

180-Day Preliminary Science Report

**STUDIES OF ORTHOSTATIC INTOLERANCE WITH THE USE OF
LOWER BODY NEGATIVE PRESSURE (LBNP)
INVESTIGATION 3.1.1:**

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I. Introduction

Exposure to weightlessness, even for short periods, induces significant changes in the cardiovascular system which are proposed to be secondary to headward fluid shifts, subsequent plasma volume contraction, and ensuing adaptations in cardio regulatory function (Hoffler, 1977; Blomqvist and Stone, 1983; Bungo, 1985; Charles, 1991; Fritsch, 1992, 1993) The resulting cardiovascular state may be inappropriate for orthostasis on Earth's surface, as revealed by tachycardia, blood pressure lability, lightheadedness, visual disturbances and presyncope. These findings mark the condition of postflight orthostatic dysfunction. In the extreme, syncope (fainting) may occur, and the dysfunction thus becomes intolerance. This dysfunction, which has been observed in a small though perhaps significant percentage of crewmembers throughout the Shuttle program, is of particular concern as spaceflight durations increase, presumably predisposing the astronauts to an even greater risk of orthostatic dysfunction during and after entry and landing (Charles and Lathers, 1991).

The U.S. investigators (Charles and Yelle) routinely test the orthostatic function of all Space Shuttle astronauts before and after spaceflight using a "stand test" in which the astronaut's heart rate and blood pressure are monitored in both the supine and standing postures for 5-10 minutes (Bungo 1985). Documentation of the development of orthostatic dysfunction during spaceflight requires a gravity-independent technique such as lower body decompression, historically referred to as "lower body negative pressure" (LBNP). Inflight LBNP, which may decompress the legs and lower abdomen by 50 mmHg, provides a cardiovascular stress similar to that induced by gravity on Earth by causing blood to pool in the lower body. Brief decompressions are used as gravity-independent tests of orthostatic function (Wolthius, 1974), while longer decompressions have been used as treatments to reverse orthostatic intolerance in bed-rested subjects (Hyatt and West, 1977) and astronauts (Fortney, 1991).

Since the late 1970s, almost all inflight use of LBNP has been directly or indirectly related to the refinement and application of a treatment, or "countermeasure", with only an occasional study examining the mechanisms of altered orthostatic tolerance as a result of weightlessness. For example, the current LBNP capability for use on the Space Shuttle was developed for the recently concluded EDOMP investigations; the effectiveness of a proposed countermeasure. However, inflight baseline measurements provided information on the adaptive changes in the mechanisms of orthostatic function that occur normally during weightlessness. Note, that this Mir investigation

used LBNP only to determine the time-course and mechanisms of the development of orthostatic dysfunction during 90 days in weightlessness. This work was part of an integrated study of changes in autonomic control of the cardiovascular system which also includes the SMSP experiments, "Studies of Mechanisms Underlying Orthostatic Intolerance Using Ambulatory Monitoring, Baroreflex Testing, and the Valsalva Maneuver" (Experiment 3.1.2) and "Fluid and Electrolyte Homeostasis and Its Regulation" (Experiment 2.1.1). Data collection was also done throughout the routine application of the Russian countermeasure program during the last days of the mission. Specific analysis of this countermeasure and its efficacy focused on comparing responses before and after the treatment. An in-depth comparison of the Russian and NASA LBNP countermeasure was not performed.

A. Objectives of Experiment

1. To determine the time-course and mechanisms of the loss of orthostatic tolerance associated with extended weightlessness.
2. To confirm and extend previous U.S. and Russian research, and provide a standardized, reproducible measure of integrated circulatory control against which other planned specific measurements of autonomic function can be interpreted.

B. Hypotheses

This investigation will test the following hypotheses:

- (1) During the first month in orbit, at each level of LBNP stress, there will have been a significant increase in heart rate (HR) and diastolic blood pressure (DBP), a significant decrease in systolic blood pressure (SBP) and pulse pressure (PP), and no significant difference in mean arterial blood pressure (MAP), compared to preflight values.
- (2) After the first month in orbit, there will be no further significant change in HR, SBP, DBP, or MAP response to each level of LBNP stress.
- (3) There will be no significant difference between the HR, SBP, DBP, MAP or PP responses to LBNP of the Mir crew (1995) and the U.S. *Skylab* crews (1973-74) before the application of the standard Russian end-of-mission countermeasures.
- (4) During LBNP on the last day inflight (that is during the last Russian required LBNP treatment session), there will be significantly smaller HR

response to each level of LBNP stress compared to values measured in the same crew member inflight before the treatment began.

(5) Immediate postflight LBNP testing will reveal smaller HR and BP responses to corresponding levels of LBNP than were found after the 84-day *Skylab* flight, but larger HR and BP responses than after Shuttle flights of 14 days or less, indicating that the Russian treatment only partially restores the responses to LBNP to their preflight values.

(6) By 6 weeks after landing, postflight HR, BP, SV, CO and TPR responses to LBNP will be indistinguishable from preflight responses.

C. Background/History of Project:

The first inflight LBNP assessment of orthostatic function was carried out on the Soviet Union's *Salyut 1* space station in 1971 (Degtyarev, 1971). Two cosmonauts were tested inflight using an early version of the now standard Chibis pneumatic vacuum suit (Barer, 1975). Since then LBNP testing has been performed on virtually every *Salyut* and Mir mission. In agreement with the U.S. *Skylab* data, testing of the crews of the *Salyut 5* mission indicated that individual responses to inflight LBNP tests were predictive of postflight responses to orthostatic stress (Degtyarev, 1980)

The *Skylab* program (1973-1973) allowed U.S. investigators to use LBNP to determine the time course of the development of orthostatic dysfunction in weightlessness (R.L. Johnson, 1975, 1976, 1977). During all three *Skylab* missions (28-, 59-, and 84-day durations), crewmembers' heart rate (HR) and blood pressure (BP) responses to a standardized graded LBNP stress were determined at approximately 3-4 day intervals.

After a lapse of 16 years, the U.S. again used LBNP during spaceflight in our investigations on 9 Space Shuttle flights since 1990 (Charles and Fortney, 1993- DSO 478 EDOMP Status Report). Although the primary objective of our work has been to validate an LBNP-based countermeasure, we have also documented the inflight responses to weightlessness earlier than was possible on *Skylab*. Early inflight measurements on the Shuttle were made on flight days (FD) 2-3 and again on FD 5, 6, or 8; on *Skylab*, they were made on FD 4-6. Thus, the Shuttle and *Skylab* data sets together provide information on the continuum of changes from early in flight through the steady-state condition attained after several weeks in weightlessness.

U.S. (Bungo, 1986) and French researchers (Pottier, 1988; Arbeille, 1991, 1994) have used ultrasound echocardiography to investigate the

cardiovascular responses to short (7-25 days) spaceflights in resting astronauts on the Space Shuttle and the Mir. Those results show that HR and total peripheral resistance (TPR) are increased, stroke volume (SV) is decreased, and BP and cardiac output (CO) are almost unchanged compared to preflight supine values. Arbeille has investigations in work on the Mir to look at echocardiographic data during LBNP tests inflight, and U.S. investigators have combined echocardiography with LBNP testing on several Shuttle missions.

II. Methods/Science Operations

A. List & Description of All Functional Objectives

FO1. "Ramp" Protocol - LBNP Test

FO2. LBNP Training Protocol - EOM Countermeasure

B. List & Description of All Hardware Items Used

Major hardware items used in preflight, inflight, and postflight data collection for this experiment:

HW1. "Skylab" LBNP Device - NASA PI provided

HW2. Russian Chibis LBNP Device - Russian PI provided

HW3. SD-designed Collapsible LBNP Device (inflight) - NASA provided

HW4. AERISEchocardiography device - NASA provided

HW5. Biosound Echocardiography device - PI provided

HW6. Portapres and Finapres Continuous Blood Pressure Device (CBPD) - NASA and PI provided

HW7. Data Acquisition System (DAS) - NASA provided

HW8. Russian "Gamma" ECG and BP system - Russian PI provided

HW9. ECG monitors, strip chart recorders, and test equipment - PI provided

HW10. Automatic Blood Pressure Monitor - PI provided

HW11. TEAC data recorders - PI provided

HW12. Chibis Low Pressure Transducer - NASA provided

C. Sessions/Functional Objectives (FO) Table

Insert sessions table here (see example)

D. Discussion of Method/Protocol

This investigation used periodic repetitions of the standard U.S. Shuttle LBNP protocol to determine the time-course and mechanisms of the

changes in the autonomic nervous control of the cardiovascular system associated with extended exposure to a weightless environment. Three subjects first underwent preflight presyncope-limited (PSL) tests (Fortney, 1991) to determine their maximum LBNP tolerance. Baseline, inflight, and postflight data were collected using the "response" or Ramp LBNP test. This test consists of 10 minutes of data collection at baseline or control (0 mmHg), followed immediately by stepwise decreases in pressure of 10 mmHg increments down to -50 mmHg. Each stage was 5 minutes. The test was completed with a 5 minute recovery period after returning to 0 mmHg.

ECG and continuous blood pressure was collected throughout the test, as well as arterial BP from a manual arm cuff once per minute. Ultrasonographic measurements of cardiac left ventricular dimensions (2-D and M-mode) and blood flow velocity (pulsed-wave Doppler) through the mitral and aortic valves were made during the pre-test resting control period; measurements of aortic blood flow velocity (stroke volume or SV) continued throughout the LBNP decompression and recovery periods. From these ultrasound measurements, cardiac output ($CO=SV*HR$) and total peripheral resistance (mean arterial pressure/ CO) were calculated.

These Ramp tests were performed on three occasions preflight, on several occasions inflight on both Mir and the Shuttle (see sessions table) and at least once postflight. HR and BP data was also acquired during LBNP treatment sessions on each of the last two full days in orbit before Shuttle landing.

III. Results

A. List of Pre-, In-, Postflight Anomalies

Preflight Anomalies

There were no preflight anomalies.

Inflight Anomalies

There was one minor anomaly during LBNP operations on the Mir. The CBPD filled its memory buffer causing an error message to be displayed. 18-CR called this to our attention and was instructed to ignore this message as it did not affect data collection and science results.

There was one anomaly during LBNP operations on the Shuttle. The LBNP "countermeasure" protocol programmed into the LBNP Controller

was different from that printed on the cue card in the PFDF. Crewmembers were instructed to follow the protocol as programmed as this did not affect science.

Postflight Anomalies

There were no hardware related anomalies during postflight testing.

B. Completeness/Quality of Data

The quality of the data which we have is fair. However, we lost ALL "Gamma" ECG and BP data from LBNP sessions conducted on the Mir station. Evidently, cabling configuration between the Russian hardware and the U.S. recording device was not correct. We believe this was due to misinformation regarding the setup of a "handshaking" device designed to route signals from the "Gamma" system to the TEAC data recorder. Further investigation is necessary to prevent this problem in future experiments. We do, however, have Chibis decompression pressure and Portapres (CBPD) continuous blood pressure data for the LBNP sessions conducted on Mir.

Data collection on STS-71 was compromised due to the inability of one subject to participate in inflight LBNP testing. This was for medical reasons.

Completeness of preflight and postflight data was severely compromised due to inconsistent participation in the LBNP protocols by the Russian cosmonauts. Several reasons were given at the time, but we will not speculate further on this matter. The complete assessment of many hypotheses will be hampered by the protocol deviations.

C. Tables, Graphs, Figures

Index:

Figure 1. Heart Rate collected preflight and inflight during LBNP "ramp" tests on Shuttle (launch + 10-12 days), Skylab (Launch + ~ 30 days) and Mir (launch + 110 days) crewmembers. It is apparent that all three groups are similar, both preflight and inflight at their respective test times.

Figure 2. Preflight, inflight, and postflight comparisons of Systolic, Diastolic, and Mean Arterial Blood Pressure, Heart Rate, Stroke Volume, and Total Peripheral Resistance at maximum decompression (-50 mmHg). There is a significant increase in Heart Rate from preflight to inflight

($p=0.04$) as was expected for the three Mir crewmembers. There were no significant differences in any other parameters.

Figure 3. Measure of tolerance - Systolic, Diastolic, and Mean Arterial Blood Pressure, Heart Rate, Stroke Volume, and Total Peripheral Resistance are presented as the % change from 0-50 mmHg (control to maximum decompression). This figure illustrates the delta from baseline, thus factoring in the different endpoints for each crew member and presenting the result as a group average. The change in Stroke Volume was significantly greater inflight and postflight compared to preflight ($p=0.02$). No other parameters exhibited a significant change, in part due to the large individual variability and small sample size. In fact, the statistical power being low for all of these comparisons should be considered when drawing any conclusions from these data.

Heart Rate Response to LBNP

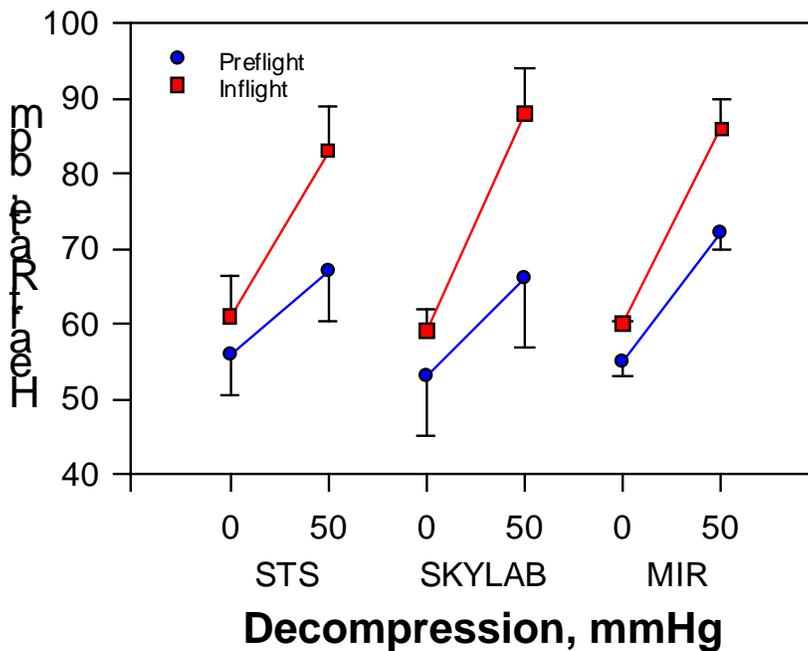


Figure 1. Heart Rate collected preflight and inflight during LBNP "ramp" tests on Shuttle (launch + 10-12 days), Skylab (Launch + ~ 30 days) and Mir (launch + 110 days) crewmembers. It is apparent that all three groups are similar, both preflight and inflight at their respective test times.

Hemodynamic Comparisons at Max Decompression LBNP - Mir Group Average

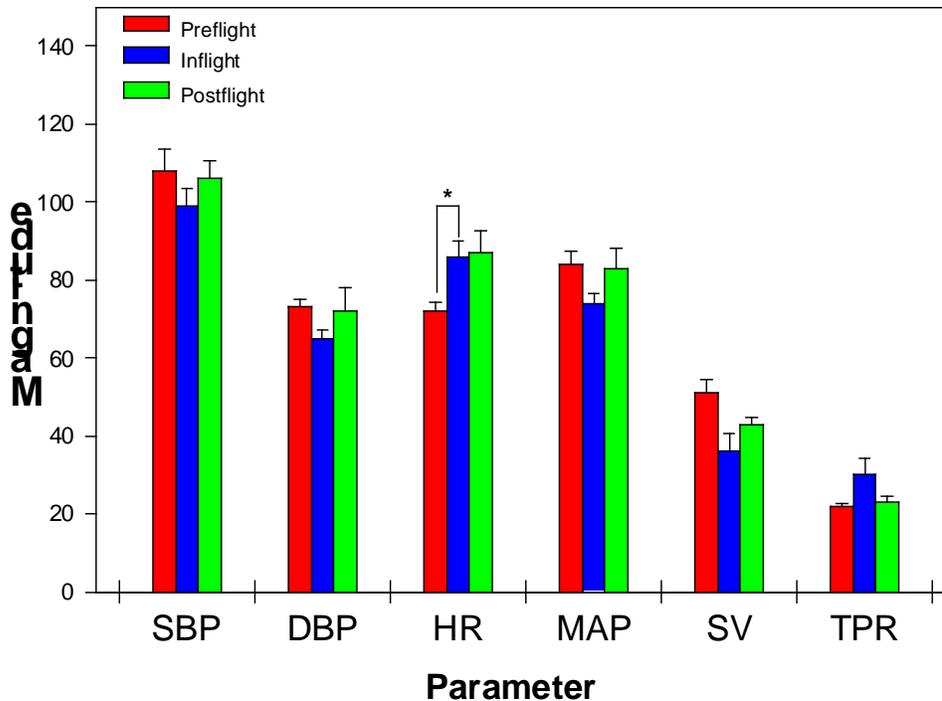


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Measure of Tolerance

LBNP - Mir Group Average

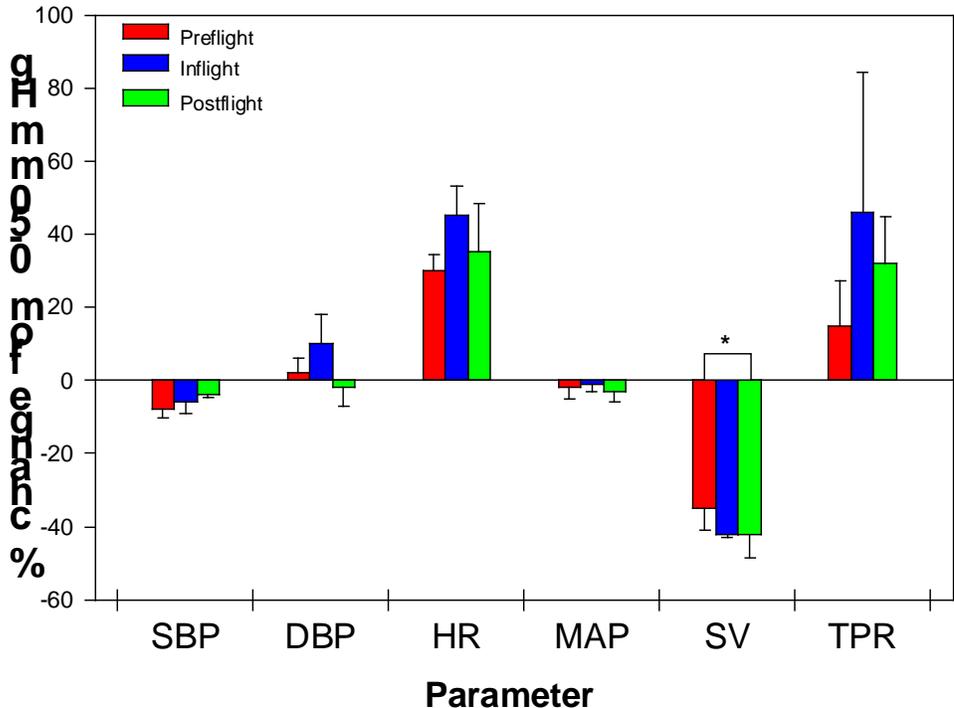


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IV. Discussion

A. Status of Data Analysis

All data has been obtained by the U.S. PI team with the exception of telemetered data, from the two cosmonauts, collected during inflight

LBNP on the Mir. We attempted to obtain this data from our Russian counterparts and we rebuffed as it is considered medically sensitive. In the PI's experience, any such telemetered data is of little value for our purposes due to the frequent interruptions of radio communication. We estimate another 2 months of analysis before final comprehensive results will be available. Our goal is to have this complete before the One-year Final Report.

B. Preliminary Science Findings

This investigation set out to test six hypotheses (stated in section **I.B.** previously) and to gather additional information regarding cardiovascular responses to lower body negative pressure after long duration spaceflight. This task was made especially difficult due to several factors beyond the principal investigator's control, including: preflight and postflight data collection scheduling difficulties, loss of inflight data due to faulty configuration of Russian hardware, and inconsistent participation in and execution of protocols which were made necessary by health concerns of the Russian medical authorities for the Russian crew members. However, analysis of the data thus far allows us to make the following statements about each hypothesis:

- 1)** Heart rate response to LBNP was significantly increased ($p=0.04$) inflight compared to preflight. Stroke volume exhibited a larger decrease ($p=0.02$) from baseline during inflight and postflight testing compared to preflight (although the necessary hardware for making this measurement was demanifested from the Mir, we were able to obtain this data during inflight testing on the Shuttle, and thus make comparisons based on that data), however, all other cardiovascular parameters measured showed no statistically significant changes. [See figures 2 and 3]
- 2)** Hypothesis #2 was unable to be fully tested due to loss of a major portion of data collected on Mir. However, the data that we do have appears to indicate that LBNP responses were altered as anticipated.
- 3)** The data indicate that there were no significant differences in the LBNP heart rate responses of the Mir crew compared to those of the *Skylab* crews [figure 1]. Blood pressure responses were equally similar.
- 4)** Small sample size and other confounding factors make us unable to determine whether heart rate response on the last day inflight was significantly less (after LBNP treatment, or "countermeasure", sessions

took place) compared to sessions earlier in the mission (before treatments).

5) Heart rate and blood pressure responses in the Mir crewmembers to postflight LBNP testing were similar to both *Skylab* and Shuttle data. Small sample size and other factors make the statistical power too low to state whether there are significant differences.

6) Postflight testing was only carried out to 6 weeks on one crew member. This one crew member's LBNP response was similar to preflight at this test time. However, the other crewmembers were unavailable for testing at R+45, thus we are unable to fully address hypothesis #6 (the original research proposal called out for testing on all crewmembers through 6 weeks postflight).

C. Conclusion

Based on the results, we can conclude the following:

- Cardiovascular deconditioning occurs early in flight, and has only partially recovered within 2 weeks postflight. Data was collected on only one subject at R+45 days, so the time course of complete recovery cannot be specifically determined for the entire group.
- Without a control group, and due to the confounding factors previously stated, we are unable to make any conclusive statements regarding the effectiveness of the Russian LBNP (or any other) countermeasure.
- We suggest that future investigations continue to document the problem of cardiovascular deconditioning in order to increase the number of subjects, so that more definitive conclusions can be made. These investigations should include in-flight catecholamine determinations, echocardiography measurements, and pre- and postflight integrated stand tests (including landing day).

In summary, we must state that a very difficult task was undertaken with this investigation. Despite the data quality problems we encountered, much was learned from the results we gathered, both scientifically and operationally. Our team of scientists and engineers worked together and overcame many obstacles, solved several engineering problems, conducted successful training sessions, and helped open a new era in the U.S. space program. We are thankful for the opportunity to participate in this phase of the NASA cooperation with the Russian Space Agency.

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