Modification of Orthostatic Tolerance with Periodic Lower Body Negative Pressure

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Returning astronauts have repeatedly displayed reduced orthostatic tolerance. Ground-based simulations of the weightless state such as water immersion and bedrest can reliably produce similar orthostatic intolerance. Using LBNP to measure orthostatic tolerance, evidence is presented demonstrating that brief, repeated exposure to LBNP is readily capable of restoring the loss of orthostatic tolerance resulting from bedrest and water immersion. In stimulating natural orthostatic mechanisms, periodic LBNP may represent a practical and efficacious method of managing orthostatic intolerance aloft without the use of artificial gravity.

Introduction

ORTHOSTATIC tolerance is the ability to remain erect and motionless without extreme tachycardia, hypotension and syncope. This capability is normally the result of postural reflexes which increase the tone of the vessels in the lower extremities so as to prevent the apparent acceleration of gravity from pooling blood in these extremities and reducing venous return to the heart. When an individual with decreased tolerance is tilted upright, he experiences a sharp increase in heart rate to perhaps twice the resting rate and a significant decrease in blood pressure which may shortly lead to syncope. As early as 1950 exposure to weightlessness was predicted to adversely affect orthostatic mechanisms[1] and indeed orthostatic intolerance has been encountered in returning astronauts[2-4] and in a variety of Earth-based simulations of weightlessness.[5-10] Orthostatic intolerance is undesirable in astronauts because it reduces natural g tolerance along the longitudinal axis and if allowed to deteriorate past some presently undefined point, complete recovery of normal orthostatic tolerance upon return to Earth may be long delayed.

Since ordinary ambulation in our one g environment provides the stimulus for normal orthostatic tolerance, an obvious solution to the prevention of orthostatic intolerance in space would be to generate a comparable artificial gravity. This however is an inefficient solution to orthostatic intolerance and more efficient solutions are worth consideration. A number of alternatives to artificial gravity have been proposed and one of these is lower body negative pressure. Lower body negative pressure (LBNP) is the application of a mild subatmospheric pressure at the level of the iliac crests. It has the advantage of being simple, utilizing little power, requiring little skill to operate and will work well in complete weightlessness.

In studies originating from various laboratories, LBNP in the supine subject has been shown to accurately reproduce those alterations in the cardiovascular system seen in upright tilting: Greenfield, et al.[11] found similar alterations in forearm blood flow and blood shifts; Plassaras[12] made comparisons of forearm flow and venous distensibility; Stevens and Lamb[13] found similar alterations in cardiac output, arterial pressure, peripheral resistance, heart rate, stroke volume, and central venous pressure; and Brown, et al.[14] described similar changes in forearm flow, heart rate, blood pressure, blood shifts and the response to several drugs. Upright tilting however has long been the traditional test of orthostatic tolerance and merely represents a controlled method of keeping the subject erect and motionless. Therefore, if LBNP accurately simulates upright tilting and upright tilting has long been used to measure orthostatic tolerance, then LBNP tolerance could also be used to measure orthostatic tolerance.[15,16] A scoring system is essential and with LBNP at higher pressures the length of time to the presyncopal, grayout state is a clear and unmistakable endpoint.

In addition to LBNP serving to measure orthostatic tolerance, there is substantial evidence that LBNP can be used therapeutically to prevent the loss of orthostatic tolerance produced by strict bedrest. Birkhead et al.[17] used -50 mm Hg for 3 out of every 10 min for 6 hr a day to maintain orthostatic tolerance over 18 days of strict bedrest; Stevens et al.[18] used -30 mm Hg for 10 hr a day for 2 days to restore orthostatic tolerance after 4 weeks of bedrest; Stevens et al.[19] then used -50 mm Hg for 4 out of every 6 min for 8 hr per day to maintain orthostatic tolerance throughout 4 weeks of strict bedrest and McCally et al.[20] restored the orthostatic intolerance induced by 6 hr of bedrest with -55 mm Hg on alternate minutes for 6 hr and -30 mm Hg for a continuous 90 min. Thus continuous exposure to -30 mm Hg LBNP and continual exposure to -50 and -55 mm Hg appear capable of restoring orthostatic tolerance as measured by upright tilting.

Conceivably the conditioning of postural reflexes producing the restoration of orthostatic tolerance could be more sensitive to the magnitude rather than the duration of the conditioning stimulus. If so, then much shorter exposure to higher pressure LBNP might restore orthostatic tolerance as effectively as lower pressures for longer durations. At the same time, a brief exposure to LBNP with a pressure high enough to produce a presyncopal endpoint within 15 min would serve as a useful measurement of orthostatic intolerance. The present study examines the use of high pressure, brief exposure LBNP, namely, -70 mm Hg for about 15 min daily, to both measure and restore orthostatic tolerance after deconditioning with bedrest and water immersion.

Methods

Subjects

Four healthy male college students ranging in age from 19 to 23 years were selected on the basis of a medical examination and

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an interview with the research staff. The medical examination was equivalent to a military flight physical with particular reference to the cardiovascular system. This included: 1) a negative history for any cardiovascular illness; 2) the absence of any physical findings suggestive of cardiovascular illness; 3) normal blood chemistries including routine hematological studies, glucose, enzymes, urea nitrogen and cholesterol; 4) a normal urinalysis; 5) a normal cardiac radiographic series; and 6) a normal 12-lead and exercise electrocardiogram while running on a treadmill at a sustained tachycardia of 180 beats/min for 3 min. The interview following the physical examination was designed to identify the more motivated individual who would readily accept the inconveniences inherent in the experimental design.

Devices

The LBNP tank is a device that applies a mild subatmospheric pressure to the lower half of a supine subject. The fit of the LBNP seal above the iliac crests is critical: it must be essentially airtight and yet not press upon the abdomen so as to interfere with the venous return to the heart. To insure a fit, individual fiberglas molds were prepared for each subject which contained a light weight latex sleeve to seal against the subject's skin. The subject lies on a foam mattress and rests against an adjustable nylon saddle inside the tank. There are numerous safety systems to avoid pressure transients, accidental sustained overpressure, or difficulty in releasing the pressure at the decision of the tank operator, attendant physician, or the subject himself. Pulse rate is taken from the continuously monitored precordial electrocardiogram and blood pressure is determined every minute with an automatically inflated cuff containing a microphone to monitor the Korotkoff sounds over the brachial artery. In practice the tank pressure is controlled by a tank operator standing at a control panel alongside the subject and the precordial ECG and blood pressure are monitored by an attendant physician on the other side of the subject.

To determine orthostatic tolerance the subject is placed in the LBNP tank and the appropriate electrodes and blood pressure cuff are attached. After five min of control data collection the pressure inside the tank is lowered to 70 mm Hg below atmospheric over 30 sec. The precordial electrocardiogram, pulse rate, and blood pressure are carefully monitored at this pressure until the subject reports a grayout endpoint and the pressure is then released over 3 sec. The length of time in minutes at -70 mm Hg is taken as the measurement of orthostatic tolerance. After another five min of control data collection the subject is removed from the tank.

The deconditioning facility consists of two 750 gallon tanks for water immersion and an adjacent ward room where subjects can be kept at strict bedrest. During the deconditioning phase of the experiment the subjects spent 8 hr per day in water immersion. While in the immersion tank the subject is supported on a horizontal nylon stretcher that is adjusted such that the surface of the normal saline breaks over his chest on inspiration. The temperature of the normal saline in the tank is critical and is kept at $95.5°F \pm 1°F$.[21] For the remaining 16 hr/day the subject was at bedrest and was allowed a small pillow for sleep and was otherwise kept horizontal except for eating when he was allowed up on one elbow. Each subject chose his meals from the general patient menu of a local hospital. Micturition and defecation was accomplished with a bedpan and constipation, when it did occur, was treated with stool softeners. Vital signs, blood counts and a routine urinalysis were determined daily to detect any cryptic disorder.

Procedure

All of the subjects chosen for this experiment had had previous experience with the LBNP tank so that further indoctrination was not necessary. Following a brief physical examination on the morning of the first experimental day, a control LBNP tolerance determination was performed on each subject to establish his orthostatic tolerance prior to deconditioning. In the afternoon of the first experimental day the subjects started the deconditioning regimen which lasted for 5 days. This regimen consisted of 8 hr/day in water immersion and the remaining 16 hr/day at strict bedrest. After completion of the water immersion on the 5th experimental day, another LBNP tolerance determination was conducted on each subject to establish the reduction of orthostatic tolerance produced by the previous 5 days of water immersion and bedrest. The subjects were then kept at strict bedrest without water immersion and exposed to daily LBNP tolerance determinations to document any improvement in orthostatic tolerance induced by the periodic LBNP. Daily LBNP tolerance determinations were then continued until all 4 subjects displayed tolerance levels equal to or greater than the original ambulatory control values.

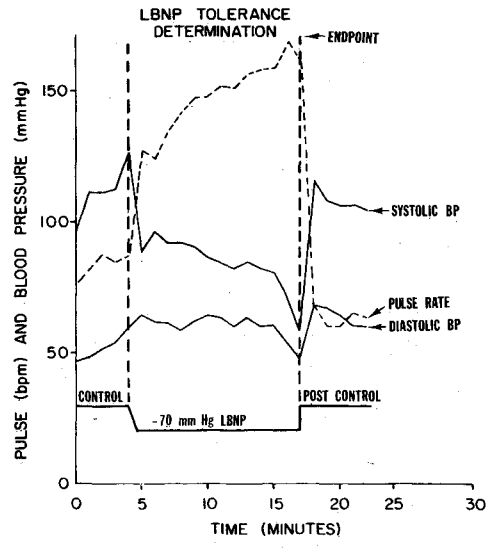

Fig. 1 Typical LBNP tolerance.

Results

The results indicate that the mean orthostatic tolerance of four subjects as measured by LBNP tolerance was reduced to approximately one-half of the mean ambulatory control by 5 days of water immersion and bedrest. Subsequent daily LBNP tolerance determinations while still at bedrest indicated a significant improvement in LBNP tolerance and presumably an equal improvement in orthostatic tolerance. The 4 subjects had LBNP tolerance endpoints nearly equal to the initial control values after 4 days of daily LBNP exposure and substantially greater than the initial controls on the 5th day. There were considerable intersubject differences, both in the degree of deconditioning and the rate and degree of improvement with daily LBNP. In spite of these differences a clear trend was evident and in only 2 of 20 instances did the LBNP tolerance endpoints actually decrease after the beginning of daily LBNP exposure.

Regardless of the length of time to the presyncopal endpoint, over 85% of LBNP tolerance determinations contain the following salient characteristics: with the onset of pressure there is an immediate increase in heart rate and a simultaneous decrease in systolic blood pressure. During the middle portion of the run the heart rate continues to rise gradually and the systolic blood pressure continues to fall similarly. Seconds before the subject signals grayout, there is an abrupt fall in heart rate and both systolic and diastolic blood pressure. The abrupt and simultaneous decline of both heart rate and blood pressure near the grayout endpoint is characteristic of vasovagal fainting and it is likely that the LBNP endpoint involves the same circulatory mechanisms.[13] With the release of pressure there is a dramatic slowing of the heart rate and a simultaneous return of systolic blood pressure to normal values. Short endpoints are characterized by a more rapid decline of systolic blood pressure in the middle portion of the run or the apparent inability to develop an

Table 1 Experimental data

		LBNP Tolerance Determinations								
		Subject 1		*Subject 2*		*Subject 3*		*Subject 4*		*Mean*
		actual[a]	% control	actual[a]	% control	actual[a]	% control	actual[a]	% control	% control
Day 1	Control and begin water immersion and bedrest	10 min	100	10 min	100	5 min	100	10 min	100	100
Day 2	Water immersion and bedrest									
Day 3	Water immersion and bedrest									
Day 4	Water immersion and bedrest									
Day 5	Water immersion and bedrest	2 min	20	5 min	50	4 min	80	7 min	70	55
Day 6	Bedrest and daily LBNP	4 min	40	6 min	60	5 min	100	10 min	100	75
Day 7	Bedrest and daily LBNP	3 min	30	9 min	90	5 min	100	11 min	110	83
Day 8	Bedrest and daily LBNP	13 min	130	9 min	90	5 min	100	10 min	100	105
Day 9	Bedrest and daily LBNP	16 min	160	11 min	110	10 min	200	19 min	190	165

[a] minutes to presyncopal state at −70 mm Hg

adequate tachycardia within the first 2 min after the pressure is lowered to −70 mm Hg. Longer endpoints are characterized by a more gradual decline of systolic blood pressure and a more gradual increase in heart rate in the middle portion of the run. LBNP tolerance appears a sensitive physiological parameter and in our experience hunger, anxiety, minor respiratory infections and mental distractions have reduced LBNP tolerance at various times in our experiments.

Figure 1 displays a typical LBNP tolerance determination. The top solid line represents systolic blood pressure, the bottom solid line is diastolic blood pressure, and the dashed line is the heart rate. The rising blood pressure and heart rate during the control period is frequently seen and has always been related to varying degrees of anxiety. The immediate tachycardia and fall in systolic blood pressure with the onset of LBNP is a constant finding but is unfortunately of little predictive value with regard to estimating the grayout endpoint. The gradually rising tachycardia and decreasing systolic blood pressure are almost always present, but again not usefully predictive of the endpoint. In the 16th minute while the heart rate was still rising, both the systolic and diastolic pressures abruptly fell about 10 mm Hg. Experience has shown that this situation indicates a grayout endpoint is near. In the 17th minute both the systolic and diastolic pressure again fell almost 10 mm Hg and at this time the decrease in blood pressure was accompanied by a decrease in heart rate. This situation reliably predicts the grayout endpoint within seconds: the subject in Fig. 1 signaled the endpoint immediately after the blood pressure determination of the 17th minute. Upon the release of pressure, there is always an immediate increase in both systolic and diastolic pressure and a substantial slowing of the pulse rate usually with variable overshoot.

Table 1 displays the results of the experiment expressed as the actual endpoints and as a percent of the initial ambulatory control determinations. The 4 subjects selected were known to have LBNP endpoints between 7 and 10 minutes from earlier experiments. Subjects 1, 2 and 4 demonstrated endpoints about as expected but subject 3 developed an endpoint at only 5 min which was some 2–5 minutes less than expected. After 5 days of water immersion and bedrest, LBNP tolerance was reduced to a mean of 55% of the initial ambulatory control values with individual values ranging from 20%–80% of controls. The rate at which subjects lose orthostatic tolerance is variable and from our experience the average young male will decrease to about 60% of ambulatory control values after being exposed to 5 days of water immersion and bedrest.

Although the subjects remained at strict bedrest, the endpoints of daily LBNP tolerance determinations rose nearly to ambulatory control levels within 4 days and substantially above the initial control levels on the 5th day. Of 20 LBNP tolerance determinations, 15 were greater than that of the previous day, 3 were equal and the remaining 2 were only 1 minute less than the determination of the previous day. The final LBNP endpoints on the 5th day of daily LBNP exposure ranged from 110%–200% of ambulatory controls with a mean of 165%.

Figure 2 displays the mean data of Table 1. Time is represented on the abscissa and on the ordinate is the mean LBNP tolerance expressed as a percent of the ambulatory control.

The reduction of LBNP tolerance through water immersion and bedrest is readily apparent as is the subsequent recovery of LBNP tolerance through daily exposure. Furthermore the significant improvement in LBNP tolerance was accomplished in the face of a known deconditioning environment, bedrest, and at the same time involved no more than 30 min of a subject's time on any given day. Inasmuch as LBNP tolerance involves fundamental cardiovascular reflexes identical to those involved in conventional orthostatic tolerance testing, the improvement in LBNP tolerance shown in this experiment presumably reflects a similar improvement in orthostatic tolerance as measured by the traditional upright tilting.

Discussion

The role of orthostatic tolerance in our familiar one g environment seems obvious; however, the role of orthostatic tolerance in space is not equally clear. In physical terms, orthostatic tolerance is basically longitudinal g tolerance in a still individual at levels of one g or less for some minutes duration. By thinking of orthostatic tolerance in these terms, the desirability of its maintenance aloft is more easily appraised. The cardiovascular system is structurally sensitive to accelerations applied along the longitudinal axis and low level accelerations of long duration are capable of shifting critical amounts of blood to or from the central circulation. Longitudinal g tolerance is the ability to with-

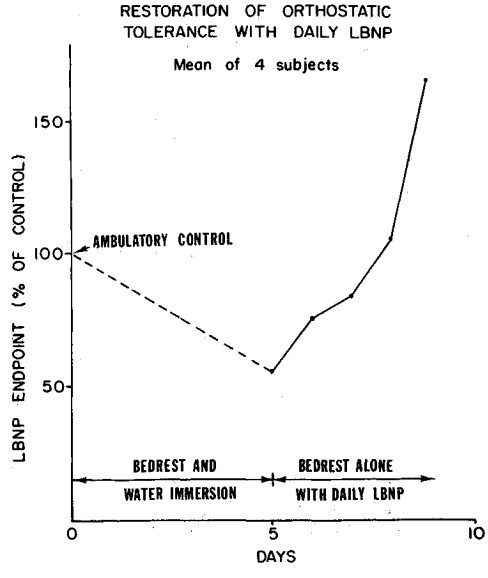

Fig. 2 Mean data from Table 1.

stand these blood shifts and insure an adequate venous return to the heart. To allow natural longitudinal g tolerance to decay to low levels would necessitate the use of special garments anytime the astronaut would be exposed to modest longitudinal accelerations. Furthermore the question arises as to when in the course of the decay, do changes take place such that upon return the recovery of normal orthostatic tolerance becomes difficult. The decay and later modification of longitudinal g tolerance can be reasonably studied with Earth-based simulations but the final decision to implement some technique to modify longitudinal g tolerance aloft will likely be made upon data collected from incrementally increasing weightlessness exposures.

LBNP represents a potential solution to the management of orthostatic or longitudinal g intolerance. Although the number of subjects in the present experiment is small, the results suggest that LBNP tolerance can be used both to measure and enhance the ability of the cardiovascular system to withstand substantial blood shifts from the thorax into the lower extremities. The capability of the cardiovascular system to withstand inappropriate blood shifts could be managed effectively by external means such as a g suit. This technique however does nothing to rehabilitate natural g tolerance and is therefore undesirable for long term use. Also related to its ability to induce significant blood shifts, LBNP can be used to expand the plasma volume[22] which has been frequently reported to be decreased in deconditioning studies[10,23,24] and in returning astronauts.[4] Some basic physiologic performance parameters including orthostatic and exercise tolerance are adversely affected by a reduced plasma volume and therefore a plasma volume normal to Earth currently seems desirable.

In summary, arguments are presented concluding that lower body negative pressure, LBNP, is capable of not only measuring orthostatic tolerance but with repeated use it can readily restore orthostatic tolerance in the previously deconditioned subject. As such it offers a practical method to measure and enhance orthostatic tolerance in long term weightlessness. This experiment explores the use of -70 mm Hg LBNP carried to a presyncopal endpoint which averaged about 15 min. Four young, adult males were deconditioned with 5 days of water immersion and bedrest followed by 5 days of daily exposure to LBNP. Orthostatic tolerance as measured by LBNP tolerance fell to 55% of the mean ambulatory control after deconditioning and with daily LBNP exposure rose to 165% of the same control at the end of 5 days.

References

[1] Gauer, O. H. and Haber, H., "Man Under Gravity-Free Conditions," *German Aviation Medicine, World War II*, Vol. 1, U.S. Air Force, Government Printing Office, Washington, D.C., April 1950, pp. 641–644.

[2] Berry, C. A., "Preliminary Clinical Report of the Medical Aspects of Apollos VII and VIII," *Aerospace Medicine*, Vol. 40, March 1969, pp. 245–254.

[3] Berry, C. A., "Status Report on Space Medicine in the United States," *Aerospace Medicine*, Vol. 40, July 1969, pp. 762–769.

[4] Berry, C. A., "Summary of Medical Experiences in the Apollo 7 through 11 Manned Spaceflights," *Aerospace Medicine*, Vol. 41, May 1970, pp. 500–519.

[5] Graybiel, A. and Clark, B., "Symptoms Resulting from Prolonged Immersion in Water: the Problem of Zero G Asthenia," *Aerospace Medicine*, Vol. 32, March 1961, pp. 181–196.

[6] Miller, P. B., Hartman, B. O., Johnson, R. L., and Lamb, L. E., "Modification of the Effects of Two Weeks of Bed Rest Upon Circulatory Functions in Man," *Aerospace Medicine*, Vol. 35, Oct. 1964, pp. 931–939.

[7] Miller, P. B., Johnson, R. L., and Lamb, L. E., "Effects of Four Weeks of Absolute Bed Rest on Circulatory Functions in Man," *Aerospace Medicine*, Vol. 35, Dec. 1964, pp. 1194–1200.

[8] Vallbona, C., Vogt, F. B., and Spencer, W. A., "The Effect of Bedrest on Various Parameters of Physiological Function—Part VIII, The Effect on the Cardiovascular Tolerance to Passive Tilt," CR-178, April 1965, NASA.

[9] Vogt, F. B., Mack, P. B., and Johnson, P. C., "Tilt Table Response and Blood Volume Changes Associated with Thirty Days of Recumbency," *Aerospace Medicine*, Vol. 37, Aug. 1966, pp. 771–777.

[10] Vogt, F. B., Mack, P. B., Johnson, P. C., and Wade, L., "Tilt Table Response and Blood Volume Changes Associated with Fourteen Days of Recumbency," *Aerospace Medicine*, Vol. 38, Jan. 1967, pp. 43–48.

[11] Greenfield, A. D. M., Brown, E., Goei, J. S., and Plassaras, G. C., "Circulatory Response to Abrupt Release of Blood Accumulated in the Legs," *Physiologist*, Vol. 6, Feb. 1963, p. 191.

[12] Plassaras, G. C., Brown, E., Goei, J. S., and Greenfield, A. D. M., "Effects of Simulated Postural Blood Shifts on the Capacity Function of the Limb Vessels," *Physiologist*, Vol. 6, Feb. 1963, p. 255.

[13] Stevens, P, M, and Lamb, L. E., "Effects of Lower Body Negative Pressure on the Cardiovascular System," *American Journal of Cardiology*, Vol. 16, Oct. 1965, pp. 506–515.

[14] Brown, E., Goei, J. S., Greenfield, A. D. M., and Plassaras, G. C., "Circulatory Responses to Simulated Gravitational Shifts of Blood in Man Induced by Exposure of the Body Below the Iliac Crests to Subatmospheric Pressure," *Journal of Physiology*, Vol. 183, April 1966, pp. 607–627.

[15] Wolthuis, R. A., Hoffler, G. W., and Johnson, R. L., "Lower Body Negative Pressure as an Assay Technique for Orthostatic Tolerance: 1. The Individual Response to a Constant Level (-40 mm Hg) of LBNP," *Aerospace Medicine*, Vol. 41, Jan. 1970, pp. 29–35.

[16] Wolthuis, R. A., Hoffler, G. W. and Johnson, R. L., "Lower Body Negative Pressure as an Assay Technique for Orthostatic Tolerance: Part II. A Comparison of the Individual Response to Incremental vs. Constant Levels of LBNP," *Aerospace Medicine*, Vol. 41, April 1970, pp. 419–424.

[17] Birkhead, N. C., Blizzard, J. J., Issekutz, B., and Rodahl, K., "Effect of Exercise, Standing, Negative Trunk and Positive Skeletal Pressure on Bedrest Induced Orthostasis and Hypercalciuria," TR-66-6, Jan. 1966, Aerospace Medical Research Lab., Wright-Patterson Air Force Base, Ohio.

[18] Stevens, P. M., Miller, P. B., Lynch, T. N., Gilbert, C. A., Johnson, R. L., and Lamb, L. E., "Effects of Lower Body Negative Pressure on Physiologic Changes Due to Four Weeks of Hypoxic Bed Rest," *Aerospace Medicine*, Vol. 37, May 1966, pp. 466–474.

[19] Stevens, P. M., Miller, P. B., Gilbert, C. A., Lynch, T. N., Johnson, R. L., and Lamb, L. E., "Influence of Long-Term Lower Body Negative Pressure on the Circulatory Function of Man During Prolonged Bed Rest," *Aerospace Medicine*, Vol. 37, April 1966, pp. 357–367.

[20] McCally, M., Piemme, T. E., and Murray, R. H., "Tilt Table Responses of Human Subjects Following Application of Lower Body Negative Pressure," *Aerospace Medicine*, Vol. 37, Dec. 1966, pp. 1247–1249.

[21] McCally, M., "Body Fluid Volumes and the Renal Response of Human Subjects to Water Immersion," TR-65-115, August 1965, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio

[22] Lamb, L. E. and Stevens, P. M., "Influence of Lower Body Negative Pressure on the Level of Hydration During Bed Rest," *Aerospace Medicine*, Vol. 36, Dec. 1965, pp. 1145–1151.

[23] Torphy, D. E., "Effects of Short-Term Bed Rest and Water Immersion on Plasma Volume and Catecholamine Response to Tilting," *Aerospace Medicine*, Vol. 37, April 1966, pp. 383–387.

[24] Vogt, F. B., "Tilt Table and Plasma Volume Changes with Short Term Deconditioning Experiments," *Aerospace Medicine*, Vol. 38, June 1967, pp. 564–568.