. Detailed computational procedures are provided for implementing this improved  $\dot{Q}_{SB}$  procedure.

120. **Loeppky, J. A., D. W. Hirshfield, and M. W. Eldridge:**  
The effects of head-down tilt on carotid blood flow and pulmonary gas exchange.  
*Aviation, Space, and Environmental Medicine* 58:637-644, 1987.

**Authors' abstract**

Common carotid artery blood flow (CCF), pulmonary gas exchange and ventilation were measured in six subjects in the supine posture (SUP I), serially during 20 min of head-down tilt at  $-30^\circ$  (HDT), and after returning to the supine posture (SUP II). CCF was approximately 6% lower during HDT, with a transient increase during the second minute, and was about 7% higher during SUP II than during SUP I. The transition from SUP I to HDT caused increases in  $O_2$  uptake ( $\dot{V}O_2$ ),  $CO_2$  output, respiratory exchange ratio and tidal volume in the first minute. Similar responses were apparent following the HDT to SUP II transition, except for  $\dot{V}O_2$  for changes in estimated lung  $O_2$  stores indicated that about 200 ml of blood were shifted within the circulation by the tilt transitions which provided a ventilatory stimulus. HDT can cause a loss in blood and tissue  $O_2$  stores and gain in  $CO_2$  stores by shifting blood volume toward and blood flow away from the dependent headward vascular compartment and perhaps by producing ischemia in the elevated lower extremities. Cerebral venous congestion during HDT appears to cause periodic breathing and reduce CCF, the latter being offset by reduced flow resistance in the carotid artery.

121. **Löllgen, H., U. Gebhardt, J. Beier, J. Hordinsky, H. Borger, V. Sarrasch, and K. E. Klein:**  
Central hemodynamics during zero gravity simulated by head-down bedrest.  
*Aviation, Space, and Environmental Medicine* 55:887-892, 1984.

**Synopsis**

*Purpose.* To define the early response of the cardiovascular system during head-down tilt (HDT), determine left ventricular function during HDT, and compare invasive hemodynamic parameters to echocardiography.

*Methods.* Eight healthy male volunteers (average age  $26 \pm 3$  yr, average weight  $71.5 \pm 6.2$  kg, average height  $188 \pm 12$  cm) participated in this study. Experiments were performed with four subjects midmorning and with four subjects in the early afternoon.

1. Right heart catheterization was performed first.
2. After heart rate (HR) and blood pressure (BP) returned to stable baseline values, all measurements were started.
3. After control measurements were performed, subjects underwent  $-6^\circ$  HDT for 2 hr.
4. Measurements were taken every 15 min and blood samples were taken every 60 min for analyses. HR and BP were obtained every minute.
5. After bed rest, a lower body negative pressure (LBNP) test was performed.

**Results.**

1. Significant increase occurred for pressures in the right atrium and the pulmonary artery in pulmonary wedge position, and for pulmonary resistance.
2. Cardiac and stroke volume index, heart rate, mean arterial pressures and total systemic resistance remained constant throughout the exposure time.

3. Pulmonary vascular resistance and pulmonary arteriolar resistance were elevated from the beginning of HDT.
4. Cardiac dimensions assessed by echocardiogram remained constant during HDT.
5. Stroke volume was significantly greater when analyzed by thermodilution as compared to echocardiogram.
6. Epinephrine and dopamine concentrations remained constant during HDT whereas plasma noradrenaline slightly increased at the end of HDT.

*Conclusions.*

1. HDT leads to an increase of preload without any evidence of disturbed left ventricular function.
2. No distinct time course of hemodynamic variables could be seen.
3. Echocardiography proved to be a useful method to study cardiovascular adaptations during HDT.

- 122. Löllgen, H., K. E. Klein, J. Beier, G. V. Neiding, H. Just, J. R. Hordinsky, and F. Baisch:**  
 Comparison of simulation of weightlessness by head-down tilt (HDT) and water immersion (WI).  
 In: *Proceedings of the 2nd European Symposium on Life Sciences Research in Space*, Porz Wahn, Germany, 4-6 June, 1984. p.169-174. (ESA Special Publication 212, 1984).

**Authors' abstract**

During 6° HDT and WI, central hemodynamics were analyzed by a semifloating pulmonary artery catheter in a group of volunteers. Echocardiography (HDT) and radionuclide angiography (WI) were also performed. During WI, cardiac and stroke volume index increased but remained constant during HDT, right heart pressures were more elevated during WI than during HDT. Ejection fraction was constant during HDT but rose during WI depending on the depth on immersion. HDT seems to be more appropriate to simulate microgravity. Echocardiography should be applied in space and invasive measurements are also possible if performed under strictly controlled conditions.

- 123. Löllgen, H., K.E. Klein, U. Gebhardt, J. Beier, J. Hordinsky, V. Sarrasch, H. Borger, and H. Just:**  
 Hemodynamic response to LBNP following 2 hours of HDT (-6°).  
*Aviation, Space, and Environmental Medicine* 57:406-412, 1986.

**Authors' abstract**

Central hemodynamics have been determined during stepwise decreasing LBP in head-down tilt (HDT) of -6°. Measurements were performed on eight healthy volunteers using right heart catheterization. During LBNP, pressures in the right atrium, pulmonary artery, and pulmonary capillary (preload) decreased in parallel with the increase of negative pressure applied to the lower part of the body. Similarly, stroke volume and cardiac output decreased with increasing negative pressure. Heart rate moderately increased (30%) as well as total peripheral resistance. The left ventricular function curve was shifted downward and to the left during LBNP indicating hypovolemia with no evidence of decreased

contractility. Cardiac dimensions determined by echocardiography changed in a similar way as those obtained by invasive measurements. There was a very close correlation between stroke volume determined by thermodilution and by echocardiography. Plasma norepinephrine and dopamine tended to increase at the end of LBNP. Echocardiography proved a useful and reliable approach to hemodynamic measurement during LBNP and is recommended for analysis of hemodynamic parameters during zero G and  $G_z$  simulation.

- 124. London, G. M., J. A. Levenson, M. E. Safar, A. C. Simon, A. P. Guerin, and D. Payer:**  
Hemodynamic effects of head-down tilt in normal subjects and sustained hypertensive patients.  
*American Journal of Physiology* 245:H194-H202, 1983.

**Authors' abstract**

Central and forearm arterial and venous hemodynamics, arterial baroreflex sensitivity, plasma renin activity, and catecholamines were studied in supine position and after  $-10^\circ$  head-down tilt in 29 patients with sustained essential hypertension and 29 normotensive controls of the same age and sex. In both populations, blood pressure, heart rate, and arterial baroreflex sensitivity did not change during the maneuver. Head-down tilt induced a similar increase in credo pulmonary blood volume in controls and hypertensives, whereas the increase in central venous pressure, cardiac output, and forearm blood flow was higher in hypertensives. Forearm venous tone decreased in controls (from  $16.6 \pm 0.8$  to  $13.8 \pm 0.9$  mmHg  $\cdot$  ml $^{-1}$ ;  $P < 0.01$ ) but did not change in hypertensive patients ( $24.9 \pm 1.6$  vs.  $25.1 \pm 1.9$ ). The magnitude of forearm vascular resistance changes induced by head-down tilt were significantly related to the basal venous tone in the overall population ( $P < 0.01$ ). The decrease in plasma renin activity and plasma catecholamines was similar in the two groups. The study provides the evidence that the higher increase in cardiac output and local flow observed in head-down tilt in hypertensive patients is probably due to a higher change in central venous pressure related to a decrease in venous distensibility.

- 125. Ludwig, D. A., V. A. Convertino, D. J. Goldwater, and H. Sandler:**  
Logistic risk model for the unique effects of aerobic fitness to  $+G_z$  tolerance before and after simulated weightlessness.  
*Aviation, Space, and Environmental Medicine* 58:1057-1061, 1987.

**Authors' abstract**

Small sample size ( $n < 10$ ) and inappropriate analysis of multivariate data have hindered previous attempts to describe which physiologic and demographic variables are most important in determining how long humans can tolerate acceleration. Data from previous centrifuge studies conducted at NASA-Ames Research Center, utilizing a 7-10 d bed rest protocol to simulate weightlessness, were included in the current investigation. After review, data on 25 women and 22 men were available for analysis. Study variables included gender, age, weight, height, percent body fat, resting heart rate, mean arterial pressure,  $\dot{V}O_{2\max}$ , and plasma volume. Since the dependent variable was time to greyout (failure), two contemporary biostatistical modeling procedures (proportional hazard and logistic discriminant function) were used to estimate risk, given a particular subject's profile. After adjusting for pre-bedrest tolerance time, none of the profile variables remained in the risk equation for post-bedrest tolerance greyout.



However, prior to bed rest, risk of greyout could be predicted with 91% accuracy. All of the profile variables except those related to fitness ( $\dot{V}O_{2\max}$ , percent body fat, resting heart rate) entered the risk equation for pre-bedrest greyout. A cross-validation using 24 new subjects indicated a very stable model for risk prediction, accurate within 5% of the original equation. The result for the fitness variables is significant in that a consensus as to whether an increased level of fitness is beneficial or detrimental has not been satisfactorily established. We conclude that tolerance to +G<sub>z</sub> acceleration before and after simulated weightlessness is independent of aerobic fitness.

**126. Machinskiy, G. B., V. P. Buzulina, V. M. Mikhaylov, and E. I. Nechayeva:**

Functional state of the cardiorespiratory system in humans after 30 days of hypokinesia with head-down tilt.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 21:46-48, 1987.

**Authors' abstract**

Six healthy males with average age of 31.5 years were exposed to hypokinesia with head-down tilt (18°) for 30 days. Before and after this period, subjects were given a provocative treadmill test, walking at a rate of 7 km/hr at a steadily increasing angle, with a 6-minute warm up walking at a slower rate. Testing stopped when subjects could not go on. The following parameters were recorded: time spent on treadmill, distance walked, maximum work performed, heart rate, respiratory minute volume, maximum oxygen consumption, respiratory rate, oxygen pulse, coefficient of oxygen consumption, EKG with bipolar chest leads, systolic and diastolic blood pressure, pulsed blood pressure, and total oxygen debt.

Before the hypokinesia treatment, subjects tolerated the test well. The major reason for stopping was fatigue in the leg muscles. Changes in bioelectric cardiac activity and blood pressure were adequate to the work performed. After hypokinesia, the test was more difficult for the subjects. The major reason for stopping was shortness of breath frequently combined with weakness and dizziness. These subjective symptoms were not accompanied by increased heart rate, while respiratory minute volume actually decreased from baseline level. Other statistically significant changes involved: decreased maximum oxygen consumption, oxygen pulse, and amplitude of T<sub>A</sub> and T<sub>D</sub> waves on the EKG. Total tolerance time decreased by 18% after treatment, distance by 21%, and work performed by 14%. Oxygen debt also decreased significantly. Decrease in maximum oxygen consumption after hypokinesia was less extreme than in other analogous studies, which the authors attribute to the amount of motor activity engaged in during bed rest.

**127. Macpherson, P., and E. Teasdale:**

Radiculography with non-ionic contrast medium: Routine bed rest is unnecessary.

*Clinical Radiology* 35:287-288, 1984.

**Synopsis**

*Purpose.* To determine whether there would be any difference in the incidence of side effects between patients staying in bed for 24 hr or remaining ambulatory after iopamidol radiculography.

**Methods.** Two hundred patients who had undergone iopamidol radiculography were randomly allocated into two groups, one confined to bed for 24 hr and the other allowed to be fully ambulant.

**Results.** The incidence of side effects was not increased by allowing the patients to remain ambulant, and headache and dizziness were significantly less frequent than in a comparable study in which metrizamide had been used.

**Conclusions.** Routine bed rest is unnecessary following radiculography with iopamidol.

**128. Macpherson, P., and E. Teasdale:**

Routine bed rest is unnecessary after cervical myelography.

*Neuroradiology* 27:214-216, 1985.

**Authors' abstract**

After undergoing myelography with iopamidol by either direct puncture (n=120) or lumbar puncture (n=232), the patients were randomly allocated into one of two groups, one group being confined to bed for 24 hr and the other allowed to be fully ambulant. Questionnaires recording the occurrence and severity of side effects were completed at specific intervals after the myelogram. Adverse reactions experienced were significantly fewer than in our previous direct puncture study using metrizamide. Neither in the direct puncture nor in the run up group were side effects adversely affected by allowing the patients to remain ambulant after the examination. There is, therefore, no necessity to confine patients to bed following cervical myelography.

**129. Maheshwari, U. R., V. S. Schneider, J. T. McDonald, A. J. Brunetti, L. Leybin, E. Newbrun, and H. Hodge:**

Fluoride balance studies in healthy men during bed rest with and without a fluoride supplement.

*The American Journal of Clinical Nutrition* 36:211-218, 1982.

**Authors' abstract**

In a program of studies of disuse osteoporosis, fluoride balances were determined in healthy men during ambulation and then during bed rest for 6 to 17 wk. Control subjects ingested basal diets containing 0.4 mg fluoride per day, whereas experimental subjects received 10-mg fluoride supplements in divided doses with meals. Fluoride and calcium were measured in diets, urine, and feces. Serum analysis included calcium and ionic fluoride. Fluoride balances during both phases were uniformly negative in control subjects (mean -0.46 mg/day) but uniformly positive in supplement subjects (mean +2.58 mg/day). Calcium balances were markedly negative during bed rest in both groups. Serum fluoride concentrations increased proportionally to fluoride intake, averaging 0.016 ppm in the controls and 0.045 ppm in the supplement subjects. The supplement of 10 mg fluoride daily did not protect against bed rest-induced calcium loss, or cause any clinical or laboratory abnormality in any subject.

- 130. Martin, D. G., V. A. Convertino, D. Goldwater, E. W. Ferguson, and E. B. Schoemaker:**  
Plasma viscosity elevations with simulated weightlessness.  
*Aviation, Space, and Environmental Medicine* 57:426-431, 1986.

**Authors' abstract**

Bed rest studies which simulate weightlessness have demonstrated marked changes in the state of hydration of subjects as well as decrements in aerobic capacity. These two phenomena may be linked through increases in blood viscosity which is altered by a loss of free water and which, in turn, influences blood flow needed for aerobic muscular work. This study examines changes in rheologic properties of blood which attend changes in plasma volume with bed rest in humans and correlates these changes with alterations in aerobic capacity. Eight healthy human subjects were studied on the 6th day of bed rest during two consecutive 10-d bed rest periods separated by a 14-d recovery interval designed to simulate the flight-layover schedule of shuttle astronauts. Plasma viscosity was measured with a Wells-Brookfield viscometer, plasma volume by dye dilution, and maximal aerobic capacity ( $\dot{V}O_{2\max}$ ) by recumbant cycle ergometry. Bed rest resulted in significant increases in hematocrit and in total plasma protein concentration and fibrinogen concentration, both of which contributed to an elevation in plasma viscosity. The >20% increase in fibrinogen concentration was much greater than could be explained by hemoconcentration.  $\dot{V}O_{2\max}$  decreased significantly in the first but not the second bed rest cycle. In many individuals, a decrease in plasma volume and aerobic capacity was coupled with elevated plasma viscosity and hematocrit; however, significant correlations between these variables were lacking. Although significant rheologic perturbations do occur with bed rest, in this study, blood viscosity elevation failed to directly correlate with the reduction in  $\dot{V}O_{2\max}$ . Thus, the decrease in aerobic capacity observed following simulated weightlessness cannot be attributed to alterations in muscle blood flow resulting from increased blood viscosity.

- 131. Matthews, D. D., V. Agarwal, and T. P. Shuttleworth:**  
A randomized controlled trial of complete bed rest versus ambulation in the management of proteinuric hypertension during pregnancy.  
*British Journal of Obstetrics and Gynaecology* 89:128-131, 1982.

**Synopsis**

**Purpose.** To examine the influence of bed rest or ambulation on fetoplacental well-being and fetal outcome in patients with proteinuric hypertension during pregnancy.

**Methods.** Forty patients participated in a randomized controlled trial of complete bed rest versus ambulation as desired in the management of proteinuric hypertension during pregnancy.

**Results.** Daily increases in serum human placental lactogen and oestriol concentrations were greater in the rested group. An especially "at risk" group of 10 patients with both hyperuricemia and severe fetal growth retardation was identified. Strict confinement to bed in these cases seemed to encourage the development of the premonitory symptoms of eclampsia, but was associated with a better prognosis for the fetus.

**Conclusions.** The results suggest that strict bed rest may help the fetus in two ways. First, placental function may be improved. Secondly, it seems that in especially “at risk” patients strict confinement to bed promotes the delivery of the fetus while it is still alive.

- 132. Medkova, I. L., N. M. Nikolayeva, and O. V. Zhiznevskaya:**  
Lipid hydrolysis in man during antiorthostatic hypokinesia.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 19:40-44, 1985.

**Authors' abstract**

Using present-day techniques, we measured the activity of pancreatic lipase in the serum and duodenal juice, the activity of monoglyceride lipase in the duodenal juice, the concentration of lipoproteins in the bile, the activity of intestinal enzymes (monoglyceride lipase and alkaline phosphatase) and the concentration of lipid fractions in the feces. These parameters were determined in six test subjects who were exposed to head-down tilt ( $-4.5^\circ$ ) for 120 days. Our findings suggest that bed rest decreases lipolytic enzymes in the duodenal juice and increases pancreatic lipase in the serum. The exposure also leads to a decrease of lipoproteins in the bile, rearrangements of the lipolytic enzymes in the intestine, and to an increase in mono-, di-, and triglycerides in the feces. Our results are indicative of changes in the pancreatic function and in lipid hydrolysis and absorption. They can be interpreted as compensatory-adaptive processes of the digestive organs.

- 133. Medkova, I. L., O. V. Zhiznevskaya, K. V. Smirnov, V. I. Lebedev, and Y. M. Artamasova:**  
Change in bile acid and lipid content of human bile during exposure to antiorthostatic hypokinesia and its correction.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 20:31-37, 1986.

**Synopsis**

**Purpose.** To investigate the bile-synthesizing function of the liver and bile calcium content during long-term bed rest while using various means of correcting calcium metabolism under these conditions.

**Methods.** Fifteen healthy men (age 30-40) were kept on strict bed rest in a  $-4.5^\circ$  head-down tilt position for 120 days. There were four groups of subjects:

Group 1: Control group, no preventive measures used.

Group 2: Subjects performed physical exercise during bed rest.

Group 3: Subjects received a set of pharmacological agents to normalize  $Ca^{++}$  metabolism and systems of its regulation.

Group 4: Subjects performed exercise in addition to intake of xidiphone during bed rest.

The duodenum of each subject was probed during the control period, as well as on various other days during the bed rest period and recovery period. Quantitative assays of bile composition were then performed.

### *Results.*

1. The results of these investigations revealed that overall bile acid content diminished toward the end of the bed rest period in Group 1 subjects, and in subjects of the other groups there was elevation of the parameter of total glycoconjugates and tauroconjugates in bile.

2. Assays of serum cholesterol levels in the same study on subjects of Group 1 revealed dramatic and reliable elevation starting on the 72nd day of the study. In groups with use of preventive measures (pharmacologic agents and exercise), hypercholesterolemia was not demonstrated.

### *Conclusions.*

1. Hypercholesterolemia and the decrease in bile cholates in Group 1 indicates impaired transformation of cholesterol into bile acids during bed rest. In Groups 2, 3, and 4, hypercholesterolemia was not demonstrated, which could be related to optimization of the process of bile acid synthesis from cholesterol as a result of the preventive measures.

2. In Groups 1 and 2, the low level of bile acid was associated with high levels of total calcium and cholesterol in bile. In Groups 3 and 4, the increase of bile acid synthesis and decrease of calcium and cholesterol content of bile are factors in the decline of lithogenicity of bile. However, more studies should be done to find more effective preventive measures for normalizing the synthetic function of the liver during bed rest.

### **134. Miles, D. S., D. R. Bransford, and S. M. Horvath:**

Hypoxia effects on plasma volume shifts at rest, work, and recovery in supine posture.  
*Journal of Applied Physiology* 51:148-153, 1981.

#### **Authors' abstract**

The purpose of this study was to determine the effects of acute exposure to hypoxia (<1.5 h; gas mixture 12.6% O<sub>2</sub> -87.4% N<sub>2</sub>) has on plasma volume (PV) shifts during rest and exercise. Nine unacclimatized males performed identical protocols in the supine posture in both normoxic (N) and hypoxic (H) conditions. The protocol was rest 60 min, submaximal exercise (PWC<sub>140</sub>, work rate eliciting a heart rate of 140 beats/min) for 30 min, immediately followed by maximal exercise, and 10 min of passive recovery. There were slight but significant losses of 2.7 and 1.4% PV at rest in H and N conditions, respectively. At the same relative intensity of submaximal exercise (work loads reduced by 22% in H conditions), PV losses were nearly identical (N=11.2%, H=11.8%). There was further PV efflux subsequent to maximal exercise (N=7.9%, H=5.2%). The maximum PV efflux, from the beginning of rest to the end of maximal exercise, was 20% for both conditions. Total plasma protein (PP) content was unchanged during rest or exercise for either N or H conditions. After 10 min of recovery, restitution of PV was 10% below preexercise values for both N and H conditions. We conclude that acute hypoxic exposure does not influence the loss of PV or PP during submaximal or maximal exercise.

**135. Montgomery, L. D.:**

Body volume changes during simulated weightlessness: An overview.  
*Aviation, Space, and Environmental Medicine* 58:A80-A85, 1987.

**Author's abstract**

It has been hypothesized that many of the adaptive processes that occur in man during exposure to space involve the rapid headward shift of tissue fluids, blood, and other fluids during the first few hours of spaceflight. A total of 53 men and women between the ages of 22 and 55 years were tested during four bed rest studies lasting between 4 h and 7 d to define the segmental volume changes that took place during simulated weightlessness. Impedance plethysmography can be used to measure baseline resistance ( $R_0$ ) changes of the calf, thigh, total leg, pelvic, torso, and arm segments before, during, and after each bed rest exposure. Records of  $R_0$  were analyzed to determine the fluid volume and volume change of each segment during each test sequence.

**136. Montgomery, L. D., and D. Goldwater:**

Body fluid redistribution and volume changes during horizontal and antiorthostatic bed rest.  
*Aerospace Medical Association Preprints*, 1980. p.22-23.

**Synopsis**

*Purpose.* To better understand the segmental fluid shifts associated with weightlessness and to compare the results obtained from horizontal ( $0^\circ$ ) and antiorthostatic ( $-6^\circ$ ) bed rest (BR).

*Methods.* Ten healthy male subjects (age  $38.5 \pm 1.5$  yr) were subjected to 7 days of bed rest; one group (5 men) maintained a  $0^\circ$  BR position while the other group (5 men) was placed in a  $-6^\circ$  head-down tilt position. Subjects were tested in 2-hr sessions during a 3-day control period, the 7-day bed rest period, and a recovery period. Measurements of baseline resistance ( $R_0$ ) of the calf, thigh, total leg, pelvic, torso, arm, and total body segments were made during each test period. Segmental geometric volumes ( $V_g$ ) of the same body segments were determined. Electric impedance volumes ( $V_e$ ) were calculated from the corresponding segmental  $R_0$  values.

*Results.*

1. During BR, the  $V_e$  of the upper and lower extremities of the  $0^\circ$  group decreased. The torso and pelvic  $V_e$  values increased during the initial BR period and then returned to pre-BR values by the end of the BR period. During recovery, the  $V_e$  of all  $0^\circ$  body segments returned to their pre-BR values, but not to pre-control values.
2. The extremity  $V_e$  values of the  $-6^\circ$  group remained the same or increased slightly during the BR period. The pelvic  $V_e$  increased dramatically during the initial days of BR and then returned to pre-BR values. The torso  $V_e$ , however, increased significantly during the entire BR period.
3. The volume changes observed occurred within 24 hr of being placed in  $0^\circ$  or  $-6^\circ$  positions.
4. The calf, thigh, whole leg, and arm  $V_e$  values correlated well with  $V_g$  values when either the  $0^\circ$ ,  $-6^\circ$ , or combined subject data were considered, whereas the extent of correlations in the pelvic values between the two groups varied.

**Conclusions.** These data indicate that impedance rheography can be used to (1) demonstrate volume changes that take place in various segments of the body during the onset of bed rest, (2) determine the temporal course of these segmental changes, and (3) determine the temporal differences in fluid redistribution that occur in similar subjects who are placed in 0° or -6° head-down orientation during bed rest. These results further indicate that the segmental volumes as determined by impedance rheography compare favorably with the segmental volumes as obtained by physical anthropometry.

- 137. Mukhina, N. N., V. V. Chestukhin, V. Y. Katkov, and A. P. Karpov:**  
Effect of brief antiorthostatic hypokinesia on blood immunoglobulin content.  
*Kosmicheskaya Biologiya I Aviakosmecheskaya Meditsina* 14:74-75, 1980.

### **Synopsis**

**Purpose.** To assay immunoglobulins in blood samples from different organs, and to test the effect of head-down bed rest (BR) on immunoglobulin levels.

**Methods.** Six male subjects underwent 5 days of -4.5° head-down BR. Blood samples were collected through catheters from different parts of the cardiovascular system. IgA, IgM, and IgG were assayed by the Macini method.

### **Results.**

1. Before BR, IgM level was lower and IgA level was higher in blood flowing out of the brain than in systemic circulation; IgG level was higher in blood drained from liver ( $P < 0.05$ ).
2. After BR, a decline in IgA content was observed from brain and lower extremities.
3. The organic distribution of IgM was not affected by BR.

**Conclusions.** Brief BR causes a redistribution of the levels of immunoglobulins in blood flowing out of different organs, while their levels in the systemic circulation do not change significantly.

- 138. Muller, E. W., H. Hohlweck, G. Plath, and F. Baisch:**  
Leg volume changes. Responses to LBNP during 7 days of 0-G simulation (6° HDT).  
In: *Proceedings of the 2nd European Symposium on Life Sciences Research in Space*,  
Porz Wahn, Germany, 4-6 June, 1984. p.159-162. (ESA Special Publication 212, 1984).

### **Synopsis**

**Purpose.** To determine (1) time course of absolute leg volume responses during a 7-day 6° head-down tilt (HDT) 0-g simulation, and (2) the leg volume response to lower body negative pressure (LBNP) and its dependence on the 0-g simulation.

**Methods.** Six male volunteers (average age 23 yr) were studied as follows:

1. LBNP was applied once before (day HDT -2), once at the beginning of HDT, five times during, and twice after HDT.

2. Before each LBNP, a set of three ultrasound transducers was placed in three positions along the leg to determine leg volume (absolute volume).
3. Venous pressure was measured by transcutaneous function of a dorsal pedian vein utilizing an electromechanic pressure transducer.
4. Heart rate was obtained from ECG.

#### *Results.*

1. At the onset of negative pressure, box pressure dropped to -40 mm Hg, remained at this level for 3 min, then increased to zero.
2. Heart rate was hardly affected throughout the study period.
3. There was a configurational change during LBNP. The cross section became more circular and the circumferential line also decreased transiently but neither in the same manner nor in the same amount.
4. At the onset of negative pressure, venous pressure fell more rapidly than box pressure. An increase of venous pressure could be observed during intervals of constant box pressure and then returned to its original volume.
5. During the phase of plasma volume reduction there was an increase of leg tissue stiffness.

#### *Conclusions.*

1. The method allows measurement of leg volume changes simultaneously at several positions.
2. In connection with LBNP or occlusion cuffs the lower extremities can be tested dynamically. Changes of compliance can be assessed.
3. Since it is possible to leave the light-weight transducers in place on the leg for more than one day the accuracy of the method may be improved allowing the time course of leg volume changes to be followed. This would be useful in space flight for determination of the absolute volume shift during launch and landing.

**139. Natelson, B. H., C. DeRoshia, and B. E. Levin:**  
Physiological effects of bed rest.  
*The Lancet* 1:51, 1982.

#### **Synopsis**

*Purpose.* To determine the effects of bed rest (BR) on physiological variables in men of late middle age, a population for which bed rest is often prescribed.

*Methods.* Eight healthy male subjects (age 55-65) underwent 5 days of BR while wearing a telemetry system to monitor heart rate and core temperature. A 19 gauge "heparin lock" containing 10 units heparin/ml of normal saline was inserted into a peripheral vein of each subject, after which heart rate, core temperature, and blood pressure were again recorded. One ml of whole blood was then collected for analysis of plasma cortisol, adrenaline, and noradrenaline. This procedure was repeated every 15 min for 8 hr during two of the BR study days.



### **Results.**

1. No consistent changes were observed in the heart rate, core temperature, and plasma adrenaline during bed rest.
2. Blood pressure, plasma noradrenaline and cortisol increased significantly for the group as a result of BR.
3. There was a significant correlation between cortisol and heart rate on BR day 5 ( $r = 0.93$ ,  $p < 0.001$ ).

**Conclusions.** Bed rest produced significant increases in blood pressure and in plasma noradrenaline and cortisol for this group of late-middle-aged, healthy men. These changes have not been reported in younger men. Such small but consistent effects must be remembered when measuring these variables in sick people of similar age if confined to bed.

**140. Nikolayenko, E. M., V. Y. Katkov, S. V. Gvozdev, V. V. Chestukhin, M. I. Volkova, and M. I. Berkovskaya:**

Respiratory tract "closing volume" and structure of total lung capacity during seven-day hypokinesia in head-down position.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 17:39-43, 1983.

### **Authors' abstract**

By mass spectrography and pneumotachography structural variations in total lung capacity (TLC) were investigated in 7 test subjects during 7-day head-down tilt at  $-15^\circ$ . By the 7th hour of head-down tilt TLC, lung vital capacity, functional residual capacity (FRC) and residual volume (RV) decreased significantly and closing volume (CV) increased insignificantly. The CV/FRC ratio grew from  $0.82 \pm 0.03$  to  $1.24 \pm 0.08$  ( $p < 0.01$ ), indicating the closure of respiratory pathways in certain lung structures within the tidal volume. These changes in the TLC structure persisted till day 7 but the CV/FRC ratio fell down to  $1.01 \pm 0.07$ . The above findings can clarify the mechanism responsible for a lower oxygenation of arterial blood in the head-down position. The expiratory closure of the airways within the tidal volume causes regional changes in alveolar ventilation and ventilation-perfusion relations and, consequently, a larger venous admixture and a smaller oxygen saturation of arterial blood.

**141. Nikolayenko, E. M., V. Y. Katkov, S. V. Gvozdev, V. V. Chestukhin, M. I. Volkova, M. I. Berkovskaya, and T. G. Kediya:**

Human lung fluid content during 7-day head-down tilt.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 18:40-44, 1984.

### **Authors' abstract**

The time-course variation of the water content of the lungs of seven male volunteers were examined during 7-day head-down tilt (at  $-15^\circ$ ). As compared to the horizontal subjects, the tilted subjects showed a significant increase in the water content from  $557 \pm 19$  ml to  $612 \pm 63$  ml by the 7th hour of the tilt. Later on the parameter gradually declined and on tilt day 7 almost returned to the pretest level, i.e.,  $567 \pm 46$  ml. This can be attributed to the hydrostatic factors: higher pulmonary artery pressure and higher

cardiac output. The increase in the water content on tilt days 3-7 can be associated with changes in the permeability of lung capacities, drainage function of the lymphatic system of the lungs and colloidal-osmotic pressure in the perivascular space of the lungs.

- 142. Nishijima, H., H. Yasuda, K. Ito, R. Murakami, K. Hayashi, M. Yamazaki, and K. Hattori:**  
Acute and chronic hemodynamic effects of the basic therapeutic regimen for congestive heart failure: Diuretics, low salt diet and bed rest.  
*Japanese Heart Journal* 25:571-585, 1984.

#### **Authors' abstract**

The acute and chronic hemodynamic effects of the "basic regimen" for congestive heart failure (CHF), consisting of diuretics (furosemide) low salt diet and bed rest, was studied in 10 patients with CHF (all in NYHA class IV initially). In the acute stage, furosemide 80 mg i.v. effected rapid clinical improvement with reduction in ventricular filling pressure (VFP); however, no increase in cardiac-(CI) or stroke volume index (SVI) was observed. Subsequently, furosemide 80 mg/day, p.o. was administered for a mean of 30 days with the patients hospitalized on a low salt diet. During this period, their clinical condition was stable. The second hemodynamic study revealed that SVI increased ( $p < 0.05$ ) with reduction in VFP maintained. Next, low molecular weight dextran was infused to construct the Frank-Starling ventricular function curve (VFC) and this was compared with the VFC at the acute stage (during diuresis). As a whole, CI and SVI at the chronic stage were significantly increased ( $p < 0.05$ ) at equal pulmonary wedge pressure (PWP: mean 20 mmHG). Mean arterial pressure and systemic vascular resistance were decreased during the chronic stage. These findings suggest that the "basic CHF regimen" is effective on a chronic basis in improving left ventricular pump function through afterload and preload reduction, in addition to acute symptomatic relief due to a decrease in PWP.

- 143. Norsk, P., F. Bonde-Petersen, and J. Warberg:**  
Cardiovascular effects of clonidine during 20 hr head-down tilt ( $-5^\circ$ ).  
*The Physiologist* 24:S91-S92, 1981.

#### **Synopsis**

**Purpose.** To investigate the cardiovascular effects of clonidine during bed rest (BR) and the effects of clonidine on orthostatic tolerance and exercise capacity before and after BR.

**Methods.** Five young healthy males were subjected to 20 hr of  $-5^\circ$  head-down BR. Arterial pressures, heart rate, forearm blood flow (FBF), specific venous compliance (SVC), cardiac output (CO), lung tissue volume (LTV), antidiuretic hormone (ADH) plasma level, relative change in plasma volume, and orthostatic tolerance were measured. While exercising at submaximal and maximal capacity levels on a cycle ergometer, subjects' heart rates and oxygen uptake values were measured. The subjects received an oral dose of clonidine 24 hr before the experiment. The above procedure was repeated twice: once with clonidine and once without (control).

### **Results.**

1. Mean arterial pressure did not change during clonidine (CLO) as compared to the control without clonidine. CLO lowered heart rate and cardiac output, and increased stroke volume.
2. BR increased mean arterial pressure, and heart rate and cardiac output were lower during BR + CLO than in the control situation.
3. CLO increased forearm vascular resistance (FVR) as well as total peripheral resistance (TPR) pre-BR. CLO had no further significant influence on FVR during BR. CLO decreased specific venous compliance (SVC) in the supine position and increased the lung tissue volume (LTV). Venous tone was also increased.
4. During submaximal exercise, heart rate was increased both with and without CLO (at a lower level with CLO).
5. CLO did not affect orthostatic tolerance, while BR decreased this parameter.

**Conclusions.** The stress induced by 20 hr BR is counteracted by the central depressor effect of CLO on the heart. The peripheral effect of CLO increasing FVR, venous tone, and LTV enhances the adaptation to the  $\mu$ -G condition.

**144. Noskov, V. B., G. I. Kozyrevskaya, B. V. Morukov, Y. M. Artamosova, and L. A. Rustam'yan:**

Body position during hypokinesia, and fluid-electrolyte metabolism.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 19:31-34, 1985.

### **Authors' abstract**

Two groups of 5 healthy volunteers each were exposed for 7 days to: 1) group 1 to horizontal bed rest and 2) group 2 to head-down tilt at  $-6^\circ$ . The purpose of the study was to determine the effect of body position on fluid-electrolyte metabolism and renal function. During the control period (14 days), bed rest and the recovery period the consumption of fluids and mineral substances and their renal excretion were measured. The typical changes in fluid-electrolyte metabolism during head-down tilt developed faster than during horizontal bed rest. The fluid-electrolyte balance became negative in the course of the exposure and returned to normal during the recovery period. The group 2 subjects showed greater body weight losses due to both fluid and muscle losses.

**145. Oganov, V. S., A. S. Rakhmanov, B. V. Morukov, K. A. Yanson, A. M. Tatarinov, V. Y. Zaychik, S. K. Ternovoy, and C. Cann:**

Noninvasive examination of bones during long-term hypokinesia.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 22:30-33, 1988.

### **Synopsis**

**Purpose.** To make a comparative evaluation of demineralization in different parts of the skeleton during long-term hypokinesia to assess the efficacy of experimental means of preventing adverse changes in bone, and to compare the results of densitometric and ultrasonic tests.

### **Methods.**

1. Twenty-five volunteer subjects were divided into four groups:
  - Group 1: (control): three subjects (bed rest (BR) only)
  - Group 2: four subjects (BR + pharmaceutical agent)
  - Group 3: four subjects (BR + exercise)
  - Group 4: four subjects (BR + exercise + pharmaceutical agent).
2. The pharmaceutical agents given to the subjects were xydiphone, tocopheral, glucamak, solizim, and F-99.
3. Four modes of exercise for muscles of the leg, thigh, back, and neck were used. These involved speed, force, speed and force, and passive extension of antigravity muscle groups. Cycle ergometers, isokinetic equipment, and expanders were used for the exercises.

### **Results.**

1. Calcium loss in skeletal bones was not more than 0.5% per month; Ca<sup>+</sup> loss in leg tubular bones was 1% to 2% per month in six test subjects; and Ca<sup>+</sup> loss in heel bones was on the average 3% to 4% per month in the control, exercise, and combination groups.
2. No strict correlation between the negative balance of calcium and mineral content in leg compact bones and foot spongy bones was found.
3. There was a correlation between changes in the mineral content of leg bones and ultrasound propagation along certain compartments of the tibial median surface.
4. In terms of negative and positive trends, leg and foot bones were in better condition in the drug group.

**Conclusions.** The results of the investigation basically coincide with the findings of other studies. In addition, the chosen set of pharmaceutical agents neutralizes skeletal demineralization well. Unfortunately, no statistically reliable data were obtained to identify the principal sources of calcium loss under hypokinesia.

### **146. Panferova, N. Y., and T. A. Kabesheva:**

Fluid dynamics in human limbs in different body positions.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 21:40-45, 1987.

### **Synopsis**

**Purpose.** To examine the effect of horizontal and head-down bed rest on fluid distribution in the body.

**Methods.** Ten healthy male subjects (age 25-40) were divided into four groups:

Group 1 (control) maintained normal ambulatory activity for 4 hr, and assumed a horizontal position for 15 min each hr for measurements.

Groups 2, 3, & 4 spent 4 hr in a horizontal position, head-down tilt (HDT) of -12°, and HDT of -22°, respectively.

Anthropometric measurements of the limbs were made and plethysmography was performed in the calf and forearm. Occlusion plethysmography was also performed to determine the minute volume of blood flow in the limbs.

### **Results.**

1. The horizontal position or HDT led to a decrease in calf volume. Change in position from horizontal to HDT led to significantly smaller fluid shifts.
2. Leg volume continued to decrease over the 4-hr period during bed rest at a rate proportional to body angle.
3. Changes in arm volume were not significant.
4. Significant decreases in minute volume of blood flow were found in both arms and legs in all conditions. Decreases were less pronounced in arms than in legs.
5. Influx of blood into the legs was also decreased; the difference between  $-22^\circ$  and horizontal was significant.

**Conclusions.** The peripheral vascular bed plays an important role in adaption to horizontal and HDT positions. In addition, in horizontal and less extreme tilt positions there are effective mechanisms for regulating fluid shifts to prevent overfilling of the central vascular bed.

### **147. Pequinot, J. M., A. Güell, G. Gauquelin, E. Jarsaillon, G. Annat, A. Bes, L. Peyrin, and C. Gharib:**

Epinephrine, norepinephrine, and dopamine during a 4-day head-down bed rest.  
*Journal of Applied Physiology* **58**:157-163, 1985.

### **Authors' abstract**

Head-down bed rest at an angle of  $6^\circ$  was used as an experimental model to simulate the hemodynamic effects of microgravity, i.e., the shift of fluids from the lower to the upper part of the body. The sympathoadrenal activity during acute (from 0.5 to 10 h) and prolonged (4 days) head-down bed rest was assessed in eight healthy men ( $24 \pm 1$  yr) by measuring epinephrine (E), norepinephrine (NE), dopamine (DA), and methoxylated metabolite levels in their plasma and urine. Catecholamine (CA) and methoxyamine levels were essentially unaltered at any time of bed rest. Maximal changes in plasma were on the second day (D2): NE,  $547 \pm 84$  vs.  $384 \pm 55$  pg/ml; DA,  $192 \pm 32$  vs.  $141 \pm 16$  pg/ml; NS. After 24 h of bed rest, heart rate decreased from  $71 \pm 1$  to  $63 \pm 3$ /min ( $P < 0.01$ ). Daily dynamic leg exercise [50% maximum  $O_2$  uptake ( $\dot{V}O_{2\max}$ )] used as a countermeasure did not alter the pattern of plasma CA during bed rest but resulted in higher urinary NE excretion during postexercise recovery (+45% on D2;  $P < 0.05$ ). The data indicated no evident relationship between sympathoadrenal function and stimulation of cardiopulmonary receptors or neuroendocrine changes induced by central hypervolemia during head-down bed rest.

**148. Pequinot, J. M., A. Güell, G. Gauquelin, M. H. Mayet, J. L. Bascands, A. Bes, L. Peyrin, and C. Gharib:**

Time course of plasma levels of norepinephrine, epinephrine, and dopamine during a 4-day head-down tilt.

In: *Space Physiology*; edited by J. Garcia, M. Guerin, and C. Laverlochere. Toulouse, France: 1983. p.453-459.

(Same as Pequinot, J. M., A. Güell, G. Gauquelin, L. Peyrin, A. Bes, G. Annat, and C. Gharib. Plasma levels of norepinephrine, epinephrine, and dopamine during a 4-day head-down tilt with and without exercise. *The Physiologist* 26:S100-S101, 1983.)

**Synopsis**

**Purpose.** To determine the effects of short-term and long-term head-down tilt on plasma catecholamine levels. In a second group of subjects, the effects of regular exercise and its possible use as a countermeasure in association with bed rest were tested.

**Methods.** Eight healthy male subjects ( $24.1 \pm 0.4$  yr) participated in the study, and were divided randomly into two groups. Group I underwent head-down tilt for 5 days without exercise. Blood samples were taken twice a day, in the morning and at night. Group II was submitted to the same experimental design, but in addition, exercised in the supine position on a cycle ergometer for two 1-hr periods daily. Plasma catecholamine levels were determined for Groups I and II.

**Results.**

1. The plasma catecholamine levels were not affected by either short-term or prolonged bed rest.
2. Head-down bed rest and exercise resulted in no significant change in plasma norepinephrine levels by bed rest day 5, and did not affect epinephrine and dopamine levels.

**Conclusions.** Neither short-term nor prolonged head-down tilt altered sympatho-adrenal activity. There is therefore no evident relationship between peripheral sympathetic nerve function, as assessed by plasma catecholamine measurements, and stimulation of cardiopulmonary receptors or neuroendocrine changes induced by head-down tilt.

**149. Podrushnyak, E. P., and E. I. Suslov:**

Changes in bone tissue under conditions of hypokinesia and in connection with age.

NASA Technical Memorandum 76154, 1980. p.1-5. (Translation of Zmini kistkovoï thanini v umonakh hipokinezii ia v zv'yazku z vikom, *Fiziologichnyy Zhurnal* 19:841-843, 1973.)

**Synopsis**

**Purpose.** To study changes in the density of bone under conditions of bed rest and as a function of age.

**Methods.** X-ray micrograph method was used to study optical density (degree) of blackening of X-ray photographs of five bones (not specified) in nine people aged 24-29 yr before and after hypokinesia (strict bed rest confinement for 16-37 days).

X-ray structural analysis (studying the structure of the crystalline matter with the aid of X-ray interference) was used to investigate the cortical layer of the diaphysis of femurs from 25 cadavers of healthy individuals aged 18-70 yr who died from various injuries.

*Results.*

1. Subjects with a high initial bone density showed a 20-25% reduction in the concentration of bone matter during the period of observation (37 days). However, subjects with a low initial bone density showed a 15-24% increase in the concentration of bone matter during the same observation period.

2. It was also established that stabilization of the crystalline structure of hydroxyapatite, especially the formation of its crystals, is finished by the age of 20-25 yr. From 25 to 60 yr the crystalline lattice remains stable but a reduction in the hydroxyapatite density does occur.

*Conclusions.* Bone tissue is a highly dynamic structure and can change not only with age, but also in a relatively short period of time. A change in body position (state of hypokinesia) with respect to the gravitational field leads to essential disruption in bone (density) structures. These changes in bone tissue of different individuals are not uniform.

**150. Polese, A., D. Goldwater, L. London, D. Yuster, and H. Sandler:**

Resting cardiovascular effects of horizontal (0°) and head-down (-6°) bed rest (BR) on normal men.

*Aerospace Medical Association Preprints*, 1980. p.24-25.

**Synopsis**

*Purpose.* To describe the functional and dimensional cardiac changes that occur during bed rest (BR), and to compare the changes induced by horizontal to head-down BR.

*Methods.* Ten healthy males (age 35-40) underwent 14 days of ambulatory control and 7 days of BR, followed by 10 days of recovery. Subjects were randomly allocated to two groups; one group was horizontal (0°) during BR and the other group was in a -6° head-down position. Cardiovascular measurements were made with subjects in the horizontal position on various days of the control, BR and recovery periods. Electrocardiogram (ECG), vectocardiogram (VCG), echocardiogram (Echo), left ventricular systolic time intervals (STI), and mean arterial blood pressure (MAP) were recorded.

*Results.*

1. Neither VCG nor STI changed significantly during BR. Neither was affected by body position.

2. MAP increased in both groups during BR, but changes were more significant in the -6° group than in the 0° group.

3. Stroke volume and cardiac output changes, two variables measured or derived from the Echo, were closely related since heart rate did not alter significantly during the study. Heart rate, systolic diameter and volume, and cardiac output showed gradual declines at least to the second day of BR.

*Conclusions.* The results obtained suggest that 0° and -6° head-down BR do not affect the electrical activity of the heart to an extent detectable with ECG, STI, and VCG, which is a more sensitive

indicator. These findings rule out major myocardial metabolic disturbances occurring as a consequence of BR between 0° and -6° head-down.

**151. Popov, I. G., and A. A. Latskevich:**

Blood plasma free amino acids under hypokinetic conditions.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 18:25-34, 1984.

**Authors' abstract**

The study (in a Hitachi KLA-3B analyzer) of 17 free amino acids in plasma of six healthy men under ambulatory and hypokinetic conditions demonstrated the following trend: by day 15 of clinostatic hypokinesia the content of most amino acids increased and by day 30 decreased, reaching the pretest level or falling below it. These variations in the amino acid concentration are viewed as a consequence of the modified relations between anabolic and catabolic processes induced by adaptation to hypokinesia. It is emphasized that the nutrition pattern was different in the hypokinetic study.

**152. Popov, I. G., and A. A. Latskevich:**

Human blood free amino acids at early stage of head-down tilt.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 20:46-54, 1986.

**Synopsis**

*Purpose.* To study the levels of essential and nonessential amino acids in blood plasma of subjects during the early stages of head down tilt.

*Methods.* Six healthy men (age 20) underwent 7 days of -10° head-down tilt. Subjects were kept on a restricted diet, similar to that of the cosmonauts, and blood was drawn during the control, bed rest (BR), and recovery periods. Amino acid concentration in plasma was then assayed.

*Results.*

1. During the first 3 days of BR the increase in concentrations of all amino acids with the exception of tyrosine, alanine, and glycine was significant ( $P < 0.001$ ) as compared to the control plasma amino acid levels.

2. After 7 days of BR the concentrations of all amino acids, both the means for the group ( $P < 0.001$ ) and for each subject individually, were higher than during the control period.

3. Total essential amino acids increased, while nonessential amino acids stayed the same.

4. During the recovery period, the sum of the essential amino acids ( $P < 0.001$ ) and sum of the nonessential amino acids were lower ( $P < 0.05$ ) than during the control period. By the end of recovery the plasma levels of amino acids corresponded essentially to the control levels.

*Conclusions.* Even in the early stage of -10° HDT, there was a reliable increase in concentrations of most free amino acids in all of the subjects. This could be due to various factors: excessive intake of amino acids with food, as compared to metabolic requirements; decreased intensity of protein synthesis under hypokinetic conditions; development of catabolic processes in muscle tissues associated with



breakdown of proteins; signs of stress of immobilization; and/or increases in plasma amino acid concentrations related to signs of dehydration in the acute period of adaptation to HDT.

**153. Popova, I.A.:**

Blood serum enzyme activity in healthy men with simulation of effects of weightlessness.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 20:71-75, 1986.

**Author's abstract**

The enzymatic activity of blood of healthy male volunteers was examined during 8-day bed rest in the horizontal and head-down ( $-6^\circ$ ) position, water immersion up to the neck and 6-hour head-down tilt ( $-15^\circ$ ). Alkaline phosphatase, cholinesterase (CE), leucine arylamidase (LA), glutamate dehydrogenase (GDH), and gamma-glutamyl transpeptidase (GGTP) were measured. During horizontal bed rest the activities of all the enzymes, except for GDH, decreased in a moderate degree which was very distinct at an early stage of exposure. The activity of GDH and CE decreased significantly after the exposure. The enzymatic activity tended to decline during head-down tilt at  $-6^\circ$ . The LA and GGTP activity decreased to a greater extent, being statistically significant during head-down tilt at  $-6^\circ$  and in the recovery period. The enzymatic activity insignificantly increased during water immersion and 6-hour head-down tilt at  $-15^\circ$ , remaining in some cases elevated during 5 days after exposure. The lower activity of enzymes (which was significant for some of them) during horizontal and antiorthostatic bed rest was primarily associated with diminished motor activity, whereas increased enzymic activity was related to the gravity-induced blood shift to the intrathoracic area.

**154. Popova, I. A., B. V. Morukov, and A. S. Ushakov:**

Metabolic changes during prolonged antiorthostatic hypokinesia.  
In: *Proceedings of the 2nd International Conference on Space Physiology*, Toulouse, France, 20-22 November, 1985. p.167-172. (ESA Special Publication 237, 1986).

**Authors' abstract**

The 120-day head-down tilt test ( $-5^\circ$ ) of nine healthy male volunteers, aged 25-44, led to a negative balance of water and electrolytes with calcium losses of 5 g per month. Changes in the ionic composition of blood included a decrease of potassium and an increase of the total calcium and its ionized fraction. Weight losses averaged 1.8 kg, primarily due to muscle losses which were responsible for changes in protein homeostasis. The content of free amino acids increased, total protein decreased (mainly due to the decrease of albumins), the content of nitrogen products of protein metabolism increased although their renal excretion remained unchanged. The prolonged antiorthostatic exposure led to new level of tissue metabolism which was indicated by a change in the activity of blood enzymes. The isoenzymic specificity suggested that metabolic changes occurred primarily in bones and muscles.

- 155. Putch, L., N. M. Cintron, J. M. Vanderploeg, Y. Chen, J. Habis, and J. Adler:**  
Effect of antiorthostatic bed rest on hepatic blood flow in man.  
*Aviation, Space, and Environmental Medicine* 59:306-308, 1988.

**Authors' abstract**

Physiological changes that occur during exposure to weightlessness may induce alterations in blood flow to the liver. Estimation of hepatic blood flow (HBF) using ground-based weightlessness simulation models may provide insight into functional changes of the liver in crewmembers during flight. In the present study HBF, indirectly estimated by indocyanine green (ICG) clearance, is compared in 10 subjects during the normal ambulatory condition and antiorthostatic ( $-6^\circ$ ) bed rest. Plasma clearance of ICG was determined following intravenous administration of a  $0.5 \text{ mg} \cdot \text{kg}^{-1}$  dose of ICG to each subject on two separate occasions, once after being sealed for 1 h and once after 24 h of head-down bed rest. After 24 h of head-down bed rest, hepatic blood flow did not change significantly from the respective control value.

- 156. Samel, A., and F. Baisch:**  
Heart-rate variability during 7-day head-down tilt ( $6^\circ$ ).  
In: *Proceedings of the 2nd European Symposium on Life Sciences Research in Space*, Porz Wahn, Germany, 4-6 June, 1984. p.163-167. (ESA Special Publication 212, 1984).

**Authors' abstract**

We report on measurements of heart rate variability, body temperature and changes in the excretion rates of hormones during simulation of weightlessness over seven days. Peak-to-peak intervals of heart rate show a significant increase on the first day of simulation and a significant decrease on the first two days after simulation. The excretion of hormones alters distinctly during the simulation period. It is concluded that these alterations were induced by parasympathetic activities.

- 157. Sandler, H., D. J. Goldwater, R. L. Popp, L. Spaccavento, and D. C. Harrison:**  
Beta blockade in the compensation for bed-rest cardiovascular deconditioning: Physiologic and pharmacologic observations.  
*American Journal of Cardiology* 55:114D-119D, 1985.

**Authors' abstract**

Beta-adrenergic blockade using intravenous propranolol was evaluated as countermeasure for bedrest-induced cardiovascular deconditioning. After propranolol administration, tolerance to a maximal lower body negative pressure (LBNP) test after bed rest improved to at least the  $-70 \text{ mm Hg}$  level; following this, there was a sharp decrease in tolerance time. Propranolol decreased mean tolerance time by 36% ( $17.7 \pm 2.4$  to  $11.5 \pm 2.3$  minutes) before bed rest, and by only half as much (16.6%) after bed rest ( $14.4 \pm 2.2$  to  $12.0 \pm 2.3$  minutes). Systemic vascular resistance was maintained and even slightly increased after propranolol despite a decrease in cardiac output, indicating beta<sub>2</sub>-adrenergic blockade. Heart rates at all levels of LBNP were lower during beta blockade, yet increases occurred with successive LBNP steps, both before and after bed rest, indicating withdrawal of parasympathetic nervous system influences.

Results support the use of propranolol in small dosages as a countermeasure after bed rest, and the findings may also be extrapolated to space-flight deconditioning.

**158. Sandler, H., R. L. Popp, and D. C. Harrison:**

The hemodynamic effects of repeated bed rest exposure.

*Aviation, Space, and Environmental Medicine* 59:1047-1054, 1988.

**Authors' abstract**

Hemodynamic changes were measured during stepwise exposure to lower-body negative pressure (LBNP) (5 min, -20, -30, and -40 mmHg) in a group of seven physically active subjects before and after consecutive exposure to three 2-week bed rest periods. Bed rest exposures were separated by 3-week periods of ambulatory recovery. Dynamic exercise (68% max O<sub>2</sub>, 60 min each day) and isometric exercise (21% max leg extension, 60 min each day) performed during bed rest and reambulation failed to prevent deconditioning or accelerate the recovery process between bed rest exposures. Heart rate (HR) and end-diastolic volume index (EDVI) proved to be parameters showing greatest changes during LBNP. Heart rate increases at -40 mmHg LBNP (compared to respective pre-LBNP levels) were 13.3%, 35.1%, and 51.0% for each of the pre-bed rest exposures, while respective changes after bed rest were 57.8%, 57.2%, and 75.5%. The significantly elevated HR responses during subsequent pre-bed rest (control) periods indicated incomplete recovery despite mild exercise and ambulation. Comparison of EDVI and HR revealed a similar linear regression relationship during LBNP before and after bed rest so that  $EDVI = 112.5 - 0.85 \times HR$ ,  $r = -0.97$ . We conclude from these findings that cardiovascular deconditioning for physically active individuals involves factors other than simple loss of plasma volume, requires at least 3 weeks or longer to return to the pre-bed rest state, and is not counteracted by the levels of aerobic and/or isometric exercise used in the present study.

**159. Sandler, H., P. Webb, J. Annis, N. Pace, B. W. Grunbaum, D. Dolkas, and B. Newsom:**

Evaluation of a reverse gradient garment for prevention of bed- rest deconditioning.

*Aviation, Space, and Environmental Medicine* 54:191-201, 1983.

**Authors' abstract**

A Reverse Gradient Garment (RGG) was used to intermittently induce venous pooling in the extremities of a magnitude similar to that seen in going from a lying to standing position during the course of a 15-d period of horizontal bed rest. Venous pooling failed to improve bed-rest-induced losses in +2.5 G<sub>z</sub> and +3.0 G<sub>z</sub> centrifugation tolerance or to prevent increased heart rate responses to lower body negative pressure (LBNP). Four subjects served as controls, four were treated. Tests during the 7-d recovery period showed fluid/electrolyte and body composition values to have returned to pre-bed-rest levels with continued depression of acceleration tolerance times (56% decreased at +2.5 G<sub>z</sub> and 74% decreased at +3.0 G<sub>z</sub> compared to pre-bed-rest levels) and exaggerated blood insulin for treated group increased 95% at 1 h before bed rest and 465% during recovery). This study demonstrates that the physiologic changes after bed rest persist for significant periods of time. Acceleration tolerance time proved to be a sensitive test for the deconditioning process.

- 160. Saunders, M. C., J. S. Dick, I. M. Brown, K. McPherson, and I. Chalmers:**  
The effects of hospital admissions for bed rest on the duration of twin pregnancy: A randomized trial.  
*The Lancet* 2:793-795, 1985.

**Synopsis**

*Purpose.* Women with twin pregnancies who were prescribed bed rest (BR) in a hospital from 32 wk gestation until delivery were compared to women who were admitted usually 5 wk later.

*Methods.*

1. 212 women with twin pregnancies were admitted for BR in a hospital from 32 wk gestation until the onset of labor (105 women), or to be part of a control group in which hospital admission would be selective as necessary (107 women).
2. Data were collected from the patients' clinical case records, and assessment of duration of gestation at delivery was made by the hospital staff.

*Results.*

1. The mean duration of gestation for the 105 women allocated to BR was 32.7 weeks, whereas that of the control group was 37.4 weeks.
2. Labor was induced in 6 cases, all in the control group.
3. Preterm delivery was more common for the women undergoing BR. There were also more perinatal deaths in this group, but this may have been by chance.
4. There were more very-low-weight births in the BR group than in the control group.

*Conclusions.* The results of this study are consistent with those of two similar previous studies. Prescribing hospital BR in the third trimester of twin pregnancy increases the incidence of preterm delivery. A possible explanation may be the anxiety and stress associated with admission to a hospital. Hospital BR in twin pregnancy should therefore be used far more selectively, and should be restricted to women with other complications for which hospitalization may be beneficial.

- 161. Savilov, A. A., V. M. Mikhailov, and A. I. Grigoriev:**  
Relationship between cardiovascular functions and fluid-electrolyte metabolism during antiorthostatic hypokinesia.  
In: *Proceedings of the 2nd International Conference on Space Physiology*, Toulouse, France, 20-22 November, 1985. p.181-186. (ESA Special Publication 237, 1986).

**Authors' abstract**

This paper presents the results of investigations of the cardiovascular function and fluid-electrolyte metabolism in healthy men exposed to head-down tilt (HDT) tests of 7 days to 6 months in duration. During the first hours and days of exposure the cardiovascular changes were associated with hemodynamic shifts typical of this simulation procedure while fluid-electrolyte changes were manifestations of the compensatory-adaptive reactions aimed at maintaining an adequate circulatory homeostasis. As the exposure continued for several months, the cardiovascular changes, particularly cardiovascular deconditioning, were produced by the effect of hypokinesia as such. In this situation changes in

fluid-electrolyte balance were one of the major factors responsible for cardiovascular disorders. Water-salt supplements combined with other countermeasures may help decrease significantly the adverse effects of antiorthostatic hypokinesia and weightlessness on the human body.

**162. Schneider, V. S., and J. McDonald:**

Skeletal calcium homeostasis and countermeasures to prevent disuse osteoporosis.  
*Calcified Tissue International* 36:S151-S154, 1984.

**Authors' abstract**

Maintenance of a skeleton capable of resisting the stresses of everyday life is dependent on the mechanical forces applied to the skeleton during normal activity in a 1-g environment. When the effects of 1-g on the longitudinal skeleton are removed, as with space travel or inactivity, bone and bone mineral are lost because bone resorption is greater than bone formation.

Ninety healthy young men were studied during 5-36 weeks of continuous bed rest. During inactivity, urinary calcium increases rapidly and by the sixth week of bed rest, output has risen by 100 mg/day, plateaus for several weeks, and then decreases but remains above ambulatory baseline thereafter. This occurred even though they received vitamin D supplements throughout the study. Calcium balance becomes negative after 2 weeks and by the end of the first month, 200 mg/day is lost. The loss continues at this rate for at least 36 weeks. Calcaneal mineral loses 5% of its mass each month. Attempts to prevent disuse osteoporosis with both mechanical and biochemical means, including exercise, skeletal compression, increased hydrostatic pressure to the lower body, supplemental calcium and/or phosphorus, calcitonin, or etidronate were not useful.

**163. Semenov, V. Y.:**

Effect of spaceflight factors on hormonal regulation of fluid-electrolyte metabolism.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 19:6-8, 1985.

**Authors' abstract**

This paper presents the results of examinations of 19 test subjects exposed to head-down tilting at  $-8$  and  $-15^\circ$  and of 14 test subjects kept in water immersion for 24 hours. During the first hours of exposure the renal excretion of water and monovalent ions increased. Renin and aldosterone measurements showed that changes in the sodium and potassium excretion were produced by a lower activity of the renin-angiotensin-aldosterone system in the first 1.5 hour of hypokinesia. During immersion the renal excretion of calcium and magnesium also grew, especially in the evening and at night. The PTH production and calcium concentration in blood increased, thus augmenting the nephron load. The diurnal rhythms of the renal excretion of potassium, calcium, and magnesium remained unchanged and those of water, osmotically active substances and sodium varied. The data obtained indicate significant changes in water-salt metabolism and its regulation within the first hours of head-down tilt and water immersion.

- 164. Shen, X. Y., Y. H. Sun, Q. L. Xiang, J. R. Meng, L. H. Xu, X. X. Yan, H. F. Yu, and X. C. Zhuang:**  
The study of baroreceptor reflex function before and after bed rest.  
*The Physiologist* 31:S22-S23, 1988.

**Authors' abstract**

In order to investigate the mechanism of the lowering of orthostatic tolerance (OST) after exposure to weightlessness (WL), the changes of baroreceptor reflex function (BRF) of the two groups, 2° head-down group (n=7) and sit-up group (n=7), were studied before and after the bed rest (BR). The open-loop gain (G) was calculated during the head-up tilt (HUT) and HUT plus LBNP (-5333 Pa) before and after BR. The frequency spectrum changes of R-R intervals (RI) were also compared during neck positive pressure and LBNP between the two groups. The result was that the changes of G and RI and lowering of OST were different between the two groups after BR. Thus it indicated that the declination of BRF, which probably resulted from the change of function state of CNS, was one of the important causes responsible for the lowering of OST after WL or simulated WL.

- 165. Smirnov, K. V., I. L. Medkova, O. V. Zhiznevskaya, V. P. Bychkov, L. I. Mosyakina, and O. S. Khokhlova:**  
Some parameters of human lipid metabolism during antiorthostatic hypokinesia and their correction.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 20:34-37,1986.

**Synopsis**

*Purpose.* To investigate the basic classes of lipids in blood serum and cholesterol in human bile during long-term antiorthostatic hypokinesia, as well as the correction of demonstrated changes.

*Methods.* Twenty-one healthy men (30-40 yr) underwent 120 days of -4.5° head-down bed rest (BR). The subjects were divided into four groups:

Group 1 (control): Nine subjects maintained BR without use of preventive measures.

Group 2: Four subjects performed a set of exercises during BR.

Group 3: Four subjects were given vitamin F-99 three times a day from day 72 to day 120 of BR.

Group 4: Four subjects took vitamin F-99 from day 72 of BR on, combined with exercise.

Vitamin F-99 contains polyunsaturated fatty acids. Blood was drawn on various days of the control, BR and recovery periods. Bile and serum cholesterol content as well as lipoprotein fractions were assayed.

*Results.*

1. In Group 1, total serum lipid levels changed insignificantly but showed a tendency to increase. There was a significant increase in blood cholesterol ester content. Serum phospholipids decreased, serum nonesterified fatty acids decreased significantly, and there was a lower percentage of alpha-lipoprotein fraction during BR.

2. The changes in Group 2 were as in Group 1. However, total lipid content increased more.

3. Hypophospholipidemia was less marked in Group 3. No statistically significant changes in alpha- and beta-lipoprotein fractions were observed. Cholesterol ester levels dropped to control values after vitamin F-99 intake.

4. Hypercholesterolemia was the most marked in Group 4. After vitamin F-99 was ingested, the previously high serum cholesterol level decreased to the control level. Serum total lipid levels also dropped. There was no decrease in phospholipid concentration, and the decrease in alpha-lipoproteins was less marked in this group. Nonesterified fatty acids showed virtually no change.

5. There was increased elimination of cholesterol in Groups 1 and 2 as shown by bile cholesterol content assays. Vitamin F-99 had no effect on this process.

**Conclusions.** The ingestion of a product containing polyunsaturated fatty acids (i.e., vitamin F-99) during BR leads to beneficial changes in lipid metabolism, particularly that of cholesterol and phospholipids, as seen in the fourth group of subjects.

- 166. Smirnova, T. M., G. O. Kozyrevskaya, V. I. Lobachik, V. V. Zhidkov, and S. V. Abrosimov:** Individual distinctions of fluid-electrolyte metabolism during hypokinesia with head-down tilt for 120 days, and efficacy of preventive agents.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 20:21-24, 1986.

### **Synopsis**

**Purpose.** To study sodium balance and distribution of fluid during long-term bed rest with and without pharmacological agents and exercise.

**Methods.** Fifteen healthy male subjects (24 to 40 yr) underwent 120 days of  $-5^{\circ}$  head-down bed rest (BR):

- Group 1: Four men took pharmacological agents (PA).
- Group 2: Four men exercised during BR.
- Group 3: Four men combined intake of PA and exercise.
- Group 4 (control): Three men did not use any countermeasures.

Groups 1 and 3 underwent ultraviolet irradiation. There was a 32 day control period, during which baseline levels and body fluid volumes were measured. Mineral composition of diet and feces, total fluid volume, extracellular and intracellular fluid volume, interstitial fluid volume, and circulating plasma volume were determined.

### **Results.**

1. All subjects in Group 1 had a positive sodium balance by the end of the study. Intracellular fluid volume was also elevated.
2. Subjects in Groups 2, 3, and 4 showed a negative sodium (Na) balance, and intracellular fluid volume was decreased.
3. There was a decrease for all groups in all other parameters measured with the exception of circulating plasma volume for Group 2, which increased by the end of the study.
4. Intake of PA led to complicated changes in fluid-electrolyte metabolism, resulting in an elevated Na balance and intracellular fluid volume.

5. Exercise had the opposite effect on Na balance and intracellular fluid volume as compared to PA. Both parameters were lower in Group 2 as compared to Group 4, and in Group 3 as compared to Group 1.

**Conclusions.** The levels of Na in extracellular fluid indicate that Na could possibly be accumulating in tissues. The authors were not able to determine the exact tissue in which Na and fluid accumulate but speculate that the probable site of deposition is connective tissue. The dissimilar effects of pharmacologic agents and exercise are due to the fact that the "targets" for these factors are different. PA affects cell metabolism whereas exercise affects blood volume.

**167. Smolinsky, A., R. Mohr, and D. A. Goor:**  
Beneficial effects of feet-down bed position in nocturnal angina.  
*International Journal of Cardiology* 3:251-255, 1983.

### **Synopsis**

**Purpose.** To determine the effect of reverse Trendelenburg tilt of the bed on relieving nocturnal angina pain in pre-surgery patients.

**Methods.** The effect of 10° reverse Trendelenburg tilt of the bed was studied in 10 patients with refractory nocturnal angina on 2 consecutive nights before aortocoronary bypass surgery. The patients were restricted to bed rest. For the control night the bed was placed in the horizontal position, with the head up; on the test night the bed was placed in a 10° reverse Trendelenburg position. Intra-arterial (systemic), central venous, and flow-guided balloon catheter pulmonary artery pressures were measured every hour during the study and at the onset and end of every episode of chest pain. Sublingual isosorbide dinitrate (5 mg) was given to relieve angina attacks and all previously prescribed drug therapy continued throughout the study period. Sleep patterns were similar during both nights of the study.

**Results.** The number of nocturnal angina episodes during the control night averaged 3.7/patient/night (range 2-7), whereas in the test group it averaged 0.2 (range 0-2). These improvements are highly significant ( $P < 0.001$ ). Central venous pressure in the control group was  $9.9 \pm 4.6$ , and  $3.9 \pm 2.6$  in the test group ( $P < 0.03$ ). Systolic pulmonary artery pressure was  $21.7 \pm 6.6$  mmHg in the control and  $16.0 \pm 6.0$  mmHg in the test group ( $P < 0.03$ ); diastolic pressure was  $11.0 \pm 3.6$  mmHg in the control and  $6.2 \pm 2.5$  mmHg in test group ( $P < 0.03$ ). Aortic pressure did not change significantly.

**Conclusions.** The fall in central venous and pulmonary artery pressures and the relief of chest pain in all 10 patients on the test night reflects a decrease in venous return to the heart. Of the basic theories for explaining nocturnal angina, namely coronary vasospasm, peripheral vasoconstriction, elevation of blood pressure, oxygen demand, and transient increase in left ventricular filling pressures, an increase in filling pressures seems to be the most likely. Lowering the patient's filling pressure by tilting the bed to a feet-down position can nearly eliminate nocturnal angina, even if the filling pressures are initially normal.



168. Sokolov, V. I., K. K. Yarullin, N. D. Vikharev, M. V. Sazonova, and N. V. Degterenkova: Circulatory response of males 45-52 years of age to antiorthostatic hypokinesia. *Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 21:22-26, 1987.

### Synopsis

*Purpose.* To investigate regional and central circulation reactions to 30-day antiorthostatic hypokinesia.

### Methods.

1. Fifteen men aged 45 to 52 yr underwent  $-8^\circ$  head-down tilt for 30 days. These subjects were divided into two groups:
  - Group 1: 10 subjects with early signs of cerebrovascular and aortic atherosclerosis,
  - Group 2: 5 subjects with neurocirculatory dystonia of the hypertensive type and grade I essential hypertension.
2. Examination of cerebral hemodynamics in the system of the internal carotid arteries and vertebrobasilar system was performed by the bipolar rheography method.
3. Stroke volume (SV) of the heart, circulatory volume (CV), and arterial pressure were measured.

### Results.

1. Cerebral circulation examination of Groups 1 and 2 revealed increased tonus of resistive vessels.
  - Group 1: The changes were localized and were attributable to both morphological changes in the vascular intima and to extravascular factors.
  - Group 2: The increase in vascular tonus was apparent in all cerebral vessels examined.
2. Group 2 subjects showed an increase in SV to  $103.8 \pm 2.3$  ml.
3. Group 1 demonstrated a decline in HR by 14.9% on the 6th day as compared to baseline, and a 14% increase by the 27th day in association with a 26.1% decrease in CV and a 21.1% decrease in SV by the 17th day of HDT.
4. Group 2 showed a significant drop in maximum and lateral systolic pressure, which lead to the decline of pulse pressure. Also, HR decreased slightly as in the first group. SV did not change significantly.
5. Recovery: Group 2 had a slower recovery of hemodynamic parameters (HR, BP, pulsed delivery of blood to vessels of the brain, tonus of arterioles and venules) than did Group 1.

*Conclusions.* The variations in circulatory responses showed that one should consider not only age-related variations, but also the existence and severity of cardiovascular disease.

**169. Stegemann, J., D. Essfeld, and U. Hoffmann:**

Physical performance capacity after 7-day head-down tilt ( $-6^\circ$ ).

In: *Proceedings of the 2nd European Symposium on Life Sciences Research in Space*, Porz Wahn, Germany, 4-6 June, 1984. p.151-157. (ESA Special Publication 212, 1984).

**Authors' abstract**

Physical performance capacity was studied in six (6) healthy male subjects before and on the 1st and 7th day after a continuous 7-day head-down tilt (HDT). Pseudo-random binary sequences (PRBS) of work load were used as testing signals during upright bicycle ergometer exercise. From the PRBS tests, the frequency responses of both oxygen uptake ( $\dot{V}O_2$ ) and heart rate (HR) were computed at 9 harmonic frequencies (fundamental frequency: 0.0135 rad/s). After the simulated weightlessness, the  $\dot{V}O_2$  kinetics were found to be impaired at the harmonic frequencies above 0.068 rad/s.

**170. Stegemann, J., D. Essfeld, and U. Hoffmann:**

Effects of a 7-day head-down tilt ( $-6^\circ$ ) on the dynamics of oxygen uptake and heart rate adjustment in upright exercise.

*Aviation, Space, and Environmental Medicine* 56:410-414, 1985.

**Authors' abstract**

Oxygen uptake ( $\dot{V}O_2$ ) kinetics and heart rate (HR) were studied in six healthy male students before and on days 1, 3, and 5 after a continuous 7-d antiorthostatic bed rest ( $-6^\circ$ ). The exercise test protocol consisted of pseudorandom binary sequences (PRBS) of workload (W) performed on a bicycle ergometer in the upright position (20W – 80W, 15 bits, 30s per bit; the sequence was repeated three times). Amplitude ratio and phase of the W- $\dot{V}O_2$  and W-HR relations were computed at six harmonic frequencies in the range 0.014-0.084 rad · s<sup>-1</sup>. After bedrest the  $\dot{V}O_2$  kinetics was found to be impaired at the harmonic frequencies greater than 0.056 rad · s<sup>-1</sup>. Additionally, the mean heart rate during the PRBS cycles was increased ( $108 \pm 15$  as compared to  $92 \pm 10$  min<sup>-1</sup>). There were no significant effects on HR kinetics and on the static W- $\dot{V}O_2$  relation. During an endurance training program both  $\dot{V}O_2$  and HR changes were restored to the pre-bedrest levels. It is concluded that the impairment of  $\dot{V}O_2$  kinetics can be attributed mainly to muscular factors.

**171. Stuart, C. A., R. E. Shangraw, M. J. Prince, E. J. Peters, and R. R. Wolfe:**

Bed-rest-induced insulin resistance occurs primarily in muscle.

*Metabolism* 37:802-806, 1988.

**Authors' abstract**

Treatment of trauma victims and patients with severe illness may contribute to their metabolic derangements by severely restricting physical activity. We sought to quantitate the impact of absolute bed rest alone on insulin regulation of glucose metabolism in six healthy subjects. Six to seven days of strict bed rest resulted in moderate deterioration in oral glucose tolerance and increased both fasting plasma insulin concentration and the insulin response to an oral glucose challenge by more than 40%. Euglycemic insulin clamp studies demonstrated the development of resistance to insulin's stimulation of whole-body

glucose utilization. This change was characterized by a rightward shift of the insulin dose-response curve (insulin concentration at which 50% of maximal stimulation occurred was  $45 \pm 3$  (SE) uU/ml in the baseline period and  $78 \pm 8$  uU/ml after seven days of bed rest ( $P < 0.01$ ) with little alteration in the maximal response in the rate of glucose uptake (baseline  $15.4 \pm 1.4$  mg/kg · min and bed rest  $14.0 \pm 1.3$  mg/kg · min). In contrast to the shift of sensitivity of whole-body glucose utilization to insulin, suppression of hepatic glucose output by insulin was unchanged by seven days of bed rest. Insulin binding to circulating mononuclear cells was not changed by bed rest. These studies demonstrate that the limited physical activity dictated by bed rest for as little as seven days is associated with substantial resistance to insulin's effects on glucose metabolism. Further, the data suggest that these effects occur primarily in skeletal muscle with little change in insulin action on the liver.

**172. Teasdale, E., and P. Macpherson:**

Incidence of side effects following direct puncture cervical myelography: bed rest versus normal mobility.

*Neuroradiology* 25:85-86, 1983.

**Authors' abstract**

After cervical myelography by direct puncture at C1/2 level, 120 patients were randomly allocated to one of two groups, in one the patients were allowed to be fully ambulant and in the other the regimen was bed rest for 24 h. Questionnaires recording the frequency and severity of side effects were completed at intervals after the examination. Headache, nausea and vomiting were common; fits and mental changes occurred also but were uncommon. The incidence and severity of these side effects did not differ significantly between the two groups.

**173. Tomaselli, C. M., R. A. Kenney, M. A. B. Frey, and G. W. Hoffler:**

Cardiovascular dynamics during the initial period of head-down tilt.

*Aviation, Space, and Environmental Medicine* 58:3-8, 1987.

**Authors' abstract**

The cardiovascular response to 1 h of  $6^\circ$  head-down tilt was studied in 12 male subjects, ages 30-39 years, to simulate the early effects of weightlessness. Fluid shifts, hemodynamic variables, and indices of myocardial contractility were evaluated by utilizing electrocardiography, systolic time intervals, impedance cardiography, sphygmomanometry, and measurement of calf circumference. Most cardiovascular variables remained stable throughout the initial 30 min of the protocol, even though translocation of fluid from the legs to the thorax commenced immediately with the onset of head-down tilt. In contrast, minutes 30-60 were characterized by reduced stroke volume, cardiac output, mean stroke ejection rate, and Heather index concomitant with an elevation in mean arterial pressure. Intrathoracic fluid volume continued to increase while leg volume continued to decrease. This latter physiological response suggests intrathoracic sequestration of fluid volume; blood was apparently redistributed to the pulmonary circulation rather than being retained in the great veins.

- 174. Torikoshi, S., K. Yokozawa, M. Inazawa, K. Itoh, Y. Fukase, J. Nagano, and Y. Suzuki:**  
Effect of acutely exposing to 40 mmHg LBNP on cardiovascular responses during rest and mild exercise after 6 hr rest in 5° head-down tilting (HDT).  
*The Physiologist* 31:S16-S17, 1988.

**Authors' abstract**

To investigate the tolerance of sympathetic control to 40 mmHg lower body negative pressure (LBNP) acutely exposed after 6 hrs bed rest at head-down tilting (HDT) and the effect of mild pedalling (40%  $\dot{V}O_{2\max}$ ) on restoring cardiovascular functions; 6 female students participated as subjects. The tolerance was determined by the criteria given in the study. The averaged tolerable time was 10 min., which was a little shorter than given by NASA procedure (12 min.). At the intolerance point,  $\dot{V}O_2$  and forearm blood flow (FBF) did not change, but pulse pressure was suddenly fallen with strikingly decreasing systolic pressure (SAP) and heart rate (HR) from the peak values during LBNP. But exercising brought the pressure to restore over the control levels and further the normal exercising levels in LBNP, although HR increased and stroke volume (SV), total peripheral resistance (TPR), forearm volume conductance (FBV) decreased. LBNP tolerance might be due to decreasing sympathetic control, but it should be restored by light exercise.

**175. Turbasov, V. D.:**

Effect of prolonged antiorthostatic position on cardiac bioelectrical activity according to EKG tracings from corrected orthogonal leads.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 14:54-59, 1980.

**Synopsis**

**Purpose.** To examine the electrical activity of the heart during bed rest (BR) in order to evaluate the morphological and functional state of the myocardium.

**Methods.** Eighteen male subjects maintained -4.5° head-down BR for 182 days:

Group 1: Six subjects were submitted to a set of preventive measures (isotonic exercise and a course of electro-stimulation of muscles).

Group 2: Six subjects were exercised less intensively.

Group 3: Six subjects served as control and no preventive measures were used.

Electrocardiogram (EKG) was recorded on various days of control, BR, and recovery periods.

**Results.**

1. The mean heart rate (HR) during BR did not change significantly in any of the groups. There was a slight increase in Groups 1 and 3, and HR changes were least marked in Group 2. During recovery, HR was highest in Group 3.

2. The time parameters of the EKG (PQ, QRS, QT) remained within the normal range throughout the study for all groups. Only the PQ interval increased significantly during BR ( $P < 0.05$ ).

3. The effect of duration of BR on amplitude parameters of the QRS complex was statistically significant ( $P < 0.05$ ) and was manifested by a consistent increase.

4. The mean amplitude of T-waves remained in the normal range in all groups.

**Conclusions.** The less marked HR reaction of subjects in the second group during BR and in the recovery period could indicate less marked changes in cardiac function. Thus, it may be assumed that the exercise program used in Group 2 was optimal. The Group 3 regimen produced the most pronounced decline of cardiac function, as evidenced by the continued elevation of HR during the recovery period. The greater increase in HR in Group 1 recovery could indicate more marked changes in cardiac function. Thus, the countermeasures produce a relatively greater effect on the function of the myocardium than on its metabolism.

**176. Van den Meiracker, A. H., A. J. M. Veld, H. J. R. van Eck, G. J. Wenting, and M. A. D. H. Schalekamp:**

Determinants of short-term blood pressure variability. Effects of bed rest and sensory deprivation in essential hypertension.

*American Journal of Hypertension* 1:22-26, 1988.

#### **Authors' abstract**

In 38 hospitalized patients with uncomplicated essential hypertension intra-arterial pressure was recorded continuously for 24 hours with the Oxford technique. On the basis of beat by beat analysis, hourly and 24-hour means of mean arterial pressure (MAP) and heart rate (HR) were obtained. The standard deviations and variation coefficients of the hourly means were used as a measure of absolute and relative blood pressure variability respectively. By randomization patients were ambulant during the day (group A; n=19) or they were restricted to bed (group B). The patients of group B were sensory deprived during the first 4 hours of the blood pressure recording. During the night MAP, HR, and their respective variabilities were similar for both groups. During bed rest MAP was reduced as compared to ambulant values ( $P<0.05$ ), but bed rest had no effect on HR, or on the variability of HR and MAP. During concomitant sensory deprivation HR and the variability of MAP and HR all declined to nightly values, though MAP did not change. In group B, HR-variability (absolute and relative) was inversely correlated to age, but no relationship between these two parameters was observed in group A. During concomitant sensory deprivation, but not during bed rest alone or during night rest, relative MAP-variability was also inversely correlated to age. It is concluded that sensory stimuli have an important effect on HR and on the variability of MAP and HR, but not on MAP itself, indicating that to some extent blood pressure and its variability are regulated independently.

**177. Van de Pol, J. G., O. P. Bleker, and P. E. Trelfers:**

Clinical bed rest in twin pregnancies.

*European Journal of Obstetrics, Gynecology, and Reproductive Biology* 14:75-80, 1982.

#### **Synopsis**

**Purpose.** To study the effect of clinical bed rest (BR) from about 32 wk onward on gestational age, birthweight, placental weight, and mortality in twins.

**Methods.** A retrospective study was made of 148 sets of twins born between 1969 and 1979. From 1969 to 1974, clinical BR was prescribed on indication only. From 1975 to 1979, prophylactic clinical BR was advocated. The duration of BR was longer in the second period than in the first: the mean for

primiparae was 3 wk, and for multiparae 2 wk. The periods were compared with respect to gestational age, birthweight, placental weight and survival.

**Results.** No effect of longer BR on gestational age was found. In primiparae, a small significant increase of both birthweight and placental weight was found, possibly related to clinical BR. The improvement of survival observed could not be ascribed to BR.

**Conclusions.** Clinical BR may improve conditions for intrauterine growth in twins. However, because of emotional and economic damage, clinical BR in twin pregnancies should be advocated on a more individualized basis.

**178. Vico, L., D. Chappard, C. Alexandre, S. Palle, P. Minaire, G. Riffat, B. Morukov, and A. S. Rakhmanov:**

Effects of a 120 day period of bed-rest on bone mass and bone cell activities in man: attempts at countermeasure.

*Bone and Mineral* 2:383-394, 1987.

#### **Authors' abstract**

The effects of immobilization on bone mass and bone remodeling in patients with spinal cord injuries are known to simulate weightlessness-induced bone changes in astronauts. Nevertheless, immobilization has never been investigated using histomorphometric studies in healthy volunteers.

Twenty healthy male volunteers participated in a '120 day bed-rest' experiment in the USSR. Bone biopsy cores of iliac crest were taken before and at the end of the period of bed-rest. The subjects were divided into five groups. Five subjects underwent a normal ambulatory life (control subjects); three subjects were placed on continuous bed rest for 120 days (complete immobilization); four subjects were immobilized and underwent a controlled training program; four subjects were immobilized and received treatment with potassium diphosphonate (ethane-1,hydroxy-1,diphosphonate 900 mg/day, per os); and four subjects were immobilized and received diphosphonate plus physical exercise. Parameters of bone mass and bone cellular activities (osteoblastic formation and osteoclastic resorption) were measured using automatic and semi-automatic image analysis systems.

Bone mass remained constant in each group. Cellular activity measurements showed that in completely immobilized men, the mineralization rate was lower than in controls without change in osteoid parameters; in contrast, osteoclastic parameters were increased. In immobilized men given the training program, bone formation was normal and bone resorption was increased. In immobilized men treated with diphosphonate, osteoid parameters and resorption activity were decreased. In immobilized men with diphosphonate plus training, the osteoid parameters and the resorption activity were reduced but to a lesser degree than in immobilized men with diphosphonate alone.

Failure of bone loss in normal immobilized subjects differed from results found in paraplegic patients. However, a decrease in mineralization rate and an increase in bone resorption activity were found in both studies. Exercise stimulated bone resorption and diphosphonate inhibited the osteoclastic activity. These data emphasize the difficulties in finding good models to simulate spaceflight conditions on earth.

Comparative studies must be done using bone biopsies to determine more precisely the effects of weightlessness on the human skeleton.

**179. Vlasova, T. F., Y. B. Miroshnikova, and A. S. Ushakov:**

Investigation of some aspects of human amino acid metabolism during 120-day antiorthostatic hypokinesia.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 19:35-38, 1985.

**Synopsis**

**Purpose.** To determine the effect of long-term bed rest (BR) on free amino acid (FAA) content in blood plasma.

**Methods.** Six subjects maintained 120 days of  $-4^\circ$  head-down BR, followed by 14 days of recovery. Blood samples were drawn on various days of the control, bed rest and recovery periods, and the FAA content of blood plasma was determined by ion-exchange chromatography.

**Results.**

1. There were changes in FAA levels during BR and in recovery. Only cystine and aspartic acid remained unchanged during the study.
2. On Day 28 of BR, there was an elevation of lysine level in all subjects ( $P < 0.05$ ).
3. On Days 67-70 of BR, total FAA content of blood plasma increased by 1.5 times. There was an increase in 11 out of 17 amino acids at this point of the study.
4. By Days 94-96 of BR, the levels of virtually all the amino acids exceeded control values, with the exception of aspartic acid, cystine, and proline. Total FAA content increased 1.8 times as compared to the control.
5. During Days 109-113 of BR, the FAA levels remained high in most cases, with the exception of leucine, phenylalanine, cystine, aspartic and glutamic acids.
6. Complete restoration of FAA levels to control levels did not occur during the 14-day recovery period.

**Conclusions.** The results of this study of human plasma FAA during 120-day bed rest indicate that, starting on Day 28, there is an increase in the amino acid pool of blood, as compared to the baseline period due to increase in concentrations of most FAA. The latter is probably attributable to decrease in intensity of anabolic processes and prevalence of catabolic processes under hypokinetic conditions.

180. Vorob'yev, V. Y., V. R. Abdrakhmanov, A. P. Golikov, L. L. Stazhadze, I. B. Goncharov, I. V. Kovachevich, S. G. Voronina, and A. V. Vabishchevich:  
Effects of 120-day antiorthostatic bedrest on gas exchange and pulmonary circulation in man.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 18:23-26, 1984.

### Synopsis

**Purpose.** To compare the exchange of gases and regional pulmonary circulation in subjects during long-term bed rest (BR) and in the early recovery period.

**Methods.** Five healthy male subjects underwent 120 days of  $-4^\circ$  head-down BR. Minute respiration volume was determined, gas composition of exhaled gas was analyzed, and samples of arterial blood were drawn. Nonelastic resistance to respiration was determined, and the ventilation reaction to  $\text{CO}_2$  was tested. A plot of minute ventilation of the lungs ( $\dot{V}_E$ ) as a function of the partial pressure of  $\text{CO}_2$  ( $\text{pACO}_2$ ) tension in alveolar air was drawn. Mean  $\dot{V}_E$  was then calculated and physiological dead space was determined. In addition, rheograms of the upper, middle, and lower parts of the right lung were recorded.

### Results.

1. On day 55 of BR, a reliable elevation of blood  $\text{pCO}_2$  was observed ( $P < 0.05$ ). Minute respiration volume declined ( $P < 0.01$ ).
2. The end of the first half of the BR period was characterized by an increase in delivery of blood to the upper parts of the lung ( $P < 0.05$ ). During the second half of the BR period, the middle and lower part of the lung were found to receive the maximum blood supply, whereas the blood supply to the upper lung declined to control levels.
3. On day 75 of BR, an increase in alveolar-arterial gradient for oxygen was demonstrated ( $P < 0.05$ ) as compared to the control. There was a further drop on blood  $\text{pO}_2$  in all subjects ( $P < 0.05$ ), as well as a reliable drop of  $\text{CO}_2$  ( $P < 0.05$ ).
4. On day 100 of BR, there was a continued decline of blood  $\text{CO}_2$  ( $P < 0.01$ ). In this period, the subjects presented an increase in the nonelastic resistance to respiration ( $P < 0.05$ ).

**Conclusions.** The changes in gas exchange during the first half of the bedrest period are signs of impaired ventilation-perfusion relations in the lungs. The evaluation by means of gradients for  $\text{CO}_2$  and  $\text{O}_2$ , which revealed an increase in alveolar-arterial gradient for  $\text{O}_2$ , may be indicative of an increase in the nonuniformity of ventilation and perfusion. The results for the second half of the bedrest period indicate a relative adaptation of gas exchange under these conditions. The compensatory adaptive capabilities of the body in the presence of discrete respiratory insufficiency may be due to changes occurring in regional pulmonary circulation.



- 181. Vorob'yev, V. Y., V. R. Abdrakhmanov, I. V. Kovachevich, A. P. Golikov, L. L. Stazhadze, V. V. Bogomolov, S. G. Voronina, and L. G. Repenkova:**  
Effect of hypokinesia in antiorthostatic position on pulmonary circulation and gas exchange.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 17:16-18, 1983.

**Authors' abstract**

The purpose of this study was to investigate gas exchange and lung perfusion during 14-day head-down tilt and immediately thereafter. During head-down tilting pulmonary circulation increased, as suggested by zonal rheography of the lungs and by ECG (increase in the P<sub>II-III</sub> amplitude and width by 1-2 mm and 0.01-0.02 s, respectively). A significant decrease in O<sub>2</sub> tension and slight increase in CO<sub>2</sub> tension of the arterial blood were detected. Immediately post-test pulmonary circulation declined and metabolic acidosis developed simultaneously. Our findings suggest that drugs reducing pulmonary hypertension can be recommended for emergency medical aid in space flight.

- 182. Vorob'yev, V. Y., I. B. Goncharov, I. V. Kovachevich, and A. F. Davydkin:**  
Distinctive changes in regional hemodynamics and gas exchange in healthy men in response to moderate phlebotomy and reinfusion of blood after submitting to antiorthostatic hypokinesia.  
*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 19:45-48, 1985.

**Authors' abstract**

Nine healthy male test subjects were exposed for 7 days to head-down tilting. Within 2 hours after exposure 500 ml of blood were withdrawn. This reduced pulse blood filling of all lung compartments, particularly the upper (P<0.05) compartments, and decreased slightly finger circulation. The blood losses were then substituted but 2 hours after blood reinfusion the rheographic parameters of pulmonary circulation were still lower than before blood losses. In arterial blood pCO<sub>2</sub> remained lower (P<0.05) and the deficiency of bases increased (P<0.05). It can be concluded that in the above situation blood reinfusion in the amount exceeding blood losses should be viewed adequate. On the basis of the results obtained increased blood content of the lungs in the course of head-down tilt can be interpreted as a reflex mechanism of blood pooling in the body.

- 183. Waligora, J. M., D. J. Horrigan, M. W. Bungo, and J. Conkin:**  
Investigation of the combined effects of bedrest and mild hypoxia.  
*Aviation, Space, and Environmental Medicine* 53:643-646, 1982.

**Synopsis**

**Purpose.** To investigate changes in oxygen transport across the lung during 6° head-down bed rest (BR) combined with an operational period of mild hypoxia.

**Methods.** Seven healthy volunteer subjects (24-33 yr) participated in this study:

1. Four subjects were exposed to 20 hr of 6° head-down BR and then transferred to an altitude chamber for 8 hr (still in HDT) where the air pressure was reduced to 565±10 Torr (alveolar oxygen pressure = 69±2 Torr).

2. Three control subjects were exposed to the same altitude chamber environment for 8 hr without prior or concurrent BR.

A set of physiological measurements was taken on each subject in the BR group prior to BR, 4 hr after BR was initiated, and during the last hour of the altitude chamber exposure. The same measurements were made on the control group subjects prior to their altitude chamber exposure and during the last hour of the exposure.

### *Results.*

1. There was no statistically significant influence of BR on the effect mild hypoxia had on the subjects' heart rate, blood pressure, body temperature, minute volume, or other respiratory parameters, and no apparent effect on end expired CO<sub>2</sub>, mixed CO<sub>2</sub>, or vital capacity.

2. There were decreases in hemoglobin oxygen saturation, p<sub>a</sub>O<sub>2</sub> and p<sub>a</sub>CO<sub>2</sub> in all the subjects on exposure to altitude.

3. An 8.1% increase in hematocrit in BR subjects between the pre-BR and BR levels was measured, but there was no appreciable change in the control group or on altitude chamber exposure.

4. A consistent 20% decrease in the creatinine phosphatase level was observed in the BR group after 28 hr.

*Conclusions.* Under the conditions of this study, a 20-hr exposure to 6° head-down BR followed by an 8-hr exposure to hypoxia gave no indication of an exacerbation of hypoxia as a result of the BR when measured by a change in arterial gradient across the lung. This finding reinforces the decision to allow crew exposure to an environment providing an alveolar O<sub>2</sub> level no lower than 69 Torr in the event a contingency extravehicular activity is necessary during orbital test flights.

### **184. Wegmann, H. M., F. Baisch, and P. Esser:**

Influence of physical training on insulin responses to glucose loads during bedrest (HDT 6°).

In: *Proceedings of the 35th Congress of the International Astronautical Federation*, Lausanne, Switzerland, October 7-13, 1984. p. 1-4.

### **Authors' abstract**

Substantial changes in insulin responses to glucose loads occur as consequence of 0-g simulation by absolute bedrest. The purpose of this paper is to investigate whether these changes may be influenced by physical training. Therefore, four highly trained athletes (A) and four non-trained students (NA) were subjected to 7 days of absolute bedrest in 6° head-down tilt position. Prior to, during and after this simulation period a standard 2-h oral glucose tolerance test was administered and responses of insulin and C-peptide in blood plasma were evaluated in 30 min intervals after glucose ingestion. Both responses increased distinctly during bedrest as compared with pre-bedrest controls. However, elevations in NA were significantly more pronounced than in A. Thus it can be concluded that physical training leads to a better glucose tolerance during 0-g simulation. The response patterns of C-peptide provide evidence that the observed insulin elevations in excess controls are caused by higher secretion rates from the beta-cells of the pancreas rather than by a diminished clearance from the circulatory system. The findings are discussed in regard to their relevance for real space flights.

**185. Wegmann, H. M., F. Baisch, and G. Schafer:**

Glucose tolerance in trained and untrained subjects during head-down tilt (6°).

In: *Proceedings of the 2nd European Symposium on Life Sciences Research in Space*. Porz Wahn, Germany, 4-6 June, 1984. p.197-201. (ESA Special Publication 212, 1984).

**Synopsis**

*Purpose.* To present data on oral glucose tolerance tests conducted with human subjects in a weightlessness simulation study.

*Methods.* Four highly trained athletes and four nontrained students served as subjects. All subjects were maintained at antiorthostatic bed rest (BR) (HDT -6°) for 7 days. On one day before, two days during and two days after the study period, a standard 2-hr oral glucose tolerance test (OGTT) was administered by ingestion of 1 g glucose per kg body weight. Venous blood samples were collected immediately before and 30, 60, 90 and 120 min after ingestion.

**Results.**

1. There was a consistent trend of higher glucose responses in the athletes as compared to the untrained subjects.

2. Insulin responses to glucose load were markedly elevated during and 2 days after BR as compared with pre-BR responses. However, elevations in nontrained subjects were significantly more pronounced.

3. There were similar response patterns between insulin and C-peptide: higher maximum levels in nontrained subjects under all conditions; slower kinetics of response curves in athletes; and increased responses during HDT-BR in both groups. However, C-peptide curves appear slower to return to normal levels.

4. C-peptide curve responses are always higher in the group of untrained subjects, but athletes approach their maximum levels later than non-athletes do.

*Conclusions.* The response pattern of C-peptide provides evidence that the observed elevations of insulin during BR are caused by higher secretion rates rather than by a diminished clearance from the circulatory system.

**186. Yakovleva, I. Y.:**

Electrometric investigation of human gustatory analyzer under normal conditions and in simulated weightlessness.

*Vestnik Otorinolaringologii* 2:15-17, 1982.

**Synopsis**

*Purpose.* To study the gastrolingual reflex using electrometrical investigation of taste.

*Methods.* Sixty-two healthy men (25-45 yr) participated in this study:

1. Fifty-three men served as the normal group and nine were investigated during 5 days of antiorthostatic head-down tilt (AOH = -8° HDT).

2. Threshold sensitivity of the gustatory receptors for the right and left halves of the tongue was determined before and 10-15 min after food intake. The difference in threshold before and after eating constituted a quantitative index of the gastrolingual reflex.

3. Investigations of the gustatory analyzer were conducted prior to AOH, on days 1, 3, and 5 of bed rest (BR), and on the first day of recovery.

#### *Results.*

1. The average threshold sensitivity of taste receptors to electrostimulation was  $32.9 \pm 2.64 \mu\text{A}$  on the right half of the tongue and  $29.5 \pm 2.58 \mu\text{A}$  on the left in the normal group, and  $34.6 \pm 1.8 \mu\text{A}$  (right) and  $33.5 \pm 2.1 \mu\text{A}$  (left) in the AOH group.

2. Food intake in all subjects resulted in a significant rise in the threshold of taste which, after eating, increased by  $6.2 \mu\text{A}$  on the right and by  $2.3 \mu\text{A}$  on the left (18.8% and 7.8%, respectively).

3. In the AOH group, the threshold of taste showed a statistically significant increase during the first day of BR ( $69.3 \pm 0.8 \mu\text{A}$  on the right and  $67.8 \pm 1.6 \mu\text{A}$  on the left), and remained high throughout the entire period of AOH. However, a tendency toward normalization was noted.

*Conclusions.* Analysis of the data has made it possible to recommend electrogustometry for investigation of the human gustatory analyzer under the conditions of spaceflight.

#### **187. Yarullin, K. K., L. G. Simonov, and S. A. Vtoryy:**

Changes in regional and central hemodynamics during seven-day water immersion.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 21:45-50, 1987.

#### **Authors' abstract**

Regional and central hemodynamics were assessed at bi- and tetrapolar rheography and tachooscillography during 7-day "dry" immersion and 8-day  $-8^\circ$  head-down tilt. Blood redistribution evident from enhanced pulse filling of the brain, lungs and arms was the most pronounced on day 3-5. The onset of the blood outflow to the liver was observed on immersion day 5 due to compensatory and adaptive reactions. Lack of exercise tolerance of cardiovascular system through insufficient training was similar in the immersion and head-down tilt for all the 6 healthy males studied (aged 41-49) despite more obvious changes in regional hemodynamics during the immersion, which recovered on its fifth day.

#### **188. Zhiznevskaya, O. V., and I. L. Medkova:**

Investigation of spectrum of human bile acids during 120-day antiorthostatic hypokinesia.

*Kosmicheskaya Biologiya I Aviakosmicheskaya Meditsina* 19:33-35, 1985.

#### **Authors' abstract**

The composition of bile acids in the B and C portions of the duodenal juice of six essentially healthy test subjects exposed to 120-day head-down bed rest was investigated. As the exposure continued, the percentage content of bile acids conjugated with taurine increased and the bile acids conjugated with glycine decreased. The rapid and significant decrease of the ratio of glycine conjugated to taurine

conjugated bile acids suggests a specific modification of the synthetic function of hepatocytes under the above conditions.

**189. Zhuang, X. C., Y. M. Fan, Q. L. Xiang, and X. Y. Shen:**

The relationship between cardiovascular responses and stress tolerance before and after bed rest. *The Physiologist* 31:S102-S105, 1988.

**Synopsis**

*Purpose.*

1. To compare the results of this experiment (HUT+LBNP test) with those from a similar experiment done previously;
2. To observe what changes of the features of cardiovascular responses in the subjects of the four types had taken place during and after exposure to the hypokinetic BR;
3. To see if the tendency of the changes was consistent; and
4. To evaluate which kind of cardiovascular response could better adapt to the hypokinetic environment and readapt to a normal environment.

*Methods.*

1. Seven young men (19-20 yr) were subjected to head-up tilt (HUT) plus lower body negative pressure (LBNP) for 20 days with their heads 2° lower than their feet. Four types of cardiovascular response were:
  - a) vascular type: increased peripheral resistance (PR), decrease heart rate (HR).
  - b) mixed type: increased PR, increased HR.
  - c) cardiac type: decreased PR, increased HR
  - d) less regulating type: decreased PR, decreased HR.
2. The control period was 7 days before BR, and the recovery period was 14 days after the end of BR.
3. Cardiovascular indices were recorded every other day during BR.

*Conclusions.*

1. Under the stress of HUT + LBNP, the subjects' cardiovascular responses might be divided into four types: vascular type, mixed type, cardiac type, and less regulated type. When the stresses, environments, and health conditions were basically the same and without additional strong stresses, the features of individual responses were relatively stable.
2. During the 20 days of BR, for the subjects with the vascular and mixed types, the subjective responses were slight, the capacity for the heart to do work decreased, the compensatory responses were slight, and the adaption to hypokinetic environment was good. For the subjects with the cardiac and less regulating types the subjective responses were severe, the capacity for the heart to do work increased, the compensatory responses were great, and the adaptation to hypokinetic environment was poor.
3. The regulatory compensation and readaptation responses to the HUT + LBNP stress among the four types was as follows: the vascular type was optimal, the mixed type was second, the cardiac type was third, and the less regulating type was the poorest. This order remained the same pre- and post-BR.

**190. Zorbas, Y. G.:**

Water-mineral metabolism wavelike changes during 180-day hypokinesia.  
*Aerospace Medical Association Preprints*, 1980. p.68-69.

**Synopsis**

*Purpose.* To assess the basic tenets of the reported mechanisms of reorganization in water-mineral metabolism under prolonged hypokinesia.

*Methods.* Eight (8) healthy males 18 to 21 yr of age were subjected to a 180-day hypokinesia. Measurements were made of water consumed and urine eliminated in 24 hr, dynamics of body weight (BW), water content in the blood, plasma volume, osmolar concentration of urine and blood, rate of renal circulation, quantity of glomerular filtration, content of sodium and potassium in the blood serum and urine, and quantity of chlorine in the biological fluids.

*Results.*

1. The study of the dynamics of body weight under a balanced energy expenditure diet revealed a considerable loss of weight beginning on the first day of the experiment.
2. A comparison between urine output and water consumption indicated that the dynamics of BW alterations were associated somewhat with fluctuations of water balance.
3. Throughout the experiment, the subjects manifested a reliable degree of negative water balance and an increased urine excretion.
4. In the early stages of hypokinesia, as a result of diuresis, signs of dehydration appeared. This diuresis was accompanied by an elevation in renal excretion of osmotically active substances, including sodium; the glomerular filtration rate was elevated by 4% and renal circulation by 8-9%.
5. In addition, plasma volume was reduced by 10% and concentration of water in the blood by 3%.

*Conclusions.* The results confirm the mechanism of reorganization of man's water-mineral metabolism homeostasis and wavelike changes thereof under hypokinesia itself and hypokinetic stress.

**191. Zorbas, Y. G., V. G. Andreyev, and L. B. Popescu:**

Fluid-electrolyte metabolism and renal function in men under hypokinesia and physical exercise.  
*International Urology and Nephrology* 20:215-223, 1988.

**Authors' abstract**

It has been suggested that hypokinesia (diminished muscular activity) induces significant changes in fluid-electrolyte metabolism and renal function in physically conditioned men. Thus, the aim of this study was to investigate fluid-electrolyte metabolism and ionoregulatory renal function during 16 days of hypokinesia (HK) and 15 days of readaptation period (RP) in 12 physically conditioned male volunteers aged 19-23 years. They were divided into two equal groups. Group 1 was subjected to HK and intensive physical exercise (PE) and group 2 was submitted to pure HK, that is, without the use of any preventive measures. For the simulation of the hypokinetic effect all of the men were kept under a rigorous bed rest regime. Sodium, potassium, calcium and magnesium, creatinine, urea and osmotic concentration were calculated in blood serum and urine samples. Renal excretion of fluid, osmotically active

substances and electrolytes was insignificantly different in the two groups. The level and period of water and electrolyte retention were different with respect to the duration of HK. The basic physiological mechanisms of changes in fluid-electrolyte metabolism were consistent with a reduction of the glomerular filtration rate and a change in water and ion transport of renal tubules. It was concluded that HK induced marked changes in fluid-electrolyte metabolism and renal function in physically conditioned men regardless of their involvement in intensive physical exercise.

**192. Zorbas, Y. G., and I. O. Matveyev:**

Evaluation of efficacy of preventive measures under hypokinesia.

*International Journal of Rehabilitation Research* 10:63-68, 1987.

**Authors' abstract**

It has been demonstrated that hypokinesia (diminished muscular activity) induces changes in organs and systems of organs, including the neuromuscular system. Thus, the aim of this study was to assess the efficacy of physical exercise (PE) and combination thereof with other preventive measures under 100 days of hypokinesia (HK) on 24 healthy men aged 19 to 23 years.

They were divided into four groups. The 1st group of men was subjected to PE, the 2nd and 3rd groups were submitted to combined PE with other preventive measures and the 4th group was kept under pure HK, that is, without the use of any agents, and served as control. To simulate the hypokinetic effect, all men were kept under a rigorous bed-rest regime. Excitability and lability of the neuromuscular system (NMS) were examined by electrostimulation (ES). The excitation threshold was determined during the pre-experimental period (BGP) and under HK.

Excitability and lability of the NMS in all groups of men demonstrated marked differences between them. In the control group, excitability and lability diminished significantly on the 8th day of HK. In the other three groups the changes were unreliable, with the exception of the reduction in maximum rhythm of excitation which was manifested on the 8th day of HK. Among preventive measures used, PE was the most effective one. It was concluded that PE may be singled out as the most reliable measure in counter-acting neuromuscular system disorders under diminished activity conditions.

**193. Zorbas, Y. G., and G. E. Verentsov:**

Blood urea content changes in man under hypokinesia.

*Biochemical Medicine and Metabolic Biology* 36:267-275, 1986.

**Authors' abstract**

It has been demonstrated that hypokinesia (diminished muscular activity) leads to an increase in blood urea content in man. Against this background the objective of this investigation was to determine blood urea content under hypokinesia (HK) on 17 physically healthy men aged 19 to 23 yr. They were divided into three groups: the 1st group (5 men) was examined under HK, the 2nd group (4 men) was studied during the background period (BGP) as well as in the readaptation period (RTP), and the 3rd group (8 men) was placed under ordinary conditions and served as control. For the simulation of hypokinetic

effect the men were kept under a rigorous bed rest regime for 16 days. Blood urea, blood creatinine, urine urea, and urine creatinine were measured. The results were processed statistically. The most pronounced increased urea content was observed in the men with an initial low concentration (3.3-4.2 mmole/liter). Variations in the urea concentration were analogous and manifested a reduction during the initial days and an elevation thereafter. Creatinine excretion and clearance were reduced uniformly and significantly during the initial 10 days of HK. It was concluded that diminished muscular activity induced an increase in urea content and a decrease in creatinine clearance in man.



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16. Abstract  This compendium summarizes published results of clinical observations and of more basic studies that help to elucidate the physiological mechanisms of adaptation of humans to prolonged bed rest. If the authors' abstract or summary was appropriate, it was included. In some cases a more detailed synopsis is provided, under the subheadings Purpose, Methods, Results, and Conclusions. This volume includes material published from 1981 through 1988.					
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