

# Central venous pressure in space

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**Buckey, Jay C., Jr., F. Andrew Gaffney, Lynda D. Lane, Benjamin D. Levine, Donald E. Watenpaugh, Sheryl J. Wright, Clyde W. Yancy, Jr., Dan M. Meyer, and C. Gunnar Blomqvist.** Central venous pressure in space. *J. Appl. Physiol.* 81(1): 19–25, 1996.—Gravity affects cardiac filling pressure and intravascular fluid distribution significantly. A major central fluid shift occurs when all hydrostatic gradients are abolished on entry into microgravity ( $\mu\text{G}$ ). Understanding the dynamics of this shift requires continuous monitoring of cardiac filling pressure; central venous pressure (CVP) measurement is the only feasible means of accomplishing this. We directly measured CVP in three subjects: one aboard the Spacelab Life Sciences-1 space shuttle flight and two aboard the Spacelab Life Sciences-2 space shuttle flight. Continuous CVP measurements, with a 4-Fr catheter, began 4 h before launch and continued into  $\mu\text{G}$ . Mean CVP was 8.4  $\text{cmH}_2\text{O}$  seated before flight, 15.0  $\text{cmH}_2\text{O}$  in the supine legs-elevated posture in the shuttle, and 2.5  $\text{cmH}_2\text{O}$  after 10 min in  $\mu\text{G}$ . Although CVP decreased, the left ventricular end-diastolic dimension measured by echocardiography increased from a mean of 4.60 cm supine preflight to 4.97 cm within 48 h in  $\mu\text{G}$ . These data are consistent with increased cardiac filling early in  $\mu\text{G}$  despite a fall in CVP, suggesting that the relationship between CVP and actual transmural left ventricular filling pressure is altered in  $\mu\text{G}$ .

spaceflight; gravitation

GRAVITY HAS IMPORTANT EFFECTS on cardiac filling pressure and intravascular fluid distribution. The upright position at 1 G defines the normal operating conditions for the human cardiovascular system. The removal of all hydrostatic gradients when entering microgravity ( $\mu\text{G}$ ) produces a large (1- to 2-liter) headward fluid shift. Previous measurements have shown that the legs become thin and that the face becomes edematous in space (28). The fluid shift may be larger than the shift seen when moving from the 1 G upright to the supine or head-down tilt positions (27). This fluid shift is believed to be the primary stimulus for many of the physiological effects of spaceflight, including a reduced plasma volume and, ultimately, orthostatic intolerance on return to Earth's gravity (3). Ground-based data (with 6° head-down bed rest) show that a similar headward fluid shift transiently increases central venous pressure (CVP) and left ventricular end-diastolic volume (2, 11, 12, 20, 26). Data from short periods of  $\mu\text{G}$  produced by parabolic flight show increases in CVP (21), although this may depend on blood volume and hydration (17, 18). In space, echocardiographic data obtained

within the first 2 days show increased left ventricular end-diastolic volume (10) relative to 1 G supine levels, but peripheral (antecubital) venous pressure does not increase above 1 G levels (15, 16).

Only direct continuous measurements of cardiac filling pressure recorded during the transition from 1 G to  $\mu\text{G}$  could resolve whether CVP increases on entering  $\mu\text{G}$ . We directly measured CVP on the space shuttle during the Spacelab Life Sciences (SLS)-1 (4) and SLS-2 flights. We hypothesized that CVP would increase due to the initial  $\mu\text{G}$ -induced headward fluid shift.

## METHODS

To measure the small pressure changes expected (1–7  $\text{cmH}_2\text{O}$ ), an accurate ambulatory system with minimal drift was needed. The system for measurement of CVP (SMCVP; Engineering Development Laboratory, Newport News, VA) was designed for this purpose (5). The system consisted of a transducer (model 8510B-2, Endevco, San Juan Capistrano, CA), intravenous fluid pump, and electronics package (Fig. 1). The unit showed a drift of 0.2 mmHg over a 63-h test period. The saline-filled catheter was attached to a pump, which provided a continuous (1.5 ml/h) heparinized saline infusion to maintain catheter patency. The pressure transducer was positioned in the axilla at the level of the right atrium and was maintained in a stable position with colostomy tape. Pressure was displayed on the front panel and sent to a data recorder for later analysis.

Due to the constraints associated with research on the shuttle, only three crew members could participate. One was studied on SLS-1 in June 1991, and two were studied on SLS-2 in October 1993. Two men and one woman participated. Mean age was 43 yr (range 35–50 yr), weight 75 kg (range 64–81 kg), and height 175 cm (range 169–181 cm). All had passed a National Aeronautics and Space Administration (NASA) class III flight physical (22) and had normal supine and standing cardiovascular hemodynamics. The procedures and protocols used in the study were approved by the Institutional Review Board at the University of Texas Southwestern Medical Center (Dallas) and the Human Research Policy and Procedures Committee at the NASA Johnson Space Center (Houston, TX).

A 4-Fr polyurethane catheter (Cook, Bloomington, IN) was inserted the night before the planned launch through the median cubital vein to the superior vena cava by using fluoroscopic guidance. At the time of insertion, the arm was moved through a full range of motion while the catheter was observed by fluoroscopy to ensure that the catheter tip could not enter the right atrium and produce cardiac arrhythmias. The position of the center of the right atrium was also noted in both the anteroposterior and lateral dimensions and marked on the skin for proper positioning of the transducer. The plan called for the catheter to remain in place until the end of the first flight day for *subjects 1* and *2* (~24 h) and until

One of a series of articles that describes research conducted on dedicated life sciences missions flown on the US space shuttle.

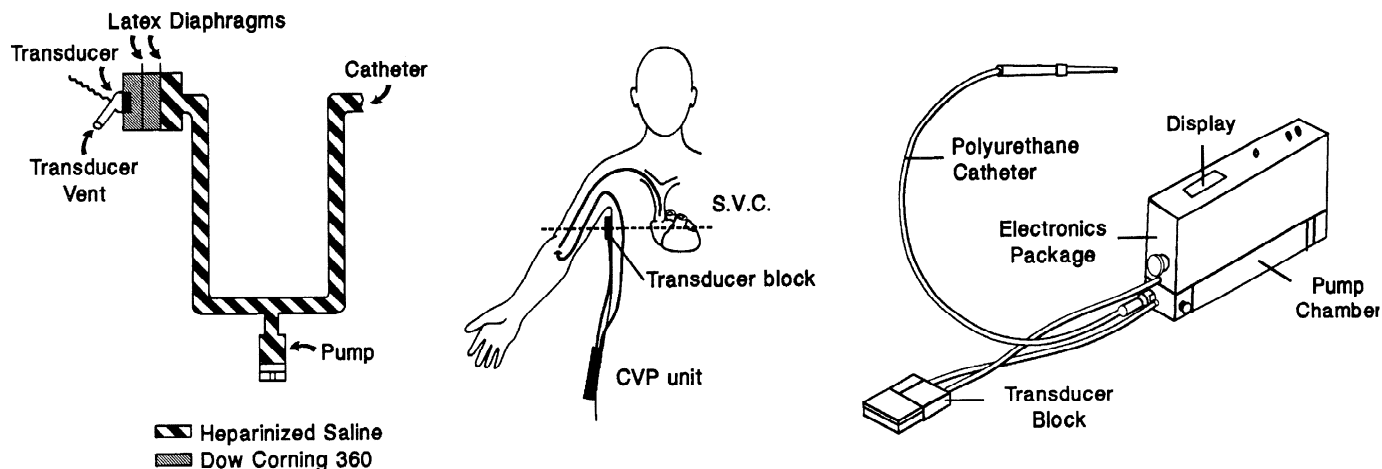


Fig. 1. Schematic configuration of system for measurement of central venous pressure (CVP). Pressure is measured with a transducer connected to a saline-filled catheter at level of right atrium. A pump provides a slow infusion of heparinized saline to keep 4-Fr polyurethane catheter patent. Units were calibrated twice preflight and were checked again postflight. *Left* panel shows that there were 2 latex diaphragms and 2 compartments filled with Dow Corning 360 medical fluid between transducer and saline line. Fluid-filled compartments were added subsequent to initial design of units (4). Because these fluid-filled compartments could contain bubbles, each unit was tested in a vacuum chamber to verify insensitivity to barometric pressure changes. SVC, superior vena cava.

the end of the second flight day for *subject 3* (~48 h). If the catheter had to remain in place longer due to a launch postponement, the insertion site was checked daily and the catheter was flushed twice daily.

The flight and backup units (one backup unit per subject was flown on each mission) were assembled the night before launch. After sterile assembly, the units were connected to a water manometer and calibrated from  $-3$  to  $35$   $\text{cmH}_2\text{O}$ . The units had multiple membranes and fluid compartments (Fig. 1) to ensure two-failure tolerance for electrical isolation from the subject (i.e., two independent failures would have to occur before the subject could be exposed to any electrical current). All air bubbles had to be eliminated from the compartment in the fluid path. After this was done, the units were placed in a small hypobaric chamber and exposed to a vacuum of  $100$   $\text{mmHg}$  ( $136$   $\text{cmH}_2\text{O}$ ) while measuring a constant  $10$ - $\text{cmH}_2\text{O}$  test pressure. This ensured that changes in barometric pressure would not cause artifactual changes in the pressure readings. The unit was considered acceptable if the measured pressure changed by  $<0.7$   $\text{cmH}_2\text{O}$  during the test.

The units had also been evaluated for inherent G sensitivity (i.e., a sensitivity to G forces within the transducer)  $\sim 1$  yr before the flight. For this test, two units were assembled and tested for barometric pressure insensitivity. Then they were secured in an apparatus that maintained the transducer in a stable orientation aboard a KC-135 aircraft. This aircraft had been modified to perform parabolic flights. The parabolic flight profile produces alternating periods of 2 and 0 G. Both units measured a constant 0-mmHg test pressure in the varying barometric pressure and G environment of the KC-135.

On launch morning, the calibration was verified, and the unit was again tested in the hypobaric chamber. Before and during launch, the astronauts wear a combination partial pressure, exposure, and anti-G suit. During astronaut suitup, the catheter was flushed, routed to the outside of the launch suit, and connected to the SMCVP. The suit was inflated and checked for leaks, and then the CVP was rechecked with a series of Valsalva and Mueller maneuvers. The crew members then rode to the shuttle, strapped themselves into the horizontally positioned seat, and remained in a supine legs-up posture before launch for 4 h on SLS-1 and 2 h on SLS-2. CVP

was measured continuously from suitup until the end of the first in-flight day for *subjects 1* and *2* (9–10 h) and until the end of the second in-flight day for *subject 3* (44 h). Due to a malfunctioning data recorder, continuous CVP measurements were lost on *subject 3* after the first 30 min in orbit. Mean CVP readings were voiced to the ground twice (at 1 and 4 h into the flight), and dynamic CVP data were transmitted to the ground on the second flight day during the echocardiographic measurement session described below.

The launch suit is removed shortly after entering space. The process of removing the suit involves disconnecting and reconnecting the catheter. Also, *subject 1* used the backup unit to verify the CVP readings, and this also involved disconnecting and reconnecting the catheter. After these procedures were performed on *subject 1*, the CVP waveform appeared damped and did not display the same dynamic response as it did early in the flight. The mean CVP reading, however, was the same, and the pressure responded appropriately to both Valsalva and Mueller maneuvers, indicating that the system was still functioning normally in all other respects.

In addition to CVP, the crew members were also instrumented for measuring heart rate (HR) and blood pressure with NASA's physiological measurement system (6). The electrocardiogram (ECG) was acquired from three chest electrodes, and blood pressure was measured indirectly with an upper arm cuff and a brachial arterial microphone to record Korotkoff sounds. The ECG, cuff pressure, and Korotkoff sound signals were recorded on a cassette data recorder mounted on the shuttle seat. The ECG was recorded continuously, and arterial blood pressure was measured approximately every 5–10 min. Before and during launch, these crew members had no assigned tasks and could sit quietly. Once in space, echocardiographic dimensions were acquired with a Hewlett-Packard (Andover, MA) 77020A echocardiograph modified for spaceflight. Left ventricular internal dimensions and left atrial dimension were acquired from the two-dimensional (2D) parasternal long-axis view. Ejection time was acquired with 2D-guided M-mode tracings. Two of the subjects (*subjects 1* and *2*) had dimensions measured on the first day in-flight, and one subject (*subject 3*) had the measure-

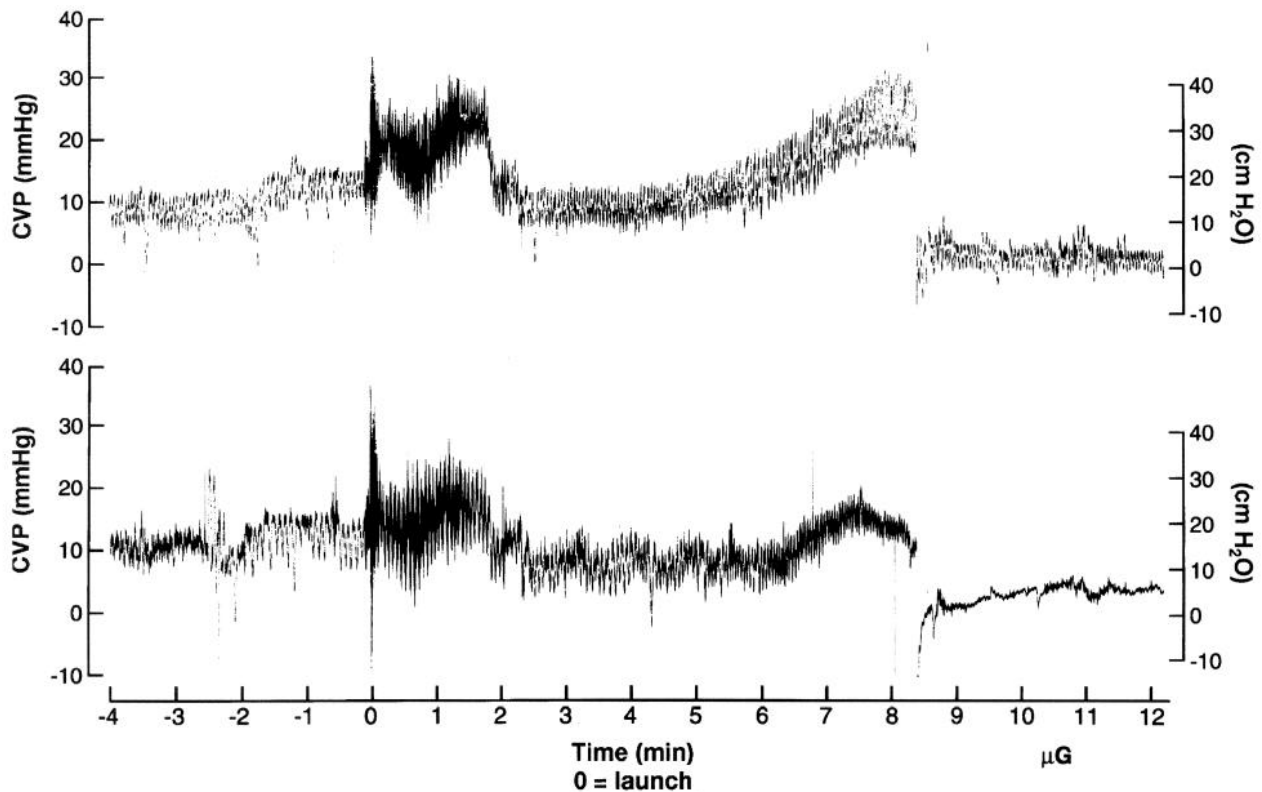


Fig. 2. Continuous CVP tracings for 2 of 3 subjects during 4 min before launch, during launch, and for 4 min after entry into microgravity ( $\mu\text{G}$ ). Continuous data for *subject 1* have been published previously (5). Launch occurs at 0 min on time scale, and entry into space occurs just after 8-min point. CVP fell promptly below preflight levels after entry into orbit. Pressure oscillations represent both cardiogenic and respiratory variations. Respiratory variations were prominent during launch when acceleration forces caused a front-to-back compression of chest. Large narrow spikes are motion artifacts.

ments made on the second day. Analysis was performed according to the American Society of Echocardiography guidelines (25).

Baseline data for HR, blood pressure, and echocardiographic measurements were recorded the day before flight after 20 min of supine rest. HR was determined from the ECG, and blood pressure from a brachial arm cuff Korotkoff sound device (Narco Electrosphygmomanometer, Houston, TX). A Hewlett-Packard Sonos 500 2D echocardiograph was used preflight. All the echocardiographs used were calibrated with an American Institute for Ultrasound in Medicine echocardiographic phantom (Nuclear Associates, Carle Place, NY) to ensure consistent results.

## RESULTS

Figure 2 shows the continuous CVP data for two of the subjects. Continuous launch data for the third subject (*subject 1*) has been published previously (5). CVP rose during the launch period when acceleration forces of up to 3.0 Gx compress the torso front to back, but, on entry into  $\mu\text{G}$ , CVP promptly dropped below prelaunch values within 60 s. During launch, larger respiratory swings in CVP can be noted when the chest is compressed. Table 1 summarizes the main CVP findings. CVP was 8.4  $\text{cmH}_2\text{O}$  seated on launch morning, 15  $\text{cmH}_2\text{O}$  1 h before launch in the supine leg-up position, and 2.5  $\text{cmH}_2\text{O}$  10 min after entry into orbit. Figure 3 shows CVP, HR, and mean blood pressure. Both HR and blood pressure showed a tendency to be

elevated above preflight values in the orbiter around the launch period. Measurements taken at the end of the CVP measurement period during echocardiography showed that HR and mean blood pressure had returned to preflight values, whereas CVP remained reduced below preflight supine values.

Despite the decrease in CVP, heart size increased (Table 2, Figure 4). The mean left ventricular end-diastolic dimension ( $n = 3$ ) increased from 4.60 cm the day before flight (supine) to 4.97 cm early in-flight. The left ventricular end-systolic dimension was 3.19 cm

Table 1. CVP data for the 3 subjects

	Subject 1	Subject 2	Subject 3
Seated CVP, $\text{cmH}_2\text{O}$	5.5	9.7	10.0
CVP 1 h prelaunch, $\text{cmH}_2\text{O}$	8.0	19.0	18.0
CVP after 10 min in orbit, $\text{cmH}_2\text{O}$	2.0	3.5	2.0
CVP last measurement, $\text{cmH}_2\text{O}$	1.0	3.5	8.0
Duration of CVP measurement, h	9	10	44
CVP postflight supine, $\text{cmH}_2\text{O}$	17.1		13.3

Central venous pressure (CVP) was measured seated immediately after suit-up on morning of launch. One hour before launch, all subjects were in legs-elevated supine posture in shuttle seats. CVP last measurement is CVP recorded before catheter was removed during echocardiography session (see Table 2). Postflight CVP was measured within 4 h of landing in 2 subjects during a supine resting period.

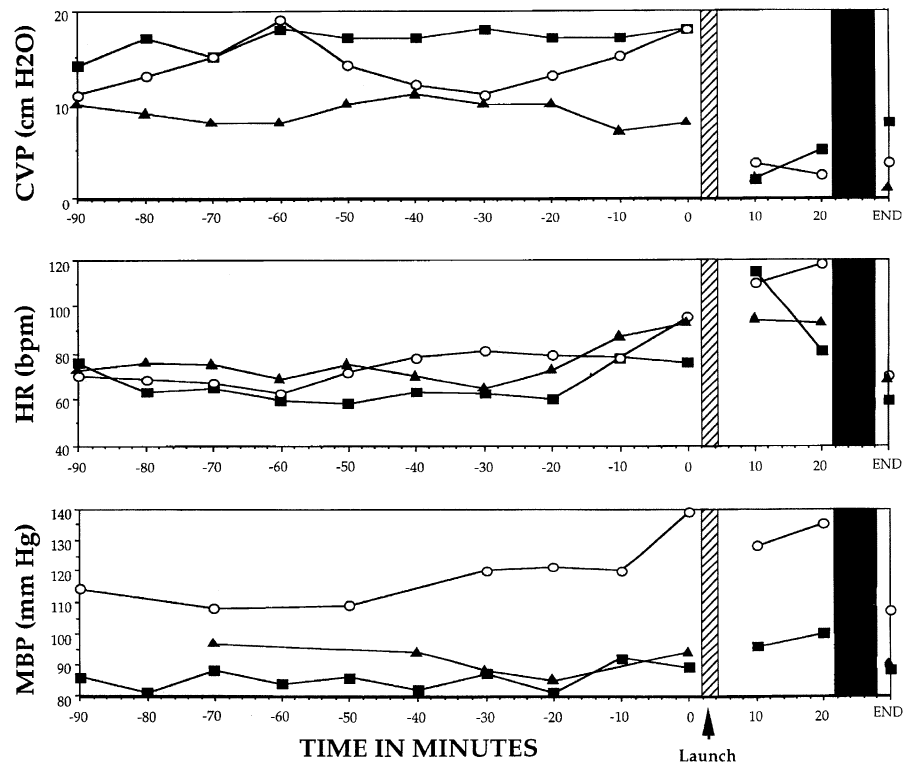


Fig. 3. CVP, heart rate (HR), and mean blood pressure (MBP) in 10-min increments in the 3 subjects.  $\blacktriangle$ , Subject 1;  $\circ$ , subject 2;  $\blacksquare$ , subject 3. Hatched bars, launch period, which lasted for 8 min. Solid bars, time between 20 min into  $\mu$ G and when echocardiographic measurements were made. End, measurements made during echocardiography; bpm, beats/min. Blood pressure measurements on subject 1 were lost during initial period in space and reestablished later in the day during echocardiography session.

preflight and 3.15 cm in-flight. Stroke volume computed from the 2D echocardiographic data on left ventricular end-diastolic and -systolic dimensions increased from 56 ml on the day before launch to 77 ml in-flight. Cardiac output increased from 4.0 l/min supine preflight to 5.0 l/min in-flight. The velocity of

circumferential fiber shortening was 0.99 circumferences/s preflight and 1.14 circumferences/s in-flight. HR was 71 beats/min supine preflight and 66 beats/min in-flight.

Table 2. Echocardiographic and CVP data for the 3 subjects

	Subject 1		Subject 2		Subject 3	
	Preflight	In-flight	Preflight	In-flight	Preflight	In-flight
Heart rate, beats/min	77	68	72	70	64	59
CVP, cmH <sub>2</sub> O	10.6	1.0	12.9	3.5	12.0	8.0
LVIDD, cm	4.61	5.20	4.50	4.74	4.68	4.96
LVIDS, cm	3.03	3.04	3.20	3.20	3.34	3.24
LAD, cm	3.16	3.29	2.76	3.30	3.11	3.16
Diastolic volume, ml	97.8	129.5	92.5	104.4	101.4	116.1
Systolic volume, ml	35.9	36.2	41.0	41.0	45.4	42.2
Stroke volume, ml	62.0	93.4	51.5	63.5	55.9	73.8
Cardiac output, l/min	4.8	6.3	3.7	4.4	3.6	4.4
V <sub>cf</sub> , circumferences/s	1.11	1.30	1.00	1.02	0.87	1.12

LVIDD, left ventricular end-diastolic internal dimension; LVIDS, left ventricular internal dimension systole; LAD, left atrial diameter; V<sub>cf</sub>, velocity of circumferential shortening. Diastolic volume is left ventricular end-diastolic volume calculated from dimension measurements. Systolic volume is left ventricular end-systolic volume calculated from dimension measurements. Preflight data were recorded on day before launch after 20 min of supine rest. In-flight data were collected on 1st flight day for subjects 1 and 2 and on 2nd in-flight day for subject 3.

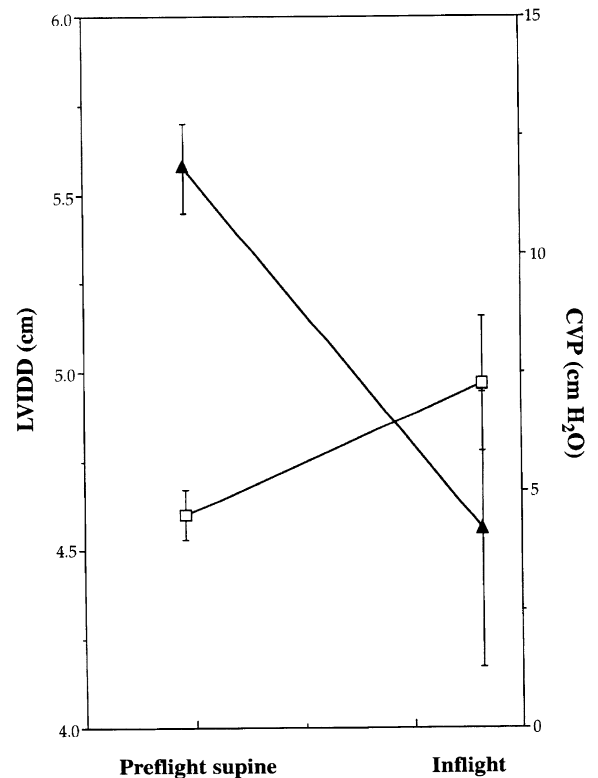


Fig. 4. Heart size [as measured by left ventricular end-diastolic internal dimension (LVIDD);  $\square$ ] and CVP ( $\blacktriangle$ ) measured during preflight supine measurement session and in-flight echocardiographic session. Heart size increased, whereas CVP decreased.

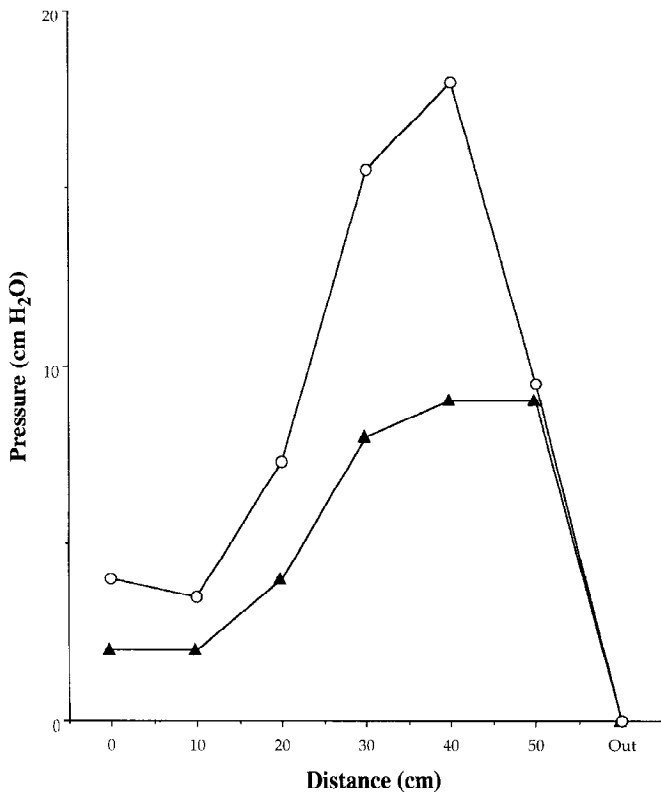


Fig. 5. CVP catheter removal in 10-cm increments in *subjects 1* (▲) and *2* (○). Pressure was recorded at each 10-cm point.

To allow for a comparison of CVP with peripheral venous pressure in space and to verify the zero reading of the units, two of the subjects (*subjects 1* and *2*) also recorded CVP in-flight while removing the catheter in 10-cm increments (Fig. 5). Pressure rose during the pullout to a peak of 9 cmH<sub>2</sub>O in *subject 1* and 18 cmH<sub>2</sub>O in *subject 2* and fell to 0 cmH<sub>2</sub>O in both subjects with complete removal.

## DISCUSSION

CVP decreased in space, refuting the hypothesis that CVP would increase significantly due to the  $\mu$ G-induced cephalad fluid shift. In fact, the pressure was below seated and supine levels as soon as the shuttle reached  $\mu$ G. The calibration of the SMCVP units was verified twice before the flight and again after landing. The units had also been tested to ensure that they were insensitive to changes in cabin pressure and G forces. The dynamics of the CVP waveform were unchanged from preflight (excluding *subject 1* during the latter part of *flight day 1*) and still showed oscillations due to respiration and the cardiac cycle at the time the catheter was removed. Taken together, this evidence supports the accuracy and integrity of the CVP measurement system. Direct CVP results from the Spacelab D-2 mission performed by Foldager et al. (9) on one subject also failed to show an increase above the 1 G supine level on entry into  $\mu$ G.

Previous arm venous pressure data taken in space arc consistent with our findings of a reduced CVP. Kirsch and colleagues (15, 16) measured peripheral

venous pressure (as an index of CVP) before, during, and after the Spacelab-1 and Spacelab D-1 flights. None of their four subjects increased peripheral venous pressure over preflight levels, and two showed substantial decreases at the time of the first in-flight measurement (22 h on Spacelab-1; 20 min on Spacelab D-1). These data, however, show peripheral rather than central pressure and also do not give the complete time course of the pressure changes before and in space.

The rapid fall in CVP after  $\mu$ G is entered is due, in part, to removal of the chest compression caused by the acceleration forces during launch, as has been seen during simulation experiments with a human-rated centrifuge (5, 19). However, CVP fell below the level established on the ground only minutes before launch. Rothe (24) has outlined three possible general mechanisms for a reduction in CVP: 1) increased cardiac contractility, 2) relaxation of venous smooth muscle, and 3) blood volume reduction. The echocardiographic data on left ventricular end-systolic dimensions and the velocity of circumferential fiber shortening indicate the absence of major changes in cardiac contractility, as previously noted by other investigators (10). In addition, the HR data do not support the possibility of increased sympathetic activation.

Venous capacity could have been increased in space for reasons other than smooth muscle relaxation. Pressure in the tissue surrounding veins and venules can alter their capacity. In space, solid tissue pressure [i.e., the compressive forces that solid structures exert on the surface of the blood vessel (14)] could be decreased due to the loss of hydrostatic pressures throughout the circulation. If this resulted in a reduced solid tissue pressure on the surface of blood vessels, then the effect would be functionally equivalent to venous smooth muscle relaxation. Evidence also exists for reduced blood volume on entry into  $\mu$ G. Astronauts routinely report that the head-down legs-elevated posture assumed for up to 4 h before launch produces a diuresis, although this was not seen in a simulation study (13). Some crew members will reduce their fluid intake before a flight so they will not have to void while on the launch pad. Insensible losses are likely to be high prelaunch due to the bulky poorly ventilated launch suit. The combination of these factors could lead to a reduced plasma volume even before entry into space. Plasma volume measurements taken early in spaceflight (29) also show marked (10–20%) reductions. Data from primates exposed to parabolic flight show that volume depletion before  $\mu$ G exposure leads to CVP reductions in  $\mu$ G (17, 18). Taken together, changes in venous capacity and blood volume could at least partially explain why CVP fell well below preflight supine levels in space.

A reduced CVP would be expected to be associated with reduced cardiac filling, stroke volume, and cardiac output. This did not occur. The echocardiographic data from this study and others (10) show that heart size increases above supine levels during the early part of a spaceflight (first 1–2 days). Also, stroke volume (measured by the foreign-gas rebreathing technique) has

been shown to be elevated early in flight (23), consistent with our echocardiographic findings. Two possible explanations exist for these results: 1) diastolic myocardial compliance rapidly increased in space and 2) effective filling pressure increased due to an increase in transmural pressure.

There is no known mechanism whereby  $\mu\text{G}$  could produce a sudden increase in intrinsic diastolic myocardial compliance, but an increase in transmural pressure could be produced by a reduction in pleural and/or solid tissue pressures on the outside of the heart. In 1 G, the fluid-filled lungs could exert a pressure on the outside of the heart due to their weight. Once in  $\mu\text{G}$ , this would be removed. In 1 G, when the subject is upright, intrapleural pressure is less negative at the base than at the apex because of the weight of the lung (30). An anteroposterior gradient exists when the subject is supine (1). Without gravity, intrapleural pressure may be more negative at heart level and contribute to a greater transmural pressure. Also, pressure surrounding the heart is affected by the diaphragm and abdominal contents when the subject is supine on Earth (1). In space, the abdominal organs are weightless and would no longer exert any pressure. Changes in intrapleural pressure could also be produced by alterations in chest wall mechanics (7, 8).

In summary, our data provide a continuous record of CVP changes from Earth to orbit and challenge traditional concepts of the early adaptation to  $\mu\text{G}$ . As expected, the launch position, similar to head-down tilt, raises CVP. During launch, CVP increases further. This change probably results from anteroposterior compression of the thorax and abdomen caused by acceleration forces up to 3.0 Gx (19). The compression of the chest also increases inspiratory effort, leading to larger respiratory variation in CVP (Fig. 2). Once in space, however, CVP dropped rapidly. The fluid shift in  $\mu\text{G}$  did not raise CVP, which suggests that there may be striking changes in the mechanical characteristics of both the central and peripheral circulatory system in space.

The limitations of this study are clear: only three subjects and many uncontrolled variables. Nevertheless, the data are unique and include the first direct measurements of CVP performed in humans during spaceflight. The pressure changes seen in space differ markedly from the responses to similar fluid shifts produced on the ground.  $\mu\text{G}$  produces unique changes in the hydrostatic forces on the body that cannot be reproduced on Earth, creating unexpected changes in CVP. The reduction seen in this study means the initial adaptation to space is more complex than initially thought and is consistent with major  $\mu\text{G}$ -induced changes in the relationship between pressure and volume in the circulatory system in space.

We are greatly indebted to Ross Goble, Dick Campbell, Greg Goble, and Bernie Poulin at Engineering Development Laboratory, Newport News, VA, for work developing the units. Boyce Moon, Willie Moore, Kim Frisk, and Harry Guy deserve thanks for help with the units and procedures. We thank Bill Young, Tim White, and John Lintott for help at the Johnson Space Center (JSC), Houston, TX. Debbie Vordermark and Bill Munsey at the Kennedy Space Center (KSC), Cape Canaveral, FL, and Gloria Salinas, Liz Kalla, Britt Walters,

and Mel Buderer at the JSC provided the facilities, equipment, and support needed before the flight. Robert Gonzalez, Carl Dillon, Ed Wagner, and Mike Justice spent long hours helping us prepare the equipment for flight. Merle Lenfest made sure we received the data intact. We thank the crews of Spacelab Life Sciences (SLS)-1 and SLS-2 for their participation. William Collins from Cape Canaveral Hospital, Cape Canaveral, FL, helped us greatly with fluoroscopy. We thank Debra Epstein for painstaking echo analysis. John Wiehe at Cook Catheter, Bloomington, IN, provided great help in designing the catheter. We also thank Rich Summers and Jim Cook for early contributions and crew surgeon John Schultz for his efforts and understanding. Carolyn Donahue deserves great thanks for all her efforts throughout the project and for help on the manuscript.

This work was supported by the National Aeronautics and Space Administration Contract NAS9-16044.

S. J. Wright was the recipient of a Will Rogers Memorial Fund Fellowship.

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Received 23 December 1994; accepted in final form 30 May 1995.

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