

LOWER BODY NEGATIVE PRESSURE: THIRD MANNED SKYLAB MISSION

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ABSTRACT

The crew of the Skylab 4 Mission exhibited physiological changes during their 84-day mission that resembled but in several important areas did not reach the magnitude of changes exhibited in crewmen of the two earlier Skylab flights. For example, calf girth diminished rapidly at first and continued throughout the flight, but at a slower rate than in the first two crews. At rest all three crewmen showed, in comparison to preflight levels, elevated mean systolic and pulse pressures and decreased mean diastolic and mean arterial pressures. Similar changes were seen in most Skylab 2 and Skylab 3 crewmen. While mean resting heart rates of both the Skylab 3 and Skylab 4 crews were elevated, those of the Skylab 2 crew were, however, lower than during preflight tests. Stressed heart rates followed previous patterns in being consistently elevated over preflight values. Again, increases of calf volume during lower body negative pressure greatly exceeded preflight increases. Postflight changes in cardiovascular parameters for the most part resembled those seen in previous crewmen of space missions. Their recovery to preflight limits occurred rapidly.

In-flight data and subjective impressions of the crewmen confirmed, as in previous Skylab flights, that lower body negative pressure in weightlessness imposed a greater stress upon the cardiovascular system than in Earth's gravity. Changed relationships in the anatomical distribution of blood volume and extravascular fluids, altered patterns of blood flow, and reduced total circulating blood volume induced by the weightless environment are offered as partial explanations for the changes in cardiovascular responses to lower body negative pressure. The exaggerated in-flight responses to lower body negative pressure generally appeared to decline after the first 30 to 50 days of flight. In-flight data served as a fairly accurate prediction of the post-flight status of orthostatic tolerance.

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INTRODUCTION

Medical evaluations after Gemini and Apollo flights demonstrated reduced orthostatic tolerance in virtually all crewmen specifically tested (1,2). This diminished ability of the cardiovascular system to function effectively against gravitational stress following exposure to weightlessness, while usually mild and never operationally significant, sometimes resulted in pronounced increases in heart rate and decreases in pulse pressure during orthostatic testing. However, forty-eight hours or less nearly always sufficed for orthostatic responses to regain their preflight status. The magnitude of this postflight loss of orthostatic tolerance showed no clear correlation with flight durations ranging between four and fourteen days. This enigma was compounded by the Russian reports of severe orthostatic intolerance in the Soyuz 9 crewmen after their eighteen-day flight (3). Against this background, concern for postflight orthostatic intolerance in the crewmen of the planned twenty-eight-day flight of the first manned Skylab Mission, Skylab 2, reached greater dimensions.

The objective of the Skylab lower body negative pressure experiment designated M092, was to determine the extent and the time course of changes in orthostatic tolerance during the weightlessness of space flight and to determine whether in-flight data from the experiment would be useful in predicting the postflight status of orthostatic tolerance.

Compared to preflight results, lower body negative pressure produced exaggerated blood pressure and heart rate responses during the first in-flight test of the Skylab 2 crewmen and showed no clear-cut trend toward preflight levels during the twenty-eight-day flight (4). Heart rate responses to the last in-flight test, however, compared quite closely to those of the first postflight test. Postflight orthostatic intolerance was not more severe than that seen after some Apollo flights and differed chiefly in requiring longer periods of time to return to preflight levels.

During the second manned mission, Skylab 3, similar exaggeration of blood pressure and heart rate responses occurred during the first in-flight test (5). Again no definite trend toward preflight values could be seen during the first twenty-eight days but cardiovascular responses to lower body negative pressure appeared to become more stable by the sixth to eighth week of flight. In general, the test results in-flight served to predict quite well the orthostatic tolerance of the individual crewmen in the immediate postflight period. The Skylab 3 crew responded surprisingly well to postflight lower body negative pressure tests. Moreover, the return of orthostatic responses to preflight values occurred more rapidly than after the

twenty-eight-day flight. During both flights the results of lower body negative pressure assumed an important role in assessing the in-flight status of crew health. The experience of the first two missions with the lower body negative pressure and other biomedical experiments greatly reduced apprehension toward extension of the third manned mission, Skylab 4, beyond the 59 days flown by the Skylab 3 crew.

METHODS AND MATERIALS

Preflight baseline data were acquired from the Skylab 4 crewmen over a four and one-half month period from four tests conducted at approximately monthly intervals and three during the last six weeks prior to launch. All tests were carried out in the Orbital Workshop one-g Trainer or the Skylab Mobile Laboratories using flight-type hardware. Training in the techniques of the test and operation of the equipment took place prior to the acquisition of baseline data, most of which was obtained from tests conducted by the astronauts acting both as subjects and observers as they would later do in flight. In-flight tests were conducted usually at three- or four-day intervals while postflight tests were carried out daily at first and then at increasing intervals of time over a period of approximately two months. Table I shows the number of tests on each Skylab 4 crewman during each period of the mission as well as those for the first two manned missions. Scheduling was such that, insofar as possible, each crewman's test was carried out at the same time of day and at least one, but if possible, two hours after meals or vigorous exercise.

TABLE I. LOWER BODY NEGATIVE PRESSURE DURING PREFLIGHT, IN-FLIGHT AND POSTFLIGHT PERIODS OF THE THREE SKYLAB MISSIONS AND TOTAL TESTS FOR EACH PHASE AND EACH MISSION.

| SkyLab Mission | | Preflight | In-flight | Postflight | Total |
|-------------------|-----------------|-----------|-----------|------------|-----------|
| 2 | Commander | 6 | 7 | 8 | 21 |
| | Scientist Pilot | 6 | 7 | 8 | 21 |
| | Pilot | <u>6</u> | <u>8</u> | <u>8</u> | <u>22</u> |
| | | 18 | 22 | 24 | 64 |
| 3 | Commander | 6 | 16 | 8 | 30 |
| | Scientist Pilot | 5 | 17 | 8 | 30 |
| | Pilot | <u>5</u> | <u>16</u> | <u>8</u> | <u>29</u> |
| | | 16 | 49 | 24 | 89 |
| 4 | Commander | 6 | 22 | 9 | 37 |
| | Scientist Pilot | 7 | 22 | 9 | 38 |
| | Pilot | <u>7</u> | <u>23</u> | <u>9</u> | <u>39</u> |
| | | 20 | 67 | 27 | 114 |
| Total: 3 Missions | | 54 | 138 | 75 | 267 |

The lower body negative pressure device, constructed of anodized aluminum, was tubular in shape and could be separated at its center to allow access to the subject's legs (figs. 1 and 2). Movable superior and lateral iris-like templates around the circular opening could be adjusted to fit snugly around the subject's waist. A waist seal of fire-resistant material encircled the end of the device and was fitted closely to the waist by means of a zippered opening and Velcro overlap, and a belt which encircled the waist just outside the metal opening. A padded post, which served as a saddle, could be adjusted footward or headward so that the iliac crests of the subject were at the level of the metal templates. Decreased pressure within the device was provided by a vacuum plenum, or during flight, the vacuum of space. In addition to a valve in this system, a second valve and a pressure gage mounted on the lower body negative pressure device permitted fine adjustment of the pressure within the device to any level between zero and 55 mm Hg below ambient pressure. Safety features included a quick-release valve, easily accessible to subject and observer, and an automatic mechanism to prevent negative pressure from exceeding 55 mm Hg. Sensors mounted inside and external to the device provided internal and ambient temperature records.

Basic measurements during all tests included blood pressure at 30-second intervals from an automatic system which detected and analyzed Korotkoff sounds, heart rate continuously from one component of a Frank lead vectorcardiogram and percentage change in calf volume continuously from capacitance plethysmographic bands encircling the legs (fig. 3). Prior to positioning these bands, a manual measurement was made of circumference of the largest portion of the calves, which also corresponded to the position where the left band was to be placed. Since the right band served solely to measure capacitance changes due to alterations of temperature and humidity within the negative pressure device, it was therefore placed around a rigid metal band which encircled the right leg at the lower level of the calf muscle. Additional measurements carried out during preflight and postflight tests included respiratory excursions from a mercury strain gage across the lower thorax, systolic time intervals from a phonocardiogram and carotid pulse transducer, and, in Skylab 4, echocardiograms. These along with vectorcardiographic findings and preflight and post-flight chest x-rays for cardiac size are discussed elsewhere (6-9). Prior to the lower body negative tests, as in Apollo 16 and 17 flight crew evaluations, lower limb volume was estimated from a series of girth measurements taken at three centimeter intervals between ankles and upper thighs. For the first time the latter measurement was also made several times during the Skylab 4 flight (10).

An Experiment Support System provided power and appropriate controls, including those necessary for calibration, to the hardware

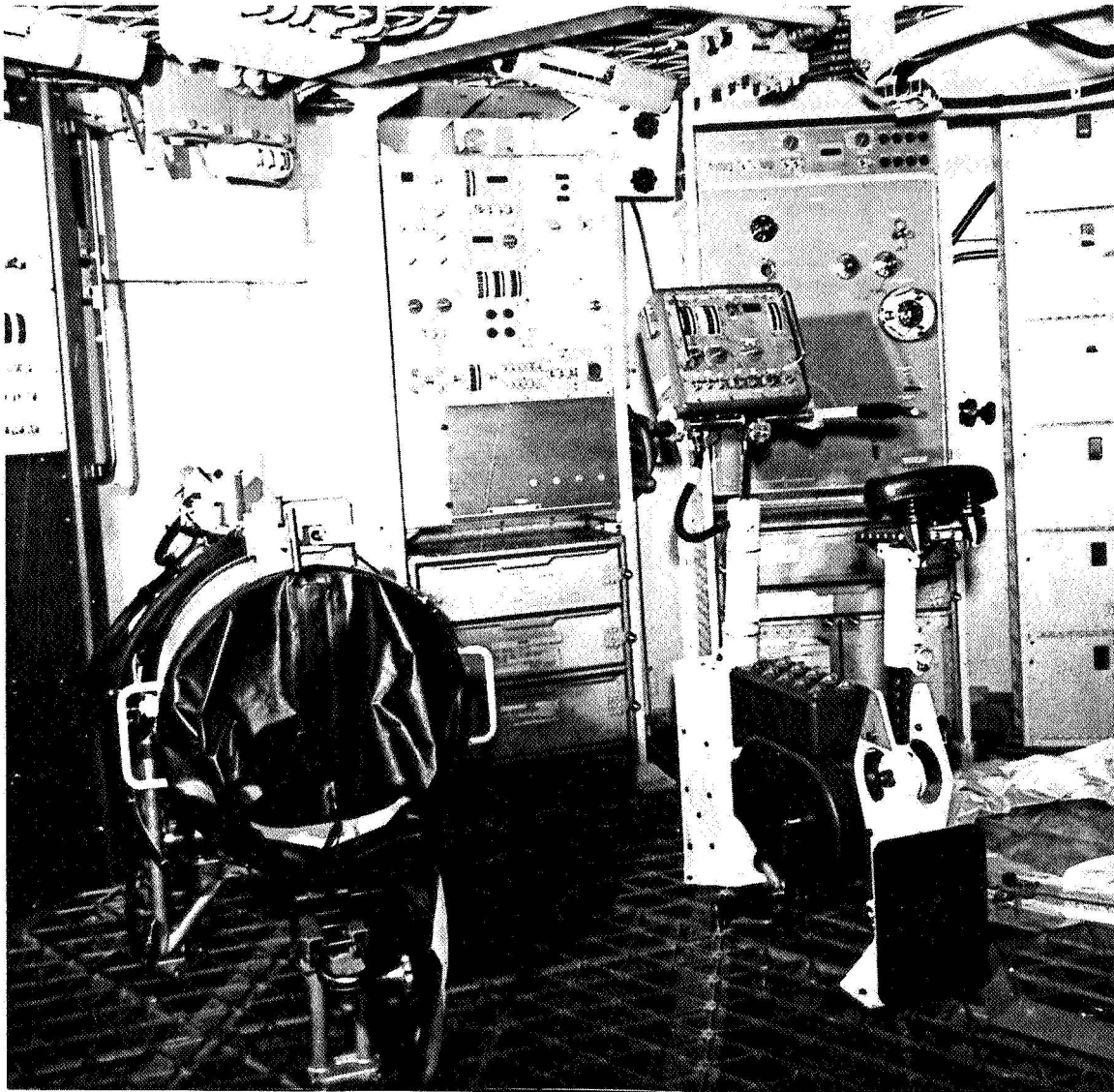


Figure 1. Photograph of the Lower Body Negative Pressure (LBNP) device, showing waist seal with zipper. Movable templates are hidden from view by the seal.

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Figure 2. Photograph showing side view of Lower Body Negative Pressure device. The ESS and its displays are in the background.

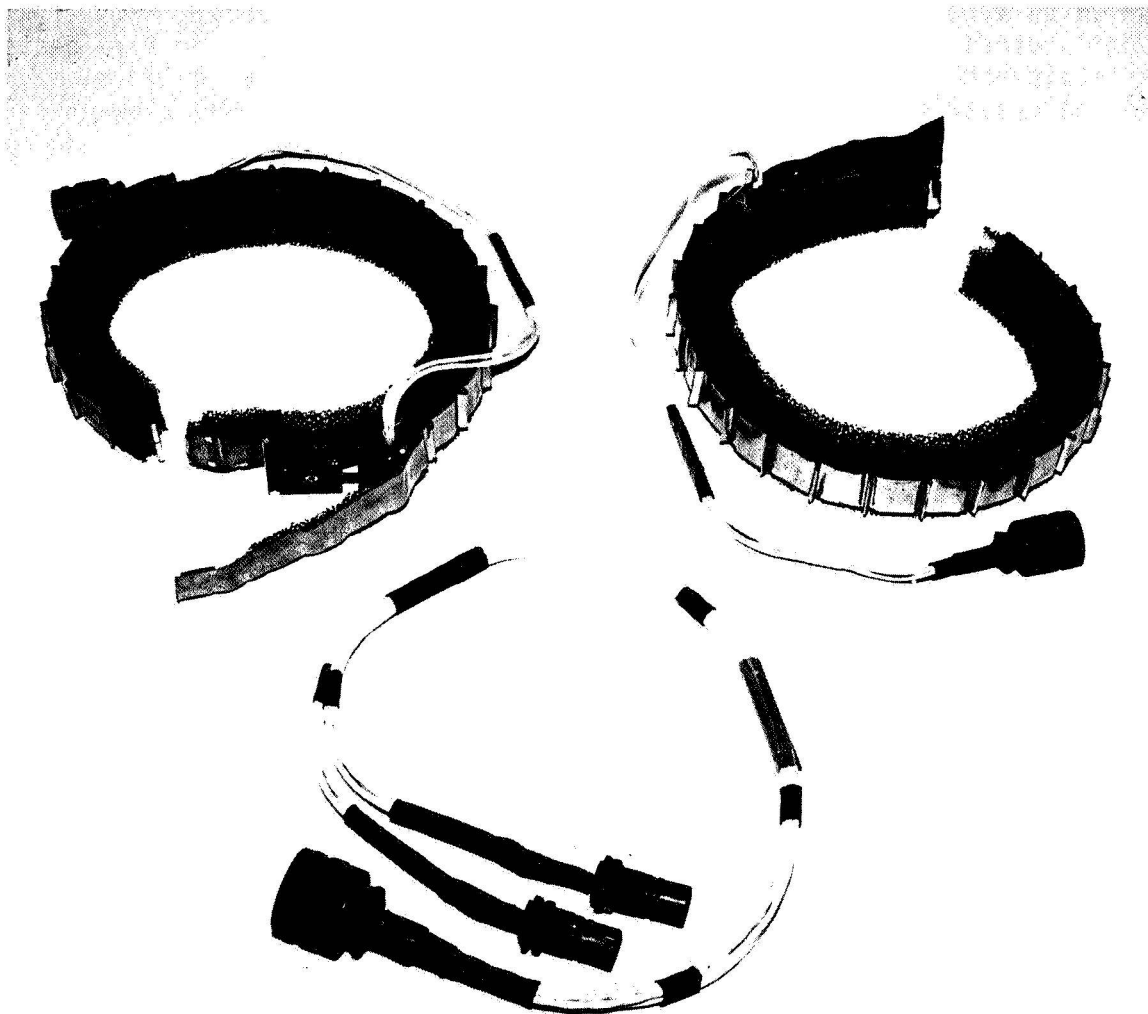


Figure 3. Photograph of capacitive plethysmographs and plug-in locking connectors.

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units already mentioned. The Experimental Support System (ESS) also contained displays for heart rate, which was updated every five beats, systolic and diastolic pressures, percentage changes in calf volume, and temperature within and exterior to the Lower Body Negative Pressure Device.

The lower body negative pressure protocol was identical to that adopted for Apollo studies. The first and last 5 minutes of the 25-minute test were at ambient atmospheric pressure to provide data from resting control and recovery periods, respectively. The 15-minute stress period consisted of five distinct levels of negative pressure applied sequentially: 8 and 16 mm Hg negative pressure for one minute each, 30 mm Hg for three minutes, and 40 and 50 mm Hg negative pressure for 5 minutes each (fig. 4).

Prior to entry, each crewman donned a garment which covered the lower body (see Skylab Medical Program Overview, fig. 6). Garment pressure against the skin was provided by lateral inflatable bladders and capstans. When inflated to gage pressure of 170 to 180 mm Hg, the capstans produced 85 to 90 mm Hg pressure at the ankles and a decreasing gradient of pressure headward which declined to 10 mm Hg at the waist. These garments remained pressurized, except during times when the crewmen could be recumbent, until beginning of the first post-flight lower body negative pressure test.

Blood pressure and heart rate data in this paper, unless otherwise specified, refer to mean values during the lower body negative pressure phase, usually the 5-minute periods during resting control and exposure to -50 mm Hg pressure. Mean values from preflight tests established fiducial limits at the $P < 0.05$ significance level for evaluating in-flight and postflight data. The subject of the Results, which follows, applies only to Skylab 4 crewmen except when otherwise specified.

RESULTS

In-flight

Heart Rate

During their first in-flight tests on mission days 5 and 6, resting heart rates of the Commander and the Scientist Pilot showed elevations of resting heart rates above fiducial limits established from preflight tests. The Pilot, on the other hand, on mission day 5 exhibited a resting heart rate that was relatively slow and well within

THE LOWER BODY NEGATIVE PRESSURE PROTOCOL USED FOR SKYLAB CARDIOVASCULAR EVALUATIONS ASSESSING ORTHOSTATIC TOLERANCE

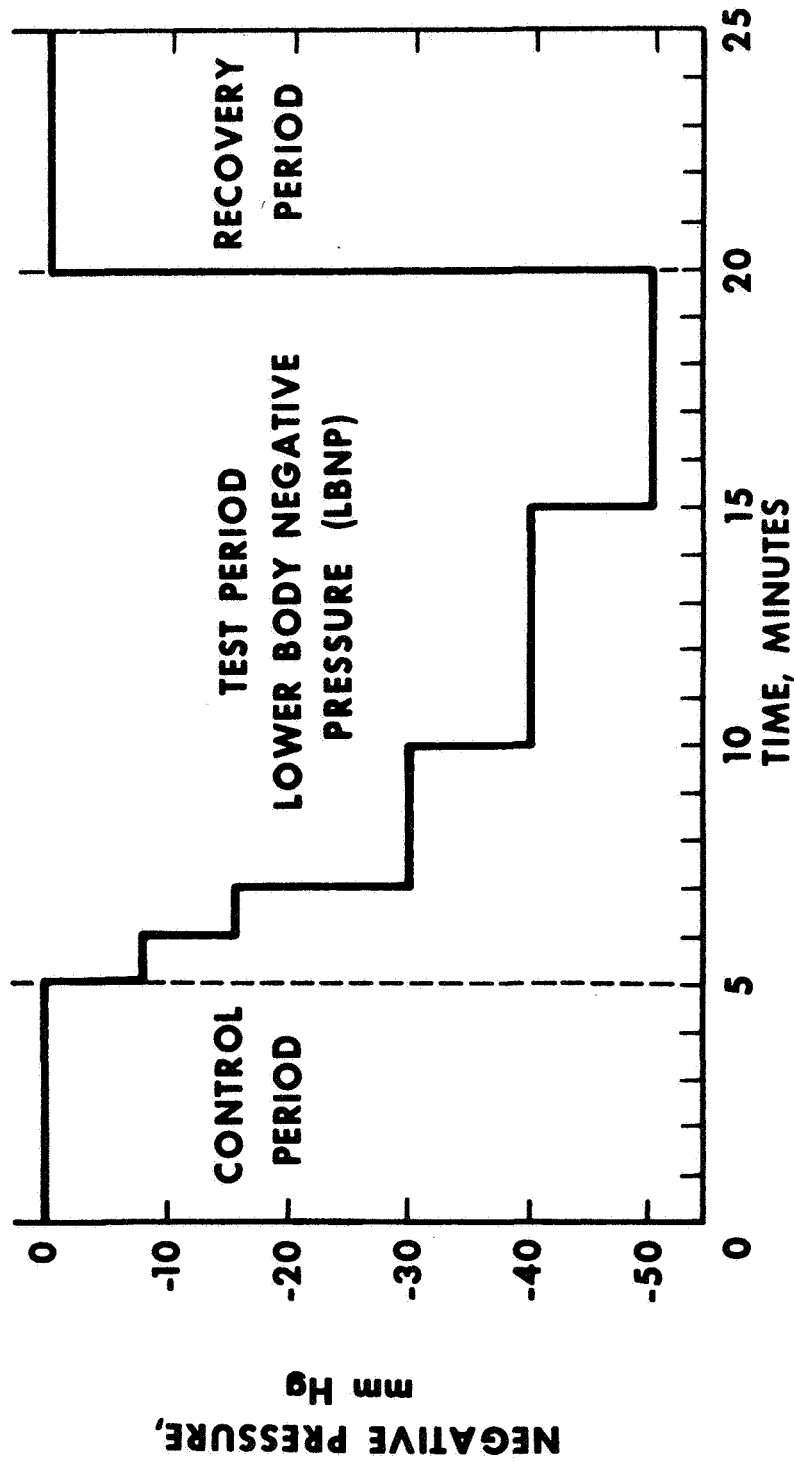


Figure 4. Levels of lower body negative pressure and time of individual phases of the lower body negative pressure protocol.

preflight limits. Typical preflight and the first in-flight tests of each crewman are shown in figures 5 through 10. After mission day 5 resting heart rates were elevated above preflight limits in nearly every test, although a probable trend toward lower rates appeared during the last third of the mission. This was more apparent in the Commander whose resting heart rates fell within preflight limits in three of nine tests after mission day 51 (fig. 11).

During the -50 mm Hg phase of lower body negative pressure heart rates became significantly elevated in all three crewmen in the first and in nearly every subsequent test throughout the flight. The degree of elevation fluctuated rather markedly from test to test. The Commander showed the least fluctuation and, after mission day 39, had no further tests in which stressed (-50 mm Hg) mean heart rates exceeded 81 beats per minute. In the majority of tests after mission day 51, his stressed heart rates remained within preflight limits. Fluctuations of mean stressed heart rates of the Scientist Pilot continued throughout the mission but remained significantly elevated above preflight limits. A slight downward trend may have been present after mission day 34 (fig. 12). Certainly after this time, tests with excessively high heart rate responses occurred less frequently. Stressed heart rate fluctuations of the Pilot became smaller after mission day 29 and a slowly declining heart rate response to lower body negative pressure may have been present after this time (fig. 13).

Blood Pressure

Mean values of systolic blood pressure (SBP) of the Commander during the resting control period of in-flight lower body negative pressure tests were usually within preflight limits. Significant elevations occurred infrequently and sporadically but were more common during the first half of the mission. Conversely, diastolic blood pressure (DBP) at rest was usually significantly lower than preflight values. Resting pulse pressure therefore usually exceeded preflight limits. Calculated mean arterial pressure ($SBP + \frac{SBP - DBP}{3}$) ranged below preflight limits in approximately one-half of the tests, occurring in four successive tests between mission day 11 and mission day 21 and in five of six tests between mission day 47 and mission day 66. The magnitude by which in-flight blood pressure and heart rate means of the Skylab 4 crewmen differed from preflight values appear in table II.

Diastolic pressure of the Commander during lower body negative pressure rose over resting values by significantly greater increments during in-flight tests than in preflight tests (fig. 14). Despite the greater in-flight rise, mean stressed diastolic pressure, while lower than preflight values, was not so to a significant degree. Higher resting levels and smaller falls of systolic pressure characterized in-flight

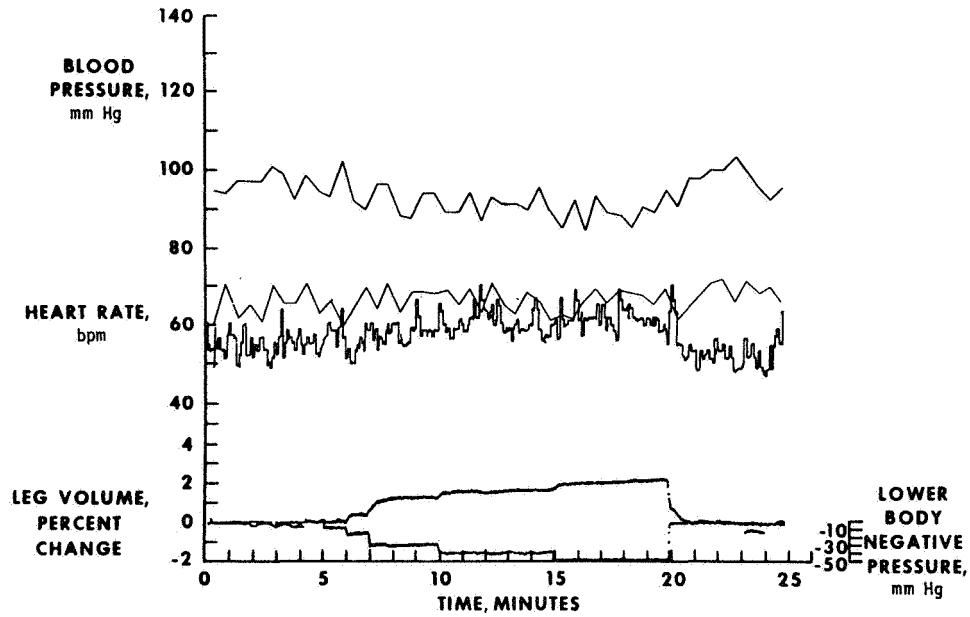


Figure 5. Cardiovascular responses of Skylab 4 Commander during test 50 days prior to flight.

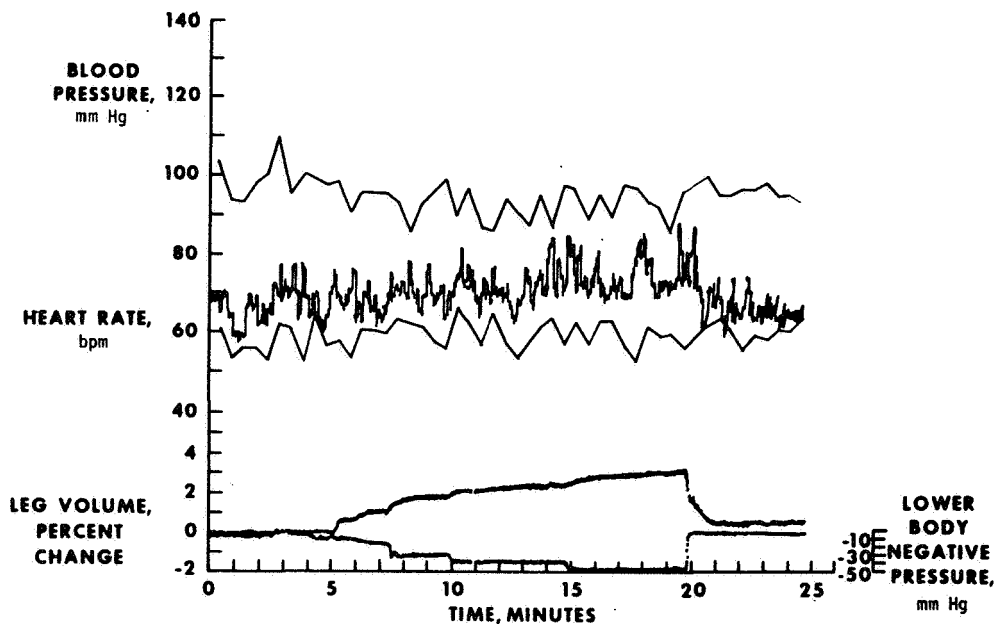


Figure 6. Cardiovascular responses during first in-flight test of Skylab 4 Commander on mission day 5. Moderate depression of diastolic pressure, elevation of systolic pressure during the resting control phase, and increased heart rate and calf volume change during lower body negative pressure are apparent.

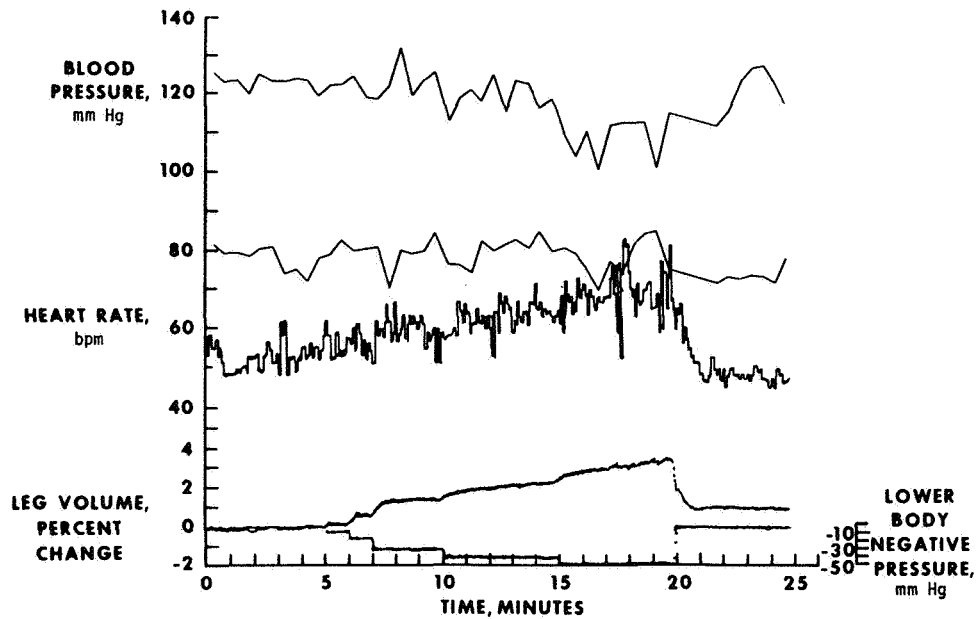


Figure 7. Cardiovascular responses of the Skylab 4 Scientist Pilot during test 21-days prior to flight.

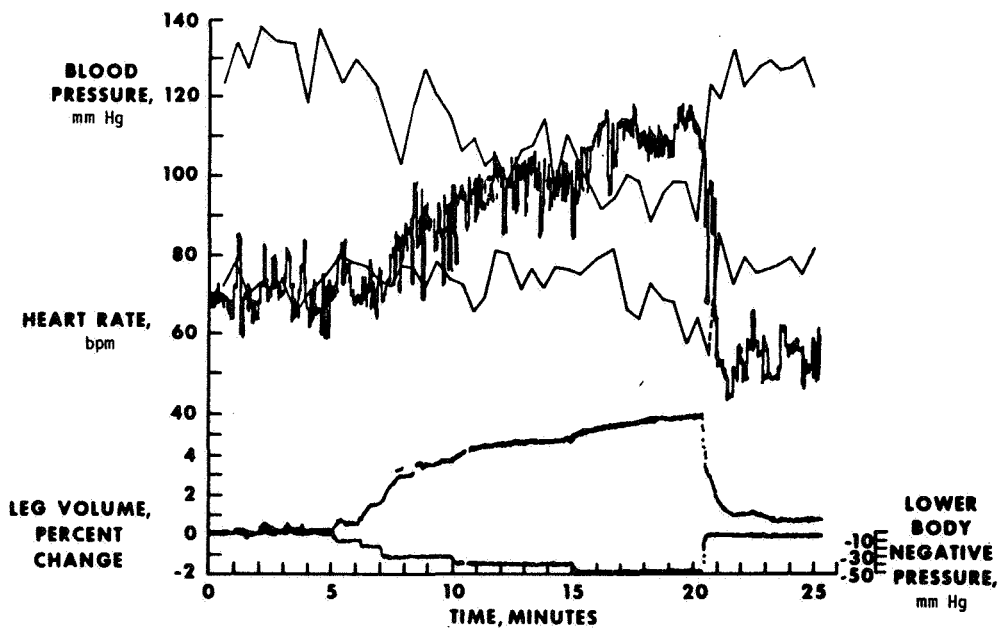


Figure 8. Cardiovascular responses during first in-flight test of the Skylab 4 Scientist Pilot on mission day 6. Changes from preflight values resemble those of the Commander in figure 6 but are more pronounced. The slightly early termination of negative pressure was not due to symptoms.

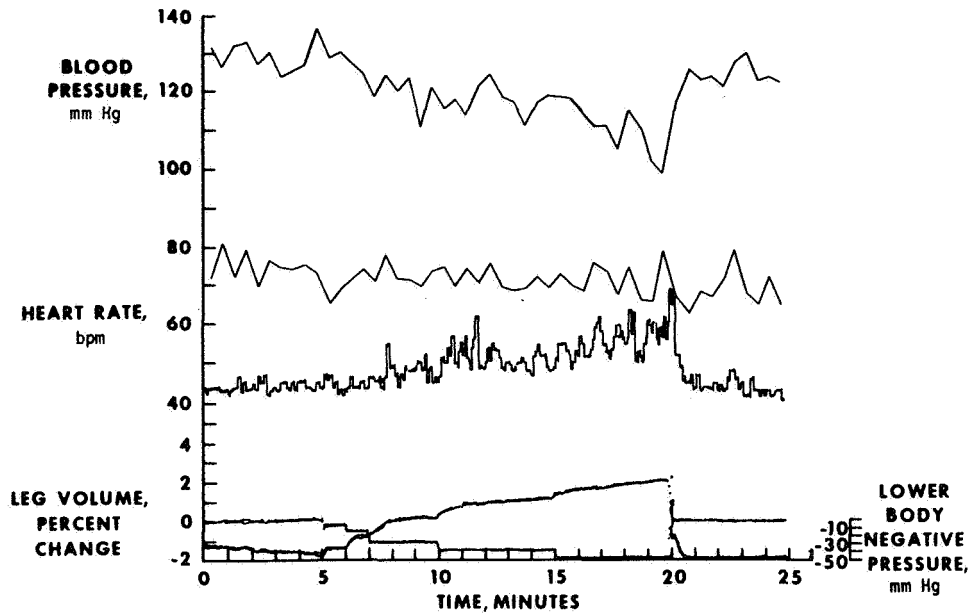


Figure 9. Cardiovascular responses of the Skylab 4 Pilot during test 35-days prior to flight.

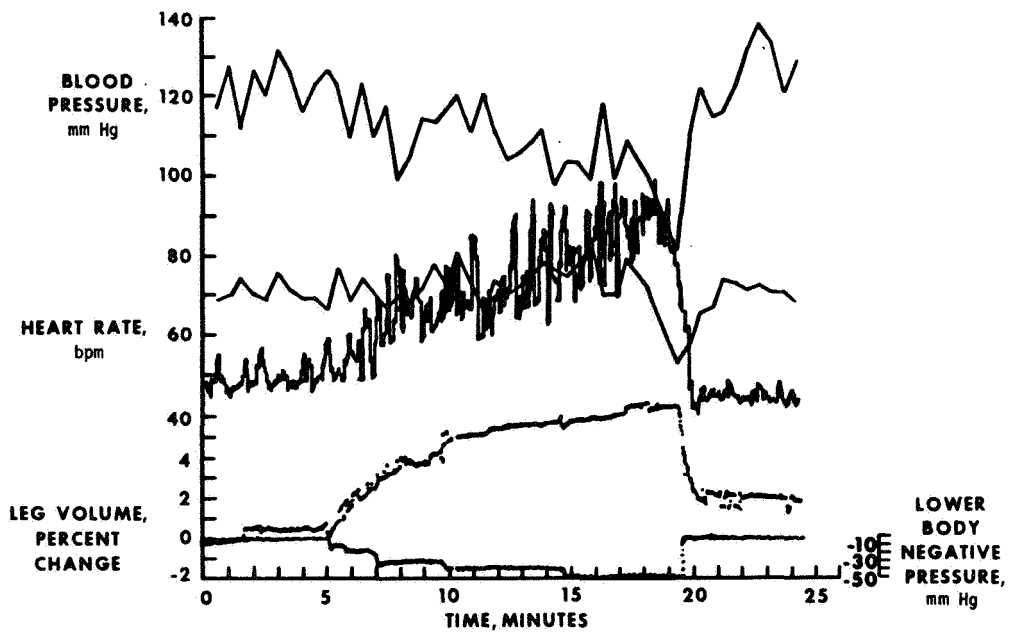


Figure 10. Cardiovascular responses during first in-flight test of the Skylab 4 Pilot on mission day 5 showing changes from preflight responses similar to those of the Scientist Pilot in figure 8.

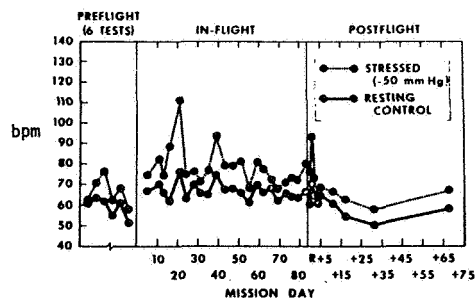


Figure 11. Mean heart rate of the Commander during resting and -50 mm Hg phases of lower body negative pressure.

Note the contracted time scale during the preflight period in this figure and similar figures that follow. Highest heart rate responses occurred on mission days 21 and 39 and post flight on recovery plus one day. A presyncopal episode on mission day 16 probably prevented higher mean heart rate on that day since the test was terminated after a little more than two minutes exposure to -50 mm Hg lower body negative pressure.

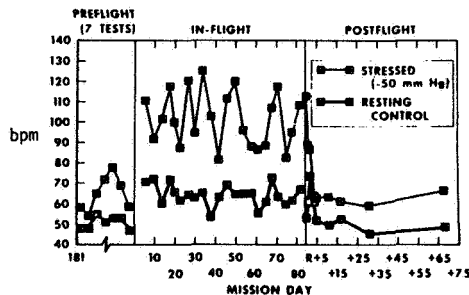


Figure 12. Mean heart rate of the Scientist Pilot during resting and -50 mm Hg phases of lower body negative pressure.

Presyncopal episodes on mission days 14 and 61 may have prevented higher stressed heart rates during these tests although such an effect was not apparent on mission days 34 and 71 when presyncopal symptoms also caused the tests to be terminated. Periodic high stressed heart rates climbed to a peak at mission day 34. Thereafter, these declined in magnitude and also in frequency.

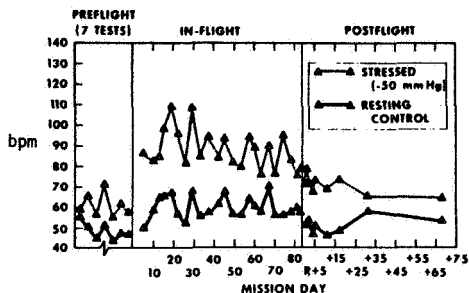


Figure 13. Mean heart rate of the Pilot during resting and -50 mm Hg phases of lower body negative pressure.

The high heart rates that appeared periodically declined in magnitude after the first month in-flight. A slight downward trend in stressed heart rates was apparent during the latter period. A presyncopal episode on mission day 10 may have been associated with the lower mean stressed heart rate on that day.

TABLE II
DIFFERENCES BETWEEN MEAN IN-FLIGHT VALUES FOR HEART RATE AND BLOOD PRESSURE OF THE SKYLAB 4 CREWMEN DURING REST AND -50 mm Hg PHASE OF LOWER BODY NEGATIVE PRESSURE FROM CORRESPONDING MEAN VALUES DURING PREFLIGHT TESTS.

| | Commander | Scientist Pilot | Pilot |
|----------------------------------|--------------------|--------------------|--------|
| Resting Control | | | |
| Heart Rate (bpm) | +7.8* | +13.3* | +11.3* |
| Systolic Blood Pressure (mm Hg) | +1.8 | + 2.5 | + 1.0 |
| Diastolic Blood Pressure (mm Hg) | -5.6* | - 2.0 | - 2.5 |
| Pulse Pressure (mm Hg) | +7.4* | + 4.5 [†] | + 3.4 |
| Mean Arterial Pressure (mm Hg) | -3.2 [†] | - 0.5 | - 1.3 |
| Stressed -50 mm Hg | | | |
| Heart Rate | +12.2 [†] | +36.7* | +26.7* |
| Systolic Blood Pressure | +6.2* | -10.9* | - 1.6 |
| Diastolic Blood Pressure | -1.0 | - 4.8 | + 1.3 |
| Pulse Pressure | +7.1* | - 6.1 | - 2.8 |
| Mean Arterial Pressure | +1.5 | - 6.8* | + 0.3 |

* Significant to 0.001 level by paired t-test

† Significant to 0.01 level by paired t-test

‡ Significant to 0.05 level by paired t-test

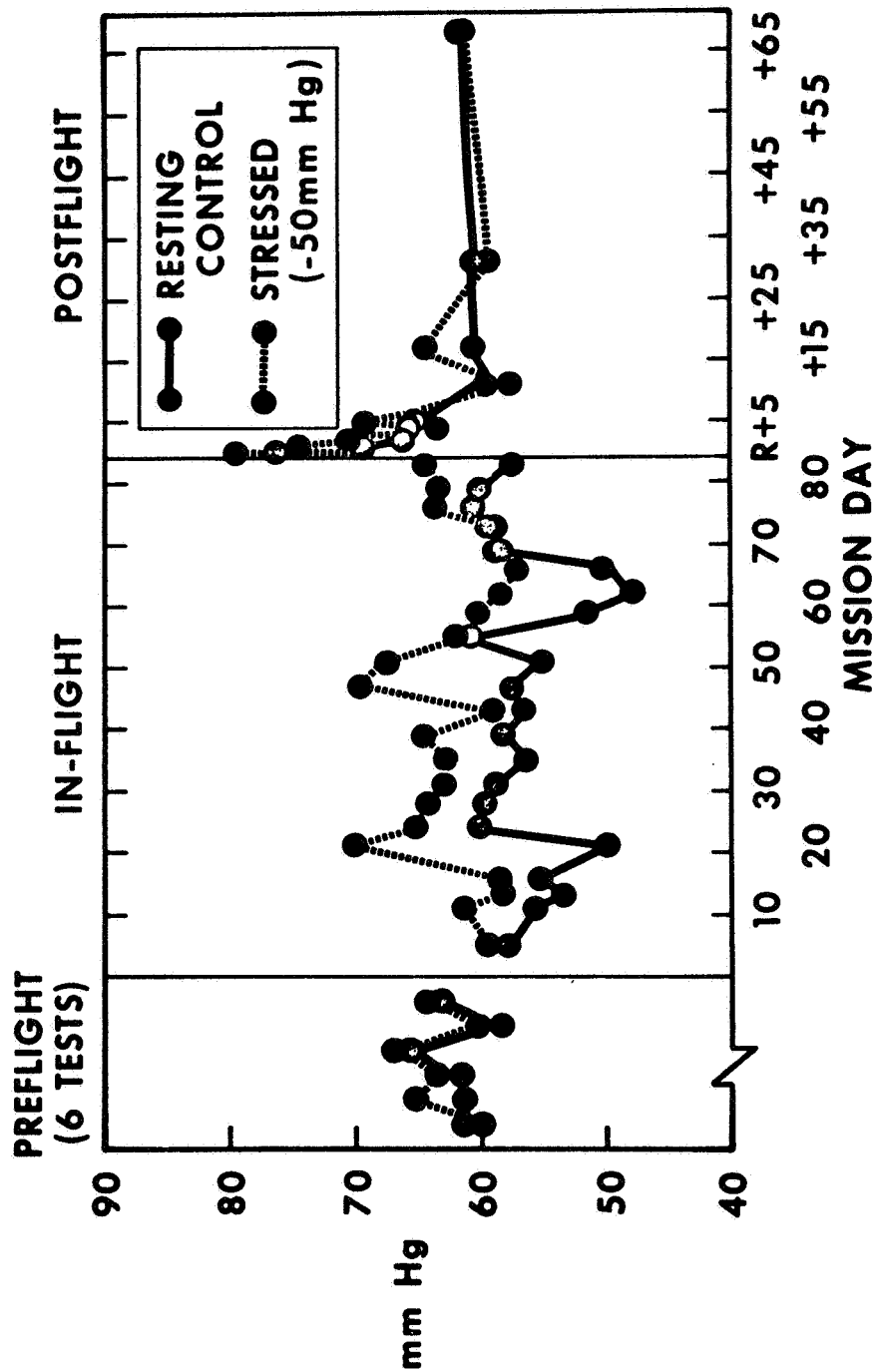


Figure 14. Mean diastolic blood pressure of the Skylab 4 Commander during resting control and -50 mm Hg pressure phases of lower body negative pressure. The marked elevation on mission day 21 was associated with the highest stressed heart rate seen in the Commander's in-flight tests. The elevated diastolic pressure on mission day 39, on the other hand, occurred in association with a heart rate that was only modestly elevated.

lower body negative pressure tests of the Commander as compared to preflight. This combination led to the unusual finding of a significantly higher in-flight mean value of pulse pressure during -50 mm Hg than preflight. Stressed pulse pressure in-flight exceeded preflight stressed pulse pressure in only two other Skylab crewmen, the Commander of Skylab 3 and the Pilot of Skylab 2. In-flight mean values for mean arterial pressure of the Commander during the -50 mm Hg phase of lower body negative pressure differed only slightly from preflight values. Evidence for any trend of change in blood pressure parameters during flight were lacking.

While blood pressure of the Commander showed less variance from test to test in the preflight period than any of the other eight Skylab astronauts, both the Scientist Pilot and the Pilot showed considerable lability of blood pressure during their preflight tests. As a consequence, in-flight changes from preflight values did not achieve statistical significance unless they were of large magnitude.

Even though resting systolic blood pressure of the Scientist Pilot during in-flight tests exceeded preflight limits rather frequently during the first half of the mission, its mean value for all in-flight tests did not depart significantly from preflight values. Diastolic pressure at rest showed little change from mean preflight values. The mean of in-flight values for resting pulse pressure of the Scientist Pilot exceeded preflight means by a significant margin. In addition, most individual tests during the first half of the mission revealed resting pulse pressures significantly higher than preflight fiducial limits. Figure 15 shows mean values of systolic and diastolic pressure of the Scientist Pilot during rest and the -50 mm Hg phase of lower body negative pressure in all tests.

Stressed systolic blood pressure of the Scientist Pilot fell below preflight limits in nearly every in-flight test. Decreases of diastolic pressure below preflight limits during lower body negative pressure occurred less frequently. Stressed pulse pressure and mean arterial pressure frequently declined below preflight limits, and the mean value of mean arterial pressure during in-flight tests were significantly lower than the mean of preflight values. Over the in-flight period there appeared to be a slight downward trend in resting systolic and diastolic pressures and a questionable downward trend in their values during stress.

Resting and stressed systolic and diastolic blood pressures of the Pilot were within the rather wide preflight limits for these values in nearly all in-flight tests. The resting pulse pressure exceeded preflight limits occasionally and sporadically in in-flight tests since systolic blood pressure tended to be higher and diastolic pressure

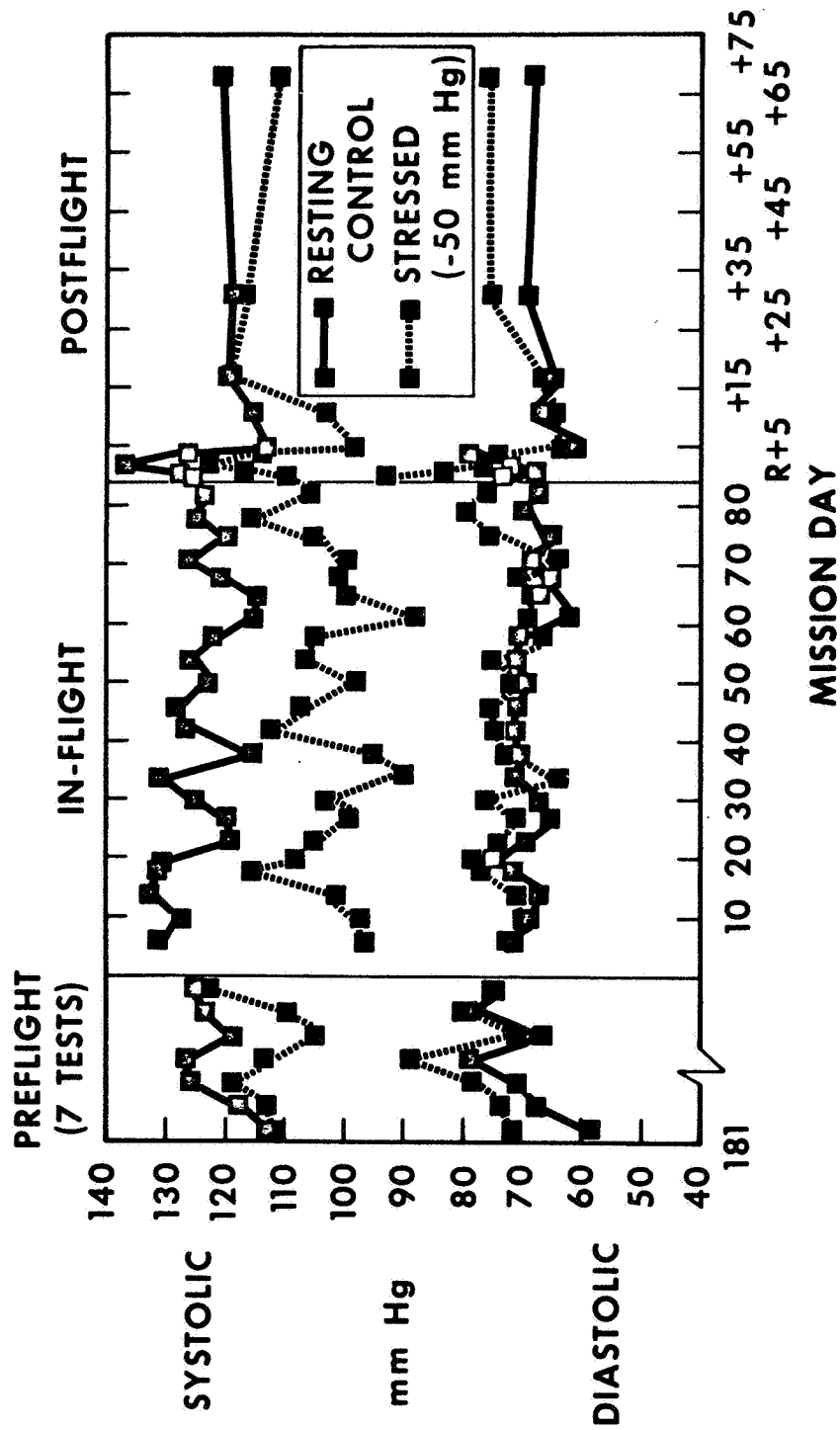


Figure 15. Mean systolic and diastolic blood pressures of the Skylab 4 Scientist Pilot during resting control and -50 mm Hg lower body negative pressure phases of individual tests. The magnitude of falls in systolic pressure during stress tended to decline during the course of the mission.

lower than preflight levels. While pulse pressure showed no definite trend or change during the flight, systolic, diastolic and mean arterial pressures, both at rest and during lower body negative pressure stress, showed definite declining trends (figs. 16, 17).

Calf Volume Increase Induced by Lower Body Negative Pressure

As had been observed in the first two Skylab Missions, calf volume increases during lower body negative pressure greatly exceeded those which had occurred in preflight tests. As illustrated in figures 18 and 19, the rate and magnitude of increase were especially pronounced at the lower levels of negative pressure, -8, -16, and -30 mm Hg. In some tests, calf volume increased so rapidly that the leveling off usually seen before the end of each minute of exposure to -8 and -16 mm Hg pressure did not occur until after the -30 mm Hg level had been reached. This pronounced change in calf volume appeared in the first test and continued, although varying considerably between tests, throughout the mission.

Calf volume increases of the Commander in preflight tests were relatively small in contrast to those of the Scientist Pilot and Pilot, which were larger than usually seen. This same pattern of difference continued throughout the flight. Even when using the least sensitive band available, calf volume of the Scientist Pilot and Pilot rather frequently reached off-scale values after increasing to about 8.5 percent. On mission day 54, following instructions from the ground, the crew made adjustments to reduce sensitivity of the band used by these two crewmen by about 30 percent. Thereafter, the off-scale condition was not reached, even though calf volume increases sometimes exceeded 11 percent. Whereas preflight calf volume increases at the end of the -50 mm Hg phase averaged between 3 and 4 percent, during in-flight tests they reached values usually between 8 and 11 percent in the Scientist Pilot and Pilot. In the Commander, calf volume increases averaged 2.4 percent preflight but usually reached levels ranging between 5 and 7 percent in-flight.

During preflight tests, calf volume decreases indicating venous drainage usually were seen during the five minutes of rest preceding negative pressure. Calf volume during this five-minute period in-flight tests usually shifted upward, indicating an increase in venous inflow. Frequently during the -8 mm Hg and -16 mm Hg phase in preflight tests, evidence of active venous contraction occurred after the initial filling period. This phenomenon was seen more often in the Commander than in either the Scientist Pilot or Pilot. During in-flight tests such indication of venous contraction occurred only infrequently and sporadically.

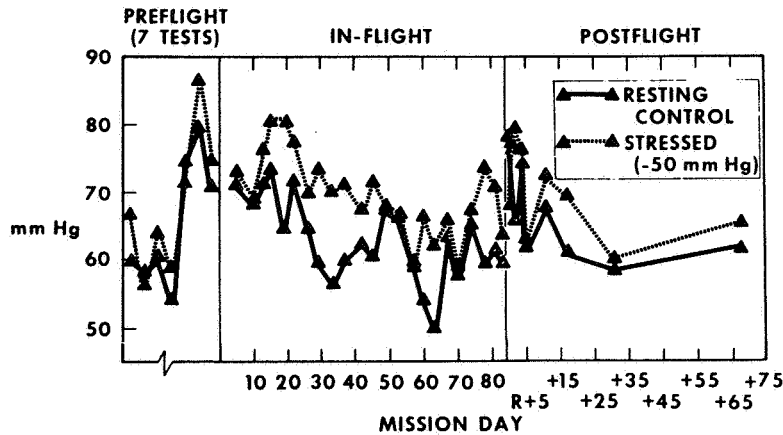


Figure 16.
Mean diastolic pressure of the Skylab 4 Pilot during resting and -50 mm Hg phases of individual lower body negative pressure tests.

In most tests, especially through the first two-thirds of the mission, elevations in diastolic pressure during stress were of large magnitude.

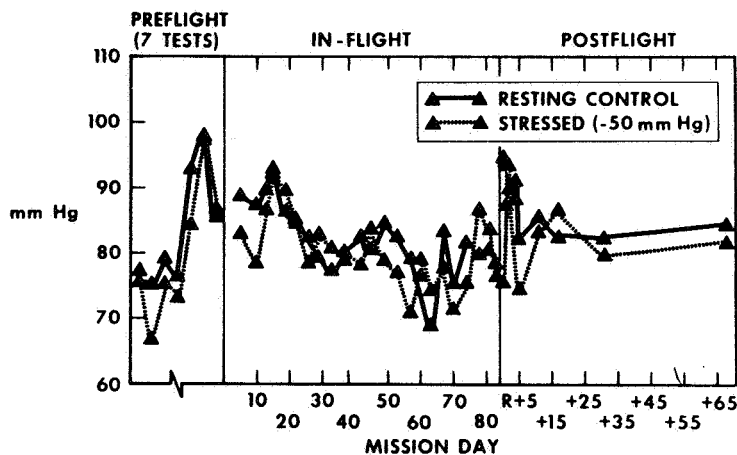


Figure 17.
Mean arterial pressure during resting and -50 mm Hg phases of individual tests of the Skylab 4 Pilot.

A trend toward lower values is extended throughout the in-flight period.

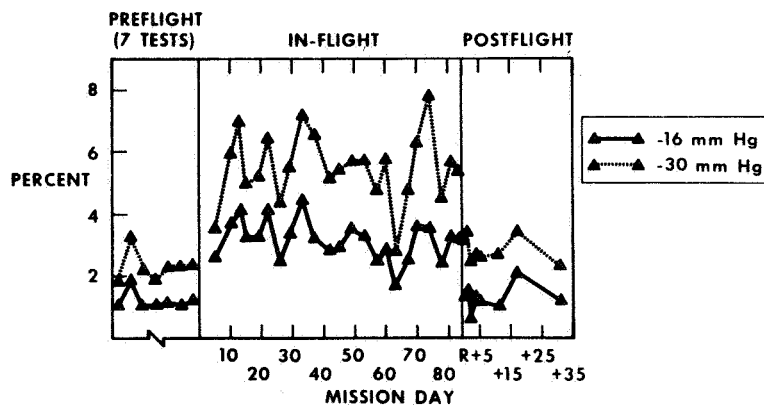


Figure 18.
Increases in calf volume, expressed as a percentage change from resting control volume, during lower body negative pressure tests of the Skylab 4 Pilot.

The values shown indicate percent volume increase at the ends of the one-minute -16 mm Hg and the three-minute -30 mm Hg phases of lower body negative pressure. Resting calf volumes are shown as zero, but actually declined during the course of the flight.

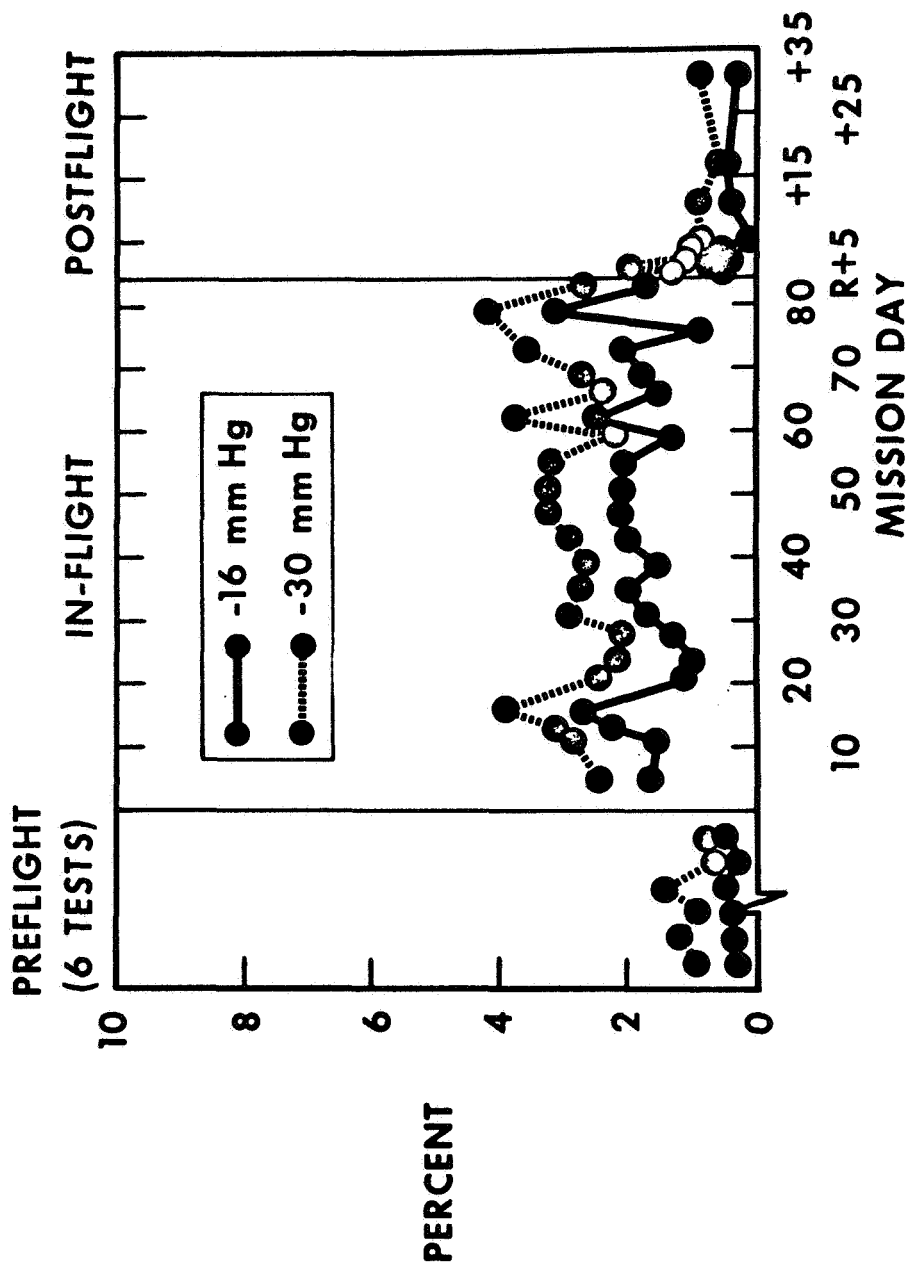


Figure 19. Percentage increase in calf volume of the Skylab 4 Commander at the end of -16 and the -30 mm Hg phases of individual tests of the Commander. Absolute values during both preflight and in-flight periods were lower than those of the Scientist Pilot and Pilot (shown in preceding figure). Proportionate increases of in-flight over preflight values were similar.

Following cessation of negative pressure, calf volume returned usually to within 0.5 percent above or below the resting value in preflight tests. Conversely, during in-flight tests, calf volume at the end of the five minute recovery period usually measured close to two percent above baseline values. In the case of the Commander, there appeared to be an upward trend in this residual volume during the first five weeks of the mission (fig. 20).

Other Measurements and Observations

Resting calf circumference measurements were made by the Skylab 4 crew on mission day 2, three days before the first lower body negative pressure experiment. At this time, both the Commander and the Pilot showed declines of approximately one centimeter from the last preflight measurement. The calf circumference of the Scientist Pilot showed a slight increase, a finding which cannot be adequately explained. These early measurements differed little, if any, from the subsequent measurements on mission day 5 and mission day 6, which showed reductions ranging from 0.8 to 2.0 percent from the last preflight values. This represented a smaller reduction than had occurred in the Skylab 2 and Skylab 3 crewmen whose decreases after comparable times in weightlessness had ranged between 3.5 and 5.0 percent (table III). Subsequent measurements throughout the Skylab 4 flight showed further rapid decreases during the first three weeks and thereafter a slow but steady decline which was apparently continuing at the end of the 84-day mission (fig. 21). The rate of decline was considerably slower than in Skylab 2 and Skylab 3 crewmen, reaching approximately the same level after 84 days that had occurred after 25 to 27 days in crewmen of the first two Skylab flights.

TABLE III
 PERCENT DECREASE FROM LAST PREFLIGHT VALUES IN MEAN CALF CIRCUMFERENCES $(\frac{R+L}{2})$
 OF THE NINE SKYLAB CREWMEN AT DESIGNATED MISSION DAYS IN-FLIGHT AND AT THE TIME OF THEIR
 FIRST FIVE POSTFLIGHT EXAMINATIONS.

| | Percent Decrease | | | | | | | | |
|-------------------|------------------|-----------------|-------|-----------|-----------------|-------|-----------|-----------------|-------|
| | Skylab 2 | | | Skylab 3 | | | Skylab 4 | | |
| | Commander | Scientist Pilot | Pilot | Commander | Scientist Pilot | Pilot | Commander | Scientist Pilot | Pilot |
| IN-FLIGHT | | | | | | | | | |
| Mission Day | | | | | | | | | |
| 2 | | | | | | | 2.0 | -0.8 | 2.5 |
| 4 | | | 4.3 | | | | | | |
| 5 | 3.7 | 5.0 | | | 3.5 | | 2.0 | | 2.5 |
| 6 | | | | 4.5 | | 4.1 | | 0.8 | |
| 25-27 | | | | 6.2 | 7.6 | 6.4 | 2.9 | 3.1 | 4.8 |
| 57-59 | 6.6 | 6.8 | 10.1 | 8.4 | 9.9 | 8.9 | 5.8 | 4.5 | 6.5 |
| 82-83 | | | | | | | 6.7 | 5.2 | 7.0 |
| POSTFLIGHT | | | | | | | | | |
| Recovery | | | | | | | | | |
| +0 | 6.0 | 6.8 | 8.3 | 9.1 | 10.3 | 7.3 | 7.2 | 5.7 | 7.7 |
| +1 | 4.8 | 5.8 | 5.6 | 8.1 | 8.1 | 8.6 | 4.7 | 4.9 | 6.1 |
| +2 | 4.6 | 5.0 | 7.5 | 8.3 | 8.1 | 7.5 | 3.2 | 3.9 | 4.9 |
| +4 | 5.4 | 4.7 | 5.6 | 5.6 | 7.0 | 2.7 | 2.9 | 1.5 | 3.5 |
| +5 | | | | | | | | | |
| +8-11 | 4.6 | 2.4 | 4.5 | 5.7 | 3.8 | 2.7 | 1.9 | 0.1 | 1.0 |

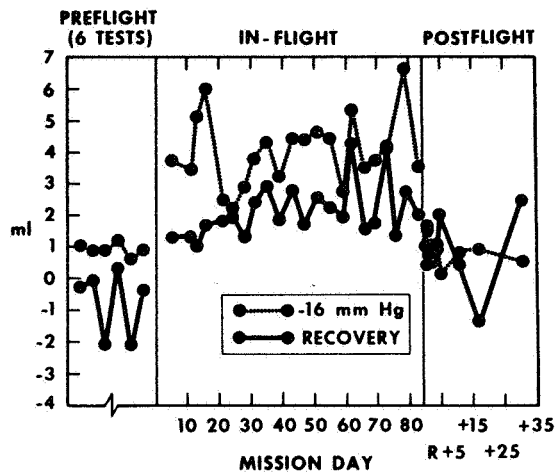


Figure 20. Absolute increases expressed in milliliters, over resting control values of leg volume at the end of the -30 mm Hg and the end of the 5-minute recovery phases of individual tests of lower body negative pressure of the Skylab 4 Commander. The latter measurement, representing residual volume increase, ranged slightly below the volume at -16 mm Hg in in-flight tests but fell below resting volumes preflight.

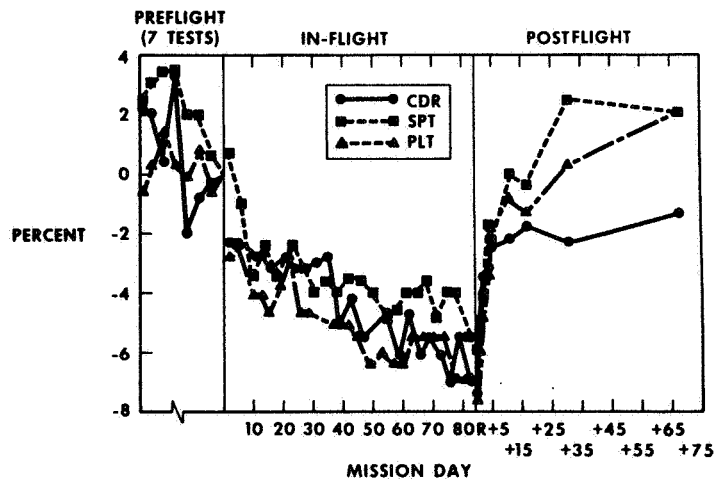


Figure 21. Calf girth of the three Skylab 4 crewmen measured just prior to each lower body negative pressure test. The mean $\frac{R+L}{2}$ of the right and left calf is shown. An eighth measurement, the last of those taken preflight, was made independently 6 days before flight and not in association with a lower body negative pressure test. This last measurement was used as a reference value, 100 percent, from which percentage difference of all other measurements were calculated.

Measurements of lower limbs to estimate volume were also made early, for the first time, in-flight. On mission day 3, estimates of lower limb volume indicated losses of 13.4 and 12.3 percent in the Commander and Scientist Pilot, respectively, compared with the mean of five pre-flight measurements. The decrease in the Pilot amounted to 9.2 percent on mission day 5. Subsequently, volume of the lower limbs appeared to decrease further as shown in table IV.

TABLE IV

PERCENT DECREASE FROM PREFLIGHT VALUES IN VOLUME OF THE LOWER LIMBS
AT THE TIME OF IN-FLIGHT MEASUREMENT, SKYLAB 4

| In-Flight | Volume of Lower Limbs Percent Decrease from Preflight Mean Values | | |
|---------------|--|-----------------|-------|
| | Commander | Scientist Pilot | Pilot |
| Mission Day 3 | 13.4 | 12.3 | |
| 5 | 12.2* | 9.7* | 9.2* |
| 8 | 13.4 | 13.5 | 13.1 |
| 31 | 15.8 | | 12.3 |
| 37 | | 15.3* | |
| 57-59 | 17.5 | 12.4* | 13.2 |
| 81 | | 12.2* | 13.4* |

* based on measurement of left lower limb only

Crewmen of the two previous missions had observed that lower body negative pressure in weightlessness forced them further into the Lower Body Negative Pressure Device. To compensate for this and to retain proper positioning of the iliac crests at the level of the iris-like templates, the saddle had usually been adjusted headward one and one-half inches from the position used preflight. This adjustment also became necessary for the Skylab 4 crew. Additionally, like previous crews they experienced abdominal discomfort from contact with the templates and seal that had not occurred on preflight tests. They also reported that the lower body negative pressure test remained subjectively very stressful throughout the flight.

The first test in which it became necessary to terminate the test early because of presyncopal symptoms occurred on mission day 10 during the second in-flight test of the Pilot (fig. 22). After nearly four

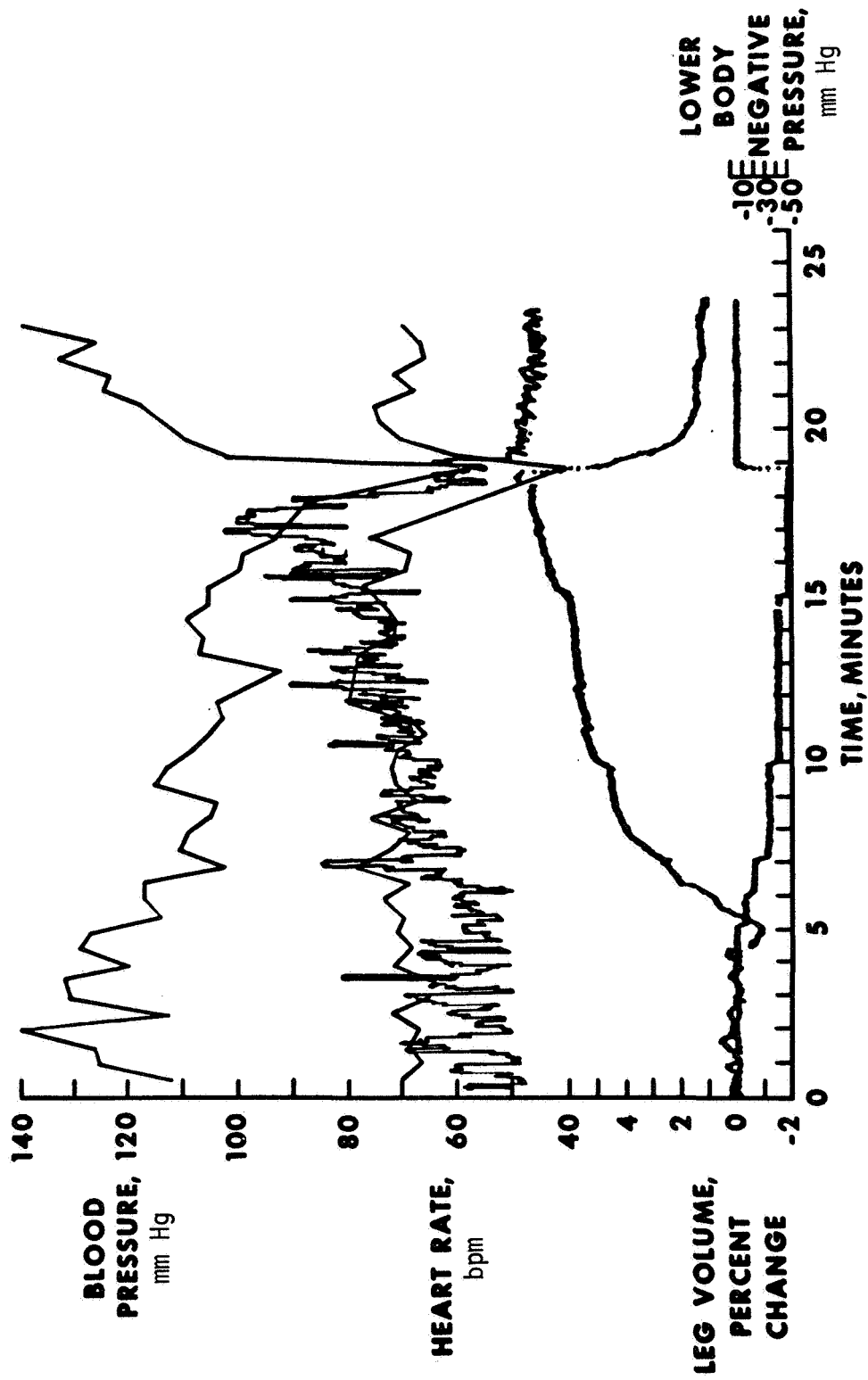


Figure 22. Cardiovascular responses of Skylab 4 Pilot during lower body negative pressure test on mission day 10. Presyncopal symptoms led to termination of the test after nearly four minutes' exposure to the -50 mm Hg phase (Skylab 4).

minutes of exposure to -50 mm Hg pressure he experienced a sensation of dizziness. Associated with this was a further marked fall in systolic and diastolic pressure and narrowing of pulse pressure. Heart rate had reached approximately 100 beats per minute and was falling prior to restoring lower body negative pressure to ambient. In his first in-flight test on mission day 5 (fig. 10), although no presyncopal symptoms had occurred, blood pressure and heart rate were falling just prior to completing the -50 mm Hg phase. In the recovery period following that test, marked sinus arrhythmia, bradycardia and atrio-ventricular dissociation had occurred suggesting a high rebound vagal tone and that a vasovagal reaction had been imminent. Heart rate had reached about the same level as during the second test although the increase in calf volume had been lower, 6.1 percent, at the end of the -50 mm Hg phase as compared with 9 percent in the test in which symptoms occurred. This test was carried out late in the afternoon following a very busy day in which the Pilot had missed lunch, and a time when he was feeling quite fatigued. Although higher mean heart rates and greater increases in calf volume during lower body negative pressure occurred on many subsequent tests of the Pilot, especially during the first month, symptoms requiring early termination did not recur.

As indicated earlier the blood pressure, heart rate and leg volume of the Scientist Pilot periodically responded quite markedly to lower body negative pressure throughout the mission. On mission day 14 during his third in-flight test, calf volume reached an off-scale condition at slightly over 7 percent increase early in the -30 mm Hg phase. Heart rate climbed rapidly and pulse pressure narrowed gradually during the ensuing minutes (fig. 23). After about two minutes of exposure to -50 mm Hg, systolic pressure fell more rapidly and diastolic pressure also began to fall. Heart rate reached nearly 120 beats per minute and then began to fall. Concurrently, light-headedness and tingling of the arms occurred and ambient pressure was restored after about 4 minutes of exposure to -50 mm Hg.

Symptoms such as tingling of the arms and shoulders and mild dizziness were commonly experienced by the Scientist Pilot but did not require another early termination of the test until mission day 34. This test terminated about two minutes early when the heart rate was falling from a peak of 140 beats per minute (fig. 24). Presyncopal manifestations including mild faintness and sudden pallor, occurred about 5 seconds before the -50 mm Hg phase was due to end on mission day 61 when ambient temperature in the orbital workshop had climbed from the usual 23.3° C (74° F) to 26.5° C (79.6° F). Again on mission day 71 symptoms led to termination of the test about 30 seconds early. Each of these four episodes were associated with the fatigue of a very busy

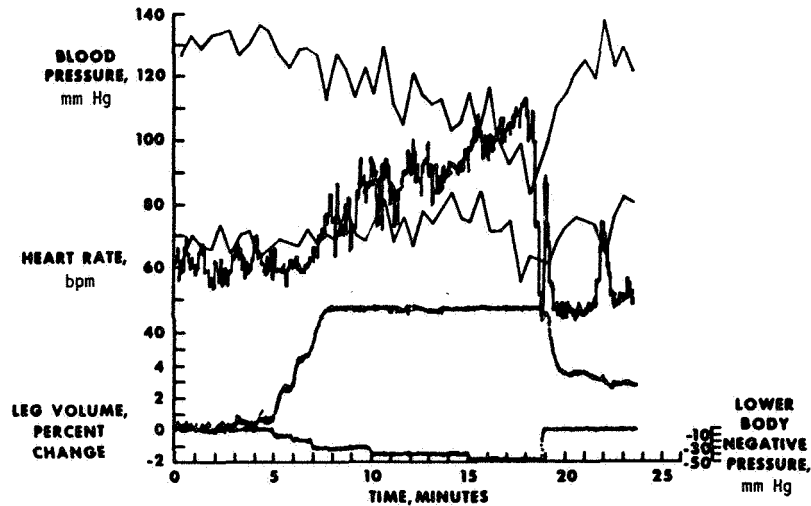


Figure 23. Cardiovascular responses of the Skylab 4 Scientist Pilot during the lower body negative pressure test on mission day 14. Presyncopal symptoms during the -50 mm Hg phase caused the test to be stopped after almost 4 minutes of exposure to this level of negative pressure. The leg volume increase reached the upper limits of transducer output a few seconds after the onset of 30 mm Hg negative pressure.

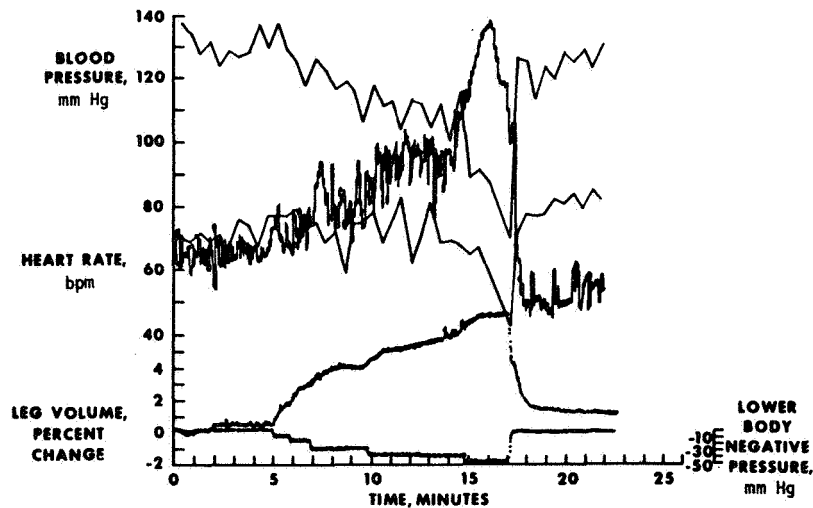


Figure 24. Cardiovascular responses of the Skylab 4 Scientist Pilot during the lower body negative pressure test on mission day 34. Presyncopal symptoms occurred soon after exposure to -50 mm Hg pressure phase which was terminated after approximately 2-1/3 minutes.

day, inadequate sleep during the previous night, and omission of his usual attempts to maintain a high fluid intake.

The only instance in which the Commander experienced presyncopal symptoms was on mission day 16 when mild dizziness and a rapid falling blood pressure after about 2 minutes of the -50 mm Hg phase caused the test to be stopped early (fig. 25). Flight planning difficulties had led to scheduling this test in the afternoon rather than during the usual morning hours. On his next test performed on the morning of mission day 21 he again experienced symptoms including dizziness and the onset of cold sweating of the face but was able to complete the test. This latter test, which was preceded by ingestion of a large amount of water and some toe-rise exercises on the "treadmill", was associated with abdominal and saddle discomfort and also a higher heart rate than in any other of his tests (fig. 26).

Postflight

Heart Rate

Resting and stressed heart rates of the Skylab 4 crewmen followed a somewhat similar pattern of change postflight during their first postflight tests on the day of recovery, all had resting heart rates which were quite slow and within preflight limits. Resting heart rates of the Commander and Scientist Pilot were elevated about 15 and 20 percent, respectively, on the following day over those on recovery. On the second day after splashdown, the Commander's resting heart rate had declined to near recovery day value whereas the Scientist Pilot's rate reached its highest postflight value, 39 percent above the recovery day value. Resting heart rate of the Pilot continued to be low in all postflight tests (fig. 27, 28, 29).

Mean heart rates of the Skylab 4 crew during -50 mm Hg lower body negative pressure at their recovery day examinations were fairly close to their respective values during their last in-flight tests (table V). Stressed heart rates of the Commander followed the same pattern as his resting heart rates with the greatest increase occurring during the day after the recovery day test. Heart rate responses to lower body negative pressure during subsequent tests returned to and remained within preflight limits.

The Scientist Pilot exhibited his highest heart rate response to lower body negative pressure during the recovery day test conducted

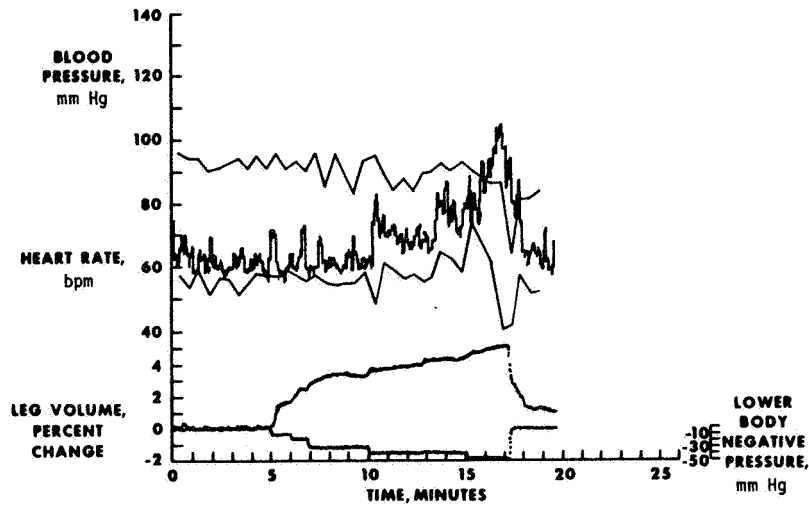


Figure 25. Cardiovascular responses of the Skylab 4 Commander during the lower body negative pressure test on mission day 16. Presyncopal symptoms developed soon after onset of the -50 mm Hg phase and negative pressure was discontinued after a little over 2 minutes at this level.

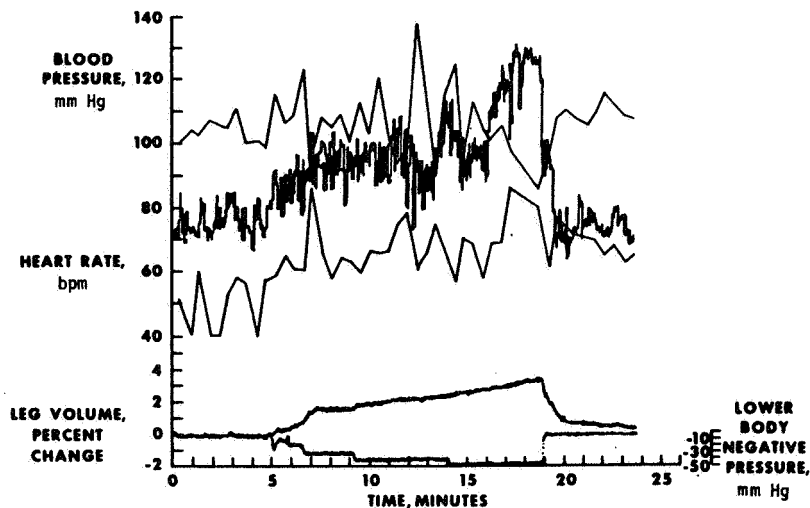


Figure 26. Cardiovascular responses of the Skylab 4 Commander during the lower body negative pressure test on mission day 21. During this test he exhibited a higher heart rate than in any other test. Symptoms did not require the test to be terminated early. The -50 mm Hg phase was continued for a full 5 minutes but the -8, -16, and -30 mm Hg pressure phases were inadvertently shortened.

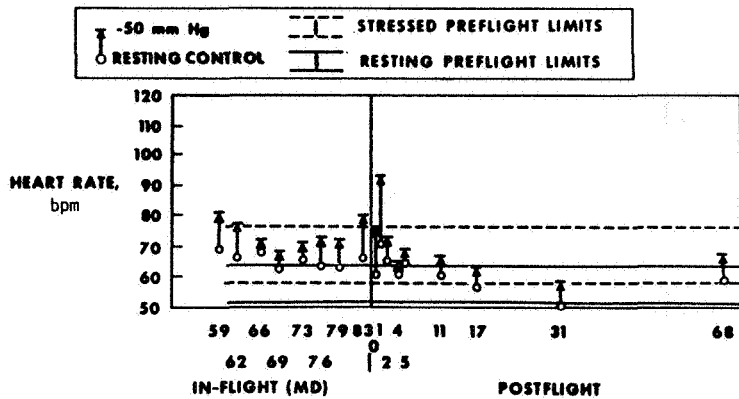


Figure 27. Mean heart rates of the Skylab 4 Commander during the resting control and the -50 mm Hg pressure phases of individual lower body negative pressure tests in the last part of the mission and in the postflight period.

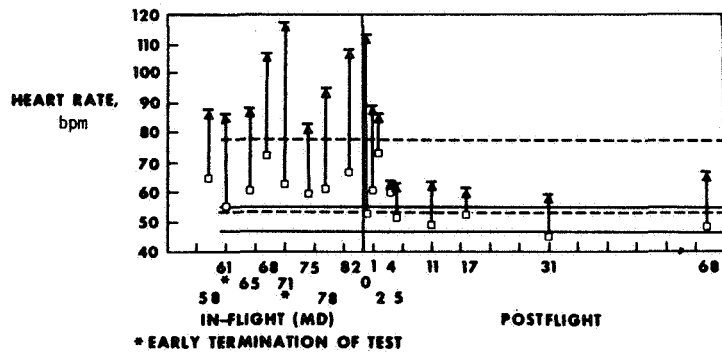


Figure 28. Mean heart rates of the Skylab 4 Scientist Pilot during the resting control and the -50 mm Hg pressure phases of individual lower body negative pressure tests in the last part of the mission and in the postflight period.

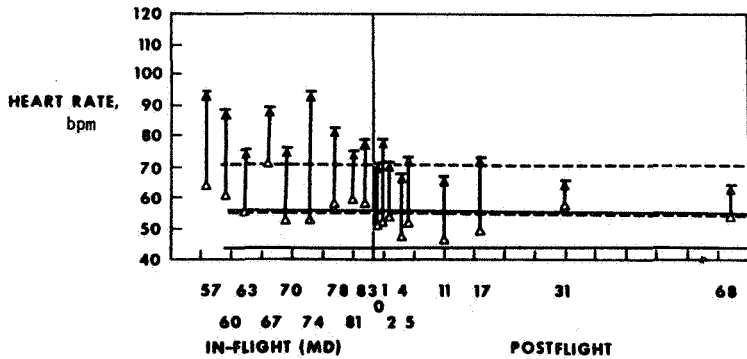


Figure 29. Mean heart rates of the Skylab 4 Pilot during the resting control and the -50 mm Hg pressure phases of individual lower body negative pressure tests in the last part of the mission and in the postflight period.

six hours after splashdown. Heart rate during tests on the following day and the second day were elevated over preflight limits by a smaller magnitude, and on subsequent tests returned to and remained within these limits.

Stressed heart rate of the Pilot was slightly elevated above preflight limits on recovery day, climbed to a slightly higher level on the day after recovery, dropped to the recovery day value on the second day after recovery and were within preflight limits on the fourth day post-mission, the heart rate response was again elevated slightly but was within preflight limits on subsequent tests.

TABLE V

MEAN HEART RATES OF THE SKYLAB 4 CREWMEN AT REST AND DURING THE -50 mm Hg PHASE OF LOWER BODY NEGATIVE PRESSURE RESULTS DURING PREFLIGHT AND IN-FLIGHT TESTS, DURING THE LAST IN-FLIGHT TEST, AND DURING EACH OF THE FIRST SIX POSTFLIGHT TESTS.

| | Mean Heart Rate (bpm) | | | | | |
|-------------------|----------------------------------|----------|-----------------|----------|---------|----------|
| | Resting and Stressed (-50 mm Hg) | | | | | |
| | Commander | | Scientist Pilot | | Pilot | |
| | Resting | Stressed | Resting | Stressed | Resting | Stressed |
| Preflight Mean | 58.9 | 66.3 | 51.1 | 64.9 | 48.0 | 61.1 |
| In-flight Mean | 66.7 | 78.5 | 64.4 | 101.6 | 59.9 | 87.8 |
| Last In-flight | 66.3 | 80.2 | 67.2 | 108.3 | 57.4 | 79.2 |
| Postflight (Days) | | | | | | |
| Recovery +0 | 60.6 | 68.1 | 53.0 | 113.0 | 51.6 | 71.2 |
| +1 | 70.6 | 82.7 | 60.9 | 88.8 | 51.9 | 78.7 |
| +2 | 64.8 | 68.5 | 73.8 | 86.3 | 53.5 | 71.6 |
| +4 | 60.9 | 62.9 | 60.4 | 63.7 | 46.5 | 67.8 |
| +5 | 64.5 | 65.8 | 52.0 | 63.0 | 51.2 | 73.4 |
| +11 | 60.7 | 61.3 | 49.7 | 63.5 | 46.2 | 69.1 |

Blood Pressure

During the first few postflight days, the three Skylab 4 astronauts exhibited marked blood pressure changes both at rest and during lower body negative pressure stress. Although the time course of the post-flight pattern differed among the three crewmen, all exhibited pronounced elevation of diastolic and mean arterial pressures both at rest and during lower body negative pressure stress on one or more of the first three post flight tests. Systolic and pulse pressure during rest were also elevated at some time during this period.

On the Commander's first postflight test, begun four hours after splashdown, resting systolic, diastolic and mean arterial pressure were markedly elevated over preflight limits during both resting control and -50 mm Hg pressure phases. Mean arterial pressure both at rest and during -50 mm Hg pressure remained above preflight limits during each test through the fifth post recovery day (fig. 30). Pulse pressure during stress also slightly exceeded preflight limits. Resting and stressed systolic blood pressure and pulse pressure climbed to higher values on the first day after recovery. Thereafter all values declined on successive tests and were within preflight limits by either the fifth or eleventh day postflight.

The Scientist Pilot, during his recovery day test 6 hours after splashdown exhibited resting systolic, diastolic, pulse and mean arterial pressures that fell within preflight limits and quite close to those seen on the last test in-flight. During lower body negative pressure, however, diastolic pressure rose quite markedly above these values and pulse pressure narrowed proportionately (fig. 31). Systolic pressure both at rest and during lower body negative pressure reached its highest post flight value on the second day post flight while diastolic pressure showed little change at rest but during the -50 mm Hg pressure fell from its initially high level on recovery day to progressively lower levels during each of the four following tests.

Resting systolic blood pressure and pulse pressure of the Pilot followed patterns similar to those of the Scientist Pilot in climbing to their highest value on the second day after recovery. Diastolic pressure at rest resembled that of the Commander in exhibiting its highest value during the first test eight hours after splashdown. Mean arterial pressure at rest remained elevated during the first four tests but during lower body negative pressure stress fell markedly during the recovery day test and reached successively higher levels during the following two tests. Stressed systolic, diastolic and pulse pressures showed the same pattern, reaching maximal levels on the second day after recovery (fig. 32).

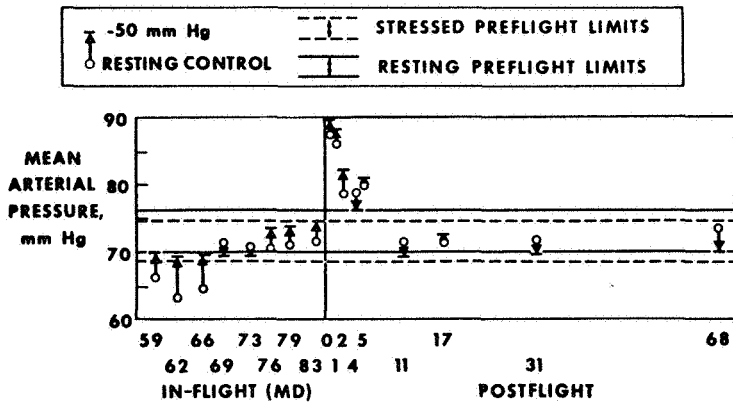


Figure 30.
Mean arterial pressure of the Skylab 4 Commander during the resting control and the -50 mm Hg pressure phases of individual lower body negative pressure tests in the last part of the mission and in the postflight period.

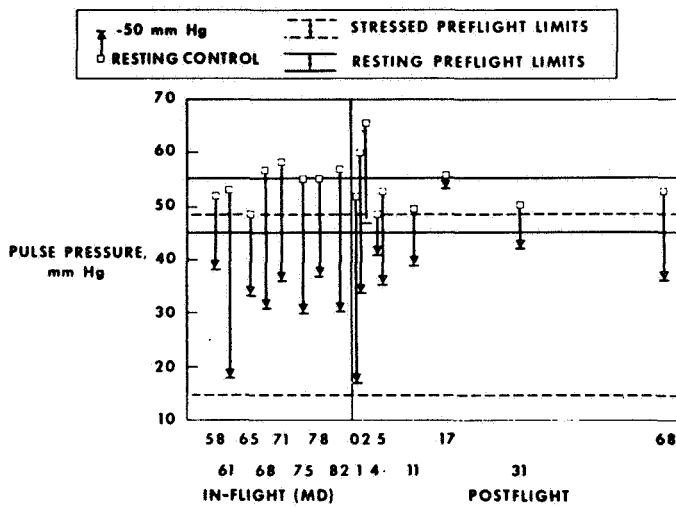


Figure 31.
Mean pulse pressure of the Skylab 4 Scientist Pilot during the resting control and the -50 mm Hg pressure phases of individual lower body negative pressure tests in the last part of the mission and in the postflight period.

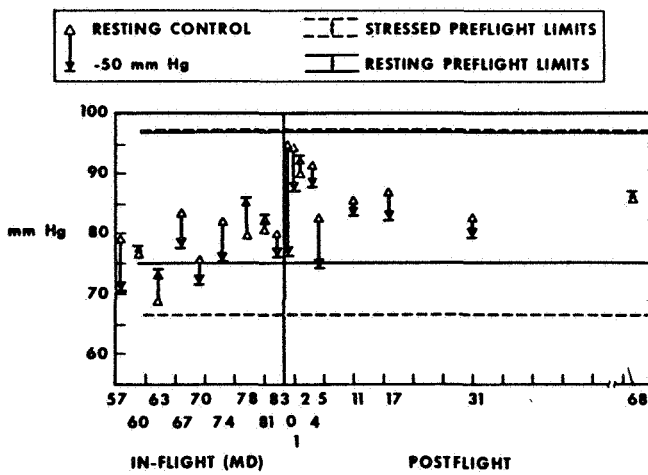


Figure 32.
Mean arterial pressure of the Skylab 4 Pilot during the resting control and the -50 mm Hg pressure phases of individual lower body negative pressure test in the last part of the mission and in the postflight period.

Calf Volume Increase Induced by Lower Body Negative Pressure

Calf volume increases at all levels of lower body negative pressure on recovery day dropped abruptly from the high values that occurred in-flight to approximately preflight values. During the next test on the day after recovery, calf volume increase climbed higher than the recovery day values. While calf volume increase reached their highest postflight value on the day after recovery in the cases of the Commander and Pilot, it climbed slightly higher on the second postmission day in the Scientist Pilot. Thereafter, increase in calf volume induced by lower body negative pressure subsided but remained slightly elevated above preflight mean values.

In contrast to in-flight patterns of increase in calf volume in which over one-half of the total increase had already occurred at the end of the -30 mm Hg phase, the greatest part of the postflight total increase took place usually during the -40 and -50 mm Hg phases. Evidence interpreted as venous drainage during the resting control phase did not appear until tests made several days after splashdown except in the Commander, where calf volume pattern indicated venous drainage in the recovery day test. Volume declines during the lower levels of lower body negative pressure thought to represent active venous contraction was similarly slow to appear. The preflight pattern of nearly complete return of calf volume to resting control values during the five minute recovery period after cessation of negative pressure was first apparent in the Commander. Calf volume during recovery returned nearly to resting levels during the recovery period of the first and most subsequent postflight tests. Similar patterns in the Scientist Pilot and Pilot were considerably delayed.

Other Measurements and Observations

Measured calf circumference after recovery, performed four, six, and eight hours after splashdown in the Commander, Scientist, and Pilot, respectively, was from 0.15 to 0.25 centimeters smaller than when determined during the last in-flight measurements on mission days 82 and 83 (fig. 21). All showed successively larger calf circumferences through the 11 days after recovery with the exception of the Scientist Pilot who showed a slight decrease on the fifth day compared to the fourth day postflight measurement. The Commander and Pilot showed their greatest increment of increase between recovery day and the day after while the increase in the Scientist Pilot was more gradual during the first 48 hours and greatest between the second and fourth day post recovery measurement. All had regained calf girth from six or more percent to approximately two percent below preflight values by the fifth day or in the case of the Scientist Pilot by the fourth day after recovery.

Volume of the lower limbs, calculated as percent change from preflight means, was moderately increased at the time of the first postflight measurement over the last volume measured in-flight a little over 48 hours earlier in the Scientist Pilot and Pilot and 28 days earlier in the Commander (fig. 33). All three postflight volume decreases on recovery day measured approximately the same as that of the Commander of Skylab 2 and slightly less than that of the Scientist Pilot of Skylab 3 at their first postflight measurement three and four hours, respectively, after splashdown.

The postflight pattern of return of lower limb volumes toward preflight values followed a somewhat different pattern than the gain in calf girth. Postflight lower limb volume increased progressively until the second day, leveled off or decreased on the third day and thereafter increased at a generally slower rate. By the second day, or a little over 48 hours after splashdown, a large part of the loss of limb volume had been regained.

During the first postflight test, the Commander exhibited higher systolic and diastolic pressures, narrower pulse pressure and slightly lower heart rates throughout the test than during his last in-flight test on mission day 83 (figs. 34, 35). The recovery day test of the Scientist Pilot produced heart rates quite similar to his last in-flight test on mission day 82 but a higher diastolic pressure and narrower pulse pressure (figs. 36, 37). In the first postflight test of the Pilot, systolic and diastolic pressures remained higher than in his last in-flight test on mission day 83 until the -40 mm Hg phase was reached. At that time, systolic pressure began to fall and pulse pressure to narrow (figs. 38, 39). After the onset of -50 mm Hg, lower body negative pressure systolic and diastolic pressure fell and shortly afterwards mild presyncopal symptoms appeared. The test was terminated after approximately one minute of exposure to the -50 mm Hg level. Of possible significance to the outcome of this test is the fact that the Pilot, because of scheduling difficulties, had performed low levels of supine and upright bicycle ergometry approximately two hours earlier.

The tests after recovery day were all completed without difficulty. Judging by heart rate responses only, preflight limits were attained by the fourth or fifth day after recovery. Blood pressure responses attained these limits by fifth or eleventh day postflight. The striking elevation of systolic pressure and widening of pulse pressure, characteristically greatest on the first day after recovery following Apollo flights and on the first and second day after recovery following Skylab flights, are illustrated in figure 40.

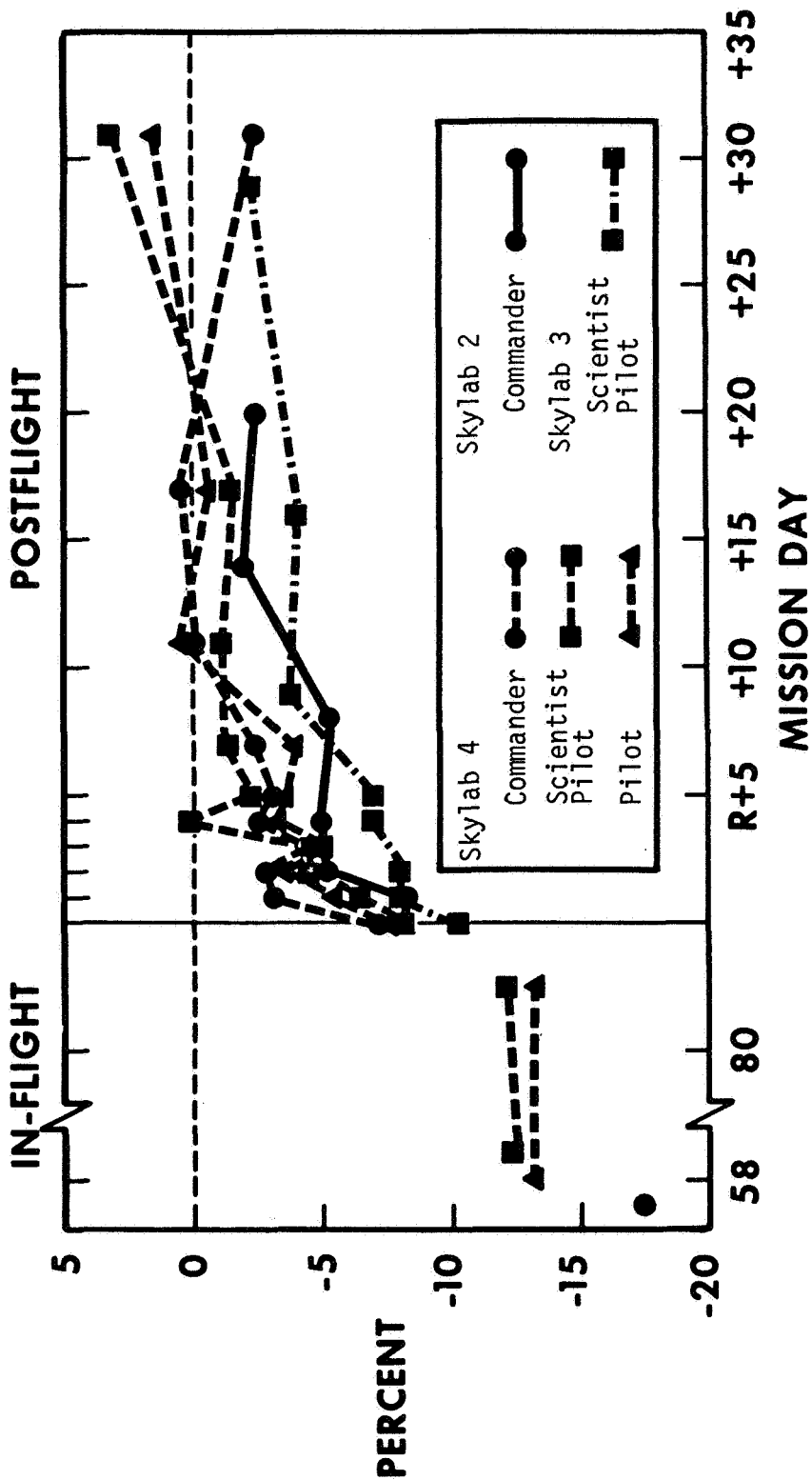


Figure 33. Percentage change in volume of the lower limbs showing volumes measured in the last third of the flight and the postflight return of volume toward preflight values (Skylab 4). Volumes of lower limbs of the Commander of Skylab 2 and the Scientist Pilot of Skylab 3, are shown for comparison.

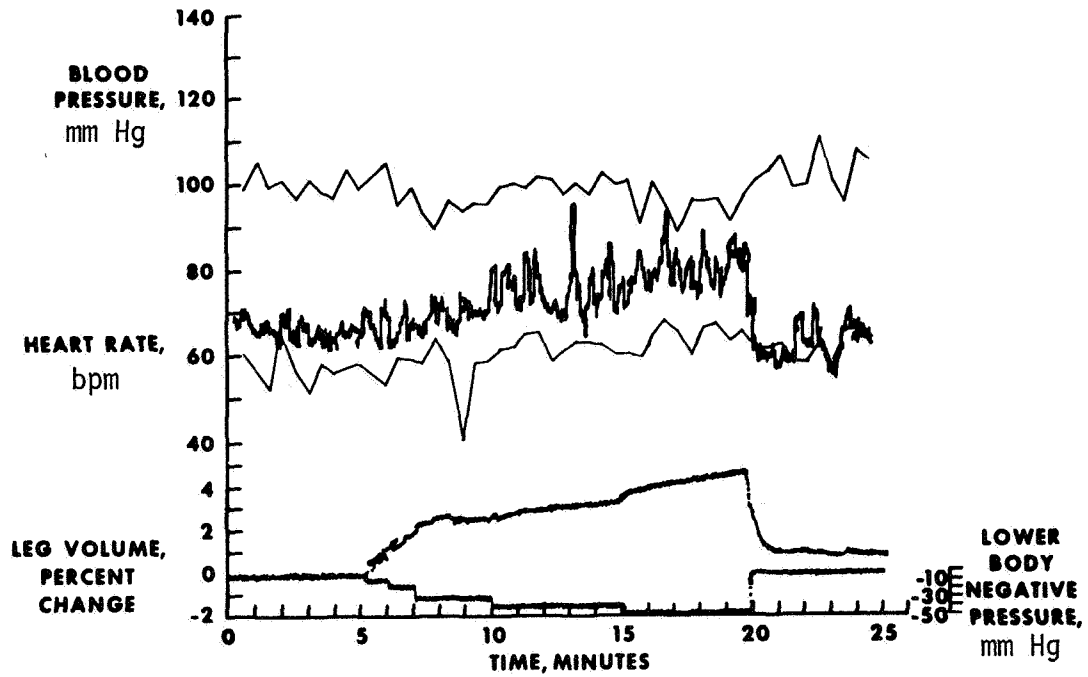


Figure 34. Cardiovascular responses of the Skylab 4 Commander during his last in-flight test on mission day 83.

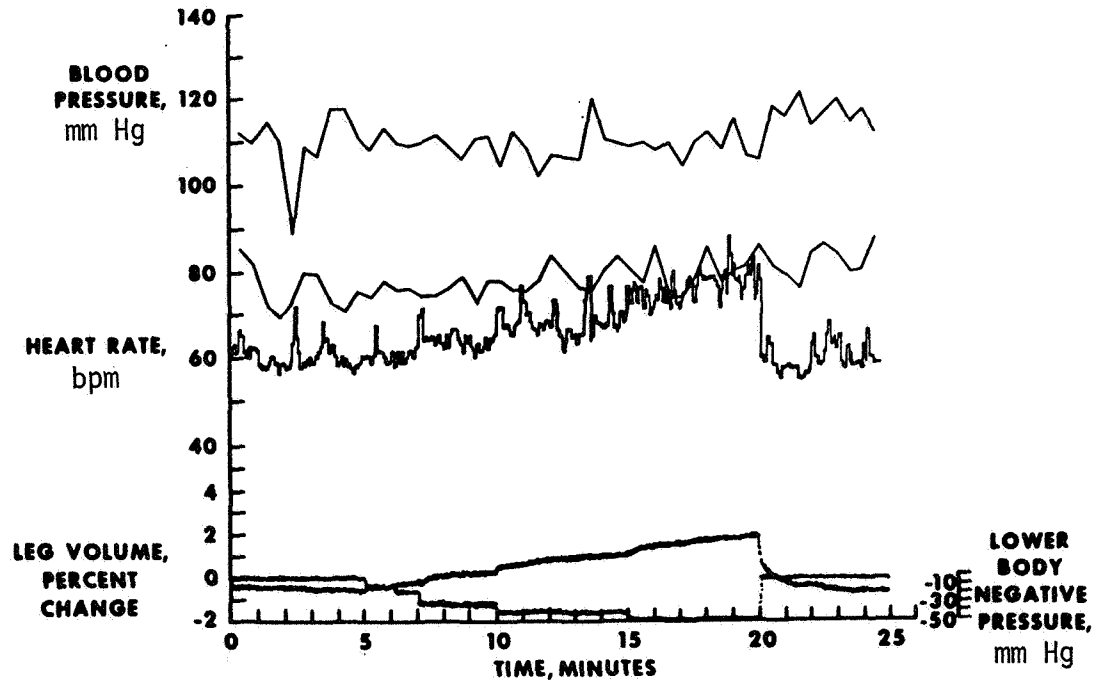


Figure 35. Cardiovascular responses of the Skylab 4 Commander during his first postflight test four hours after recovery.

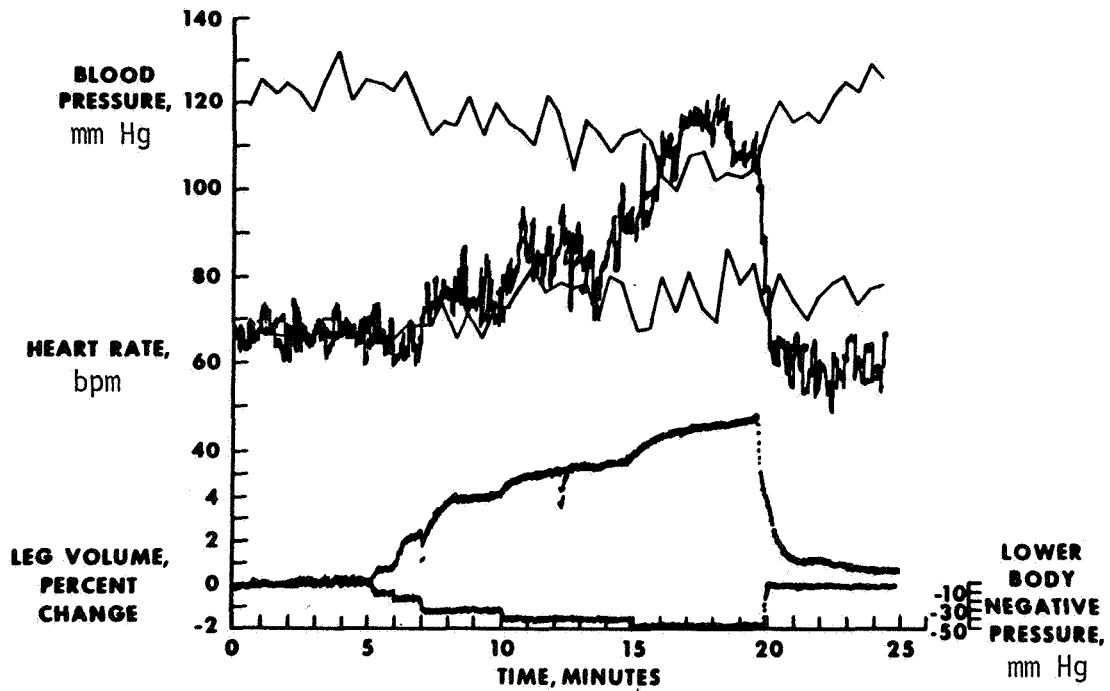


Figure 36. Cardiovascular responses of the Skylab 4 Scientist Pilot during his last in-flight test on mission day 82.

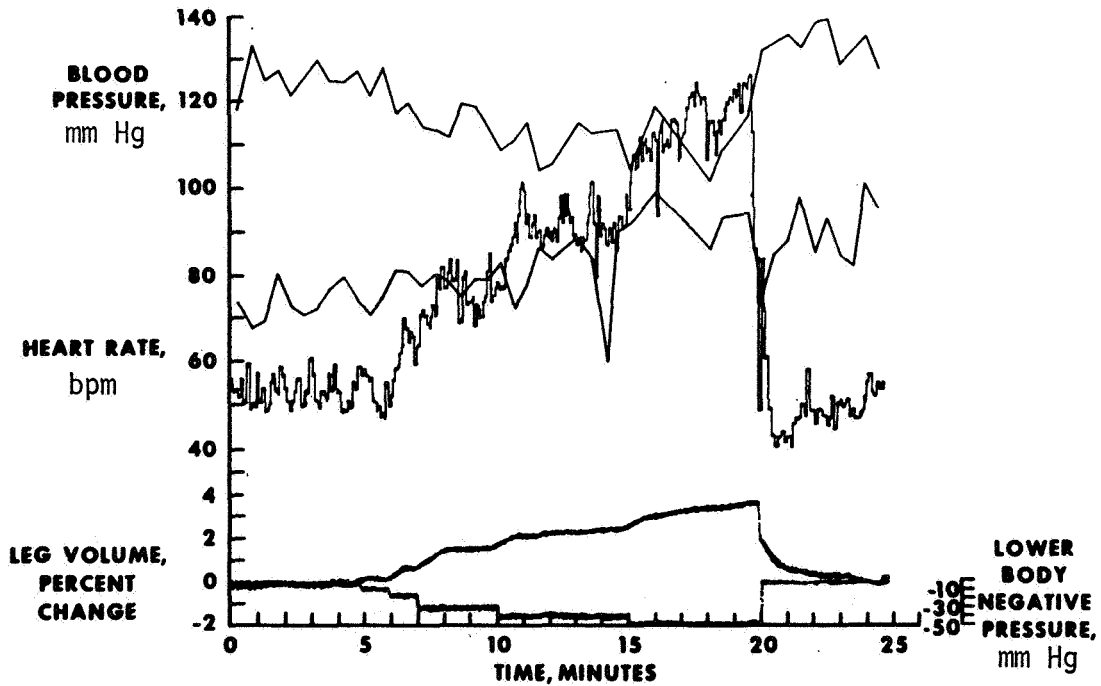


Figure 37. Cardiovascular responses of the Skylab 4 Scientist Pilot during his first postflight test six hours after recovery.

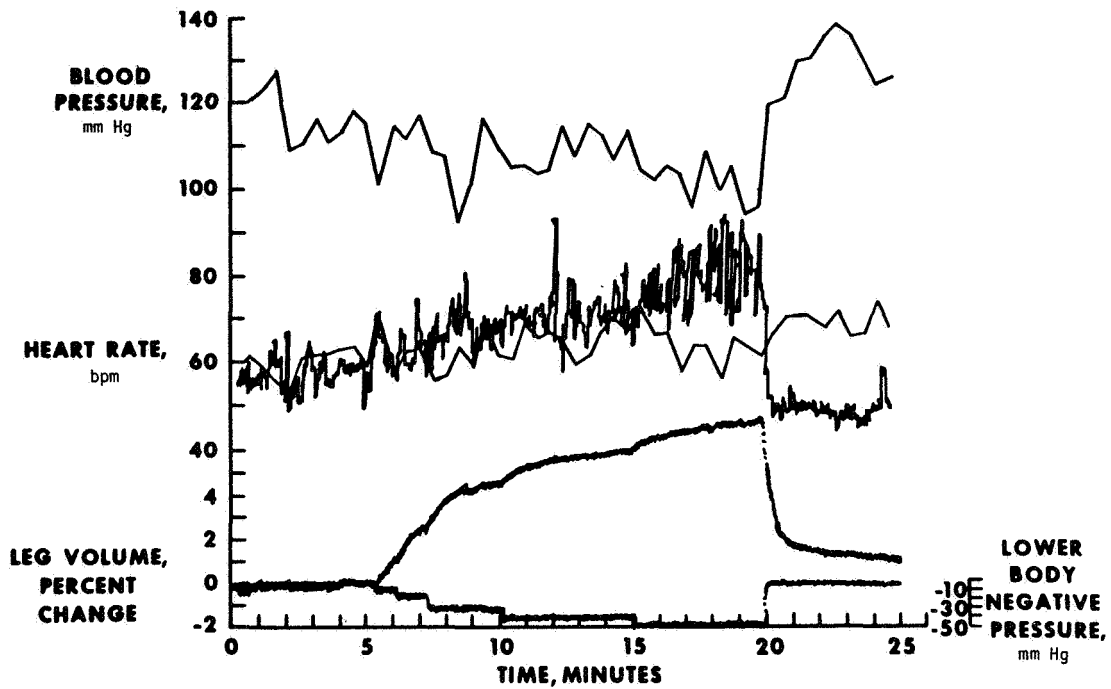


Figure 38. Cardiovascular responses of the Skylab 4 Pilot during his last in-flight test on mission day 83.

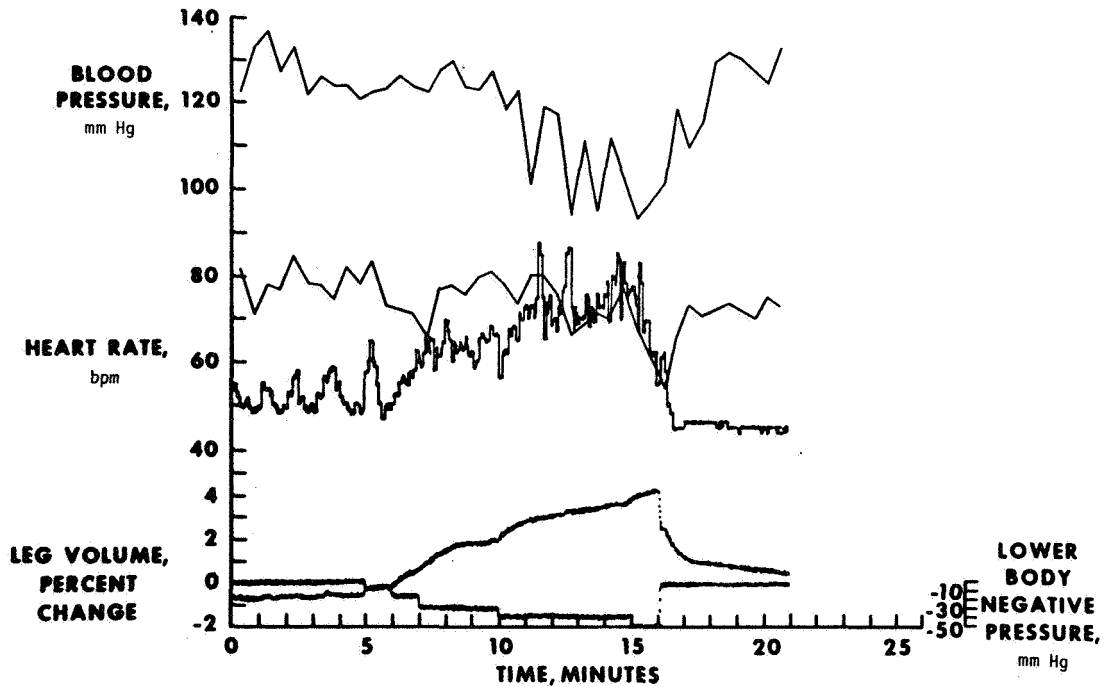


Figure 39. Cardiovascular responses of the Skylab 4 Pilot during his first postflight test eight hours after recovery.

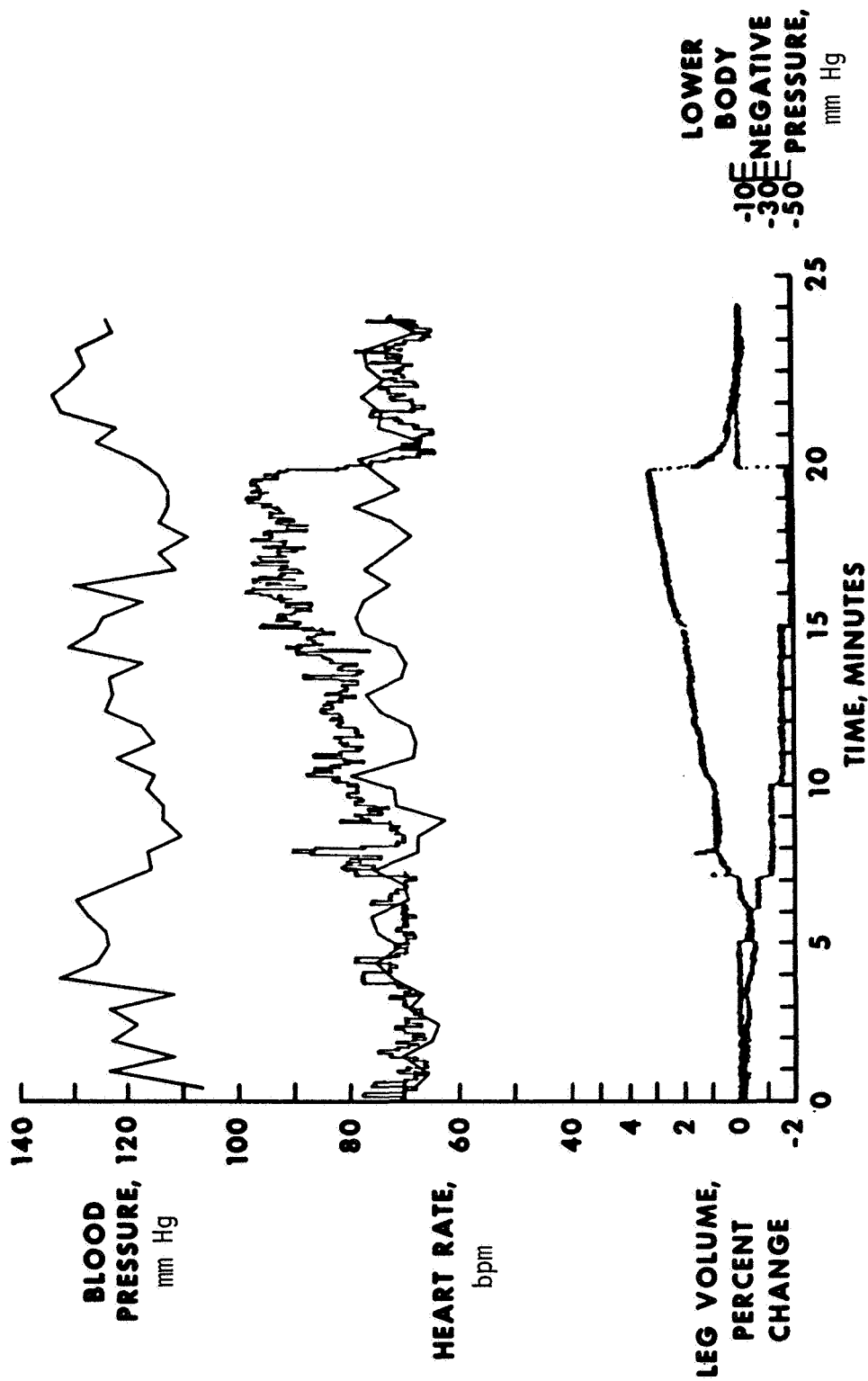


Figure 40. Cardiovascular responses of the Skylab 4 Commander during his second postflight test.

DISCUSSION

An explanation of the changes in cardiovascular responses to lower body negative pressure in a weightless environment requires understanding of the manner in which the systems of the body and their functions adjust to the weightlessness of space flight. A more comprehensive understanding of these adjustments will, in turn, require the correlation of massive volumes of data from all of the Skylab experiments, a task of monumental proportions which has barely been started.

Measurements of calf circumference of Skylab crewmen on the fourth to sixth day of flight revealed decreases of such magnitude that they could only result from loss of fluid. These rapid reductions of calf girth amounted to a mean of 1.1 centimeters or 3.0 percent below pre-flight values. If volume losses from the measured portion of the lower limbs had declined in proportion to decrease in calf volume a mean estimated loss of more than one liter would have occurred. Volumes of the lower limbs as actually measured in-flight by the Skylab 4 crewmen indicated somewhat greater losses, ranging between 1400 and 2000 milliliters within the first few days of flight. Both types of measurement support a very early loss from the lower limbs of a relatively large volume of fluid. In-flight observations of a full feeling of the head, nasal and ocular congestion, and distention of head and neck veins suggest that this process of headward fluid migration out of the lower extremities must begin simultaneously with achievement of weightlessness.

Increased outflow from veins of the legs tends to reduce local venous pressure and in turn pressure on the venous side of the local capillary bed, a condition which promotes the transfer of interstitial fluid into the capillaries. Capillary exchange of fluids is a highly dynamic process capable of moving large volumes of fluid very rapidly in either direction between capillaries and surrounding tissue. Such transfer of fluid would continue to replenish venous channels as their contents shifted upward until local tissue pressure declined to the level of venous pressure. The flow of lymph toward the central circulation would also be expected to increase. Thus, interstitial fluid, lymph and blood can participate in the rapid outflow of fluid and consequent reduction of lower limb volume.

Veins in regions above the heart are not normally subjected to venous pressure increases of more than small magnitudes and, except during recumbency, are not filled. Photographs and descriptions by the astronauts indicate, however, that cervical and cranial veins became distended early in flight and remained distended throughout flight. These superficial veins and presumably others in the upper part of the body appear then to accommodate a significant portion of the fluids

shifted upward from the lower body. Edema of the eyelids and periorbital tissues, also apparent from in-flight photographs, indicate that venous and intracapillary pressure in these regions are at least transiently increased and that interstitial spaces in the upper body also participate in storing fluid displaced to that region.

Whether and to what extent the pulmonary vessels also accommodate blood beyond their normal storage capacity of 700 to 800 milliliters of blood are unanswered and important questions. Modest reductions in vital capacity during flight (11) suggest that they do. In the acute expansion of blood volume by infusion, the lungs appear to be spared and the expanded blood volume is accommodated largely by systemic veins while in chronic circulatory congestion with normal hearts, the lungs seem to share in accommodating the expanded blood volume (12). Whatever the total blood volume in weightlessness, the pulmonary circulation must, at some time during adaptation to weightlessness, react as if total blood volume was increased.

At some time early in the process of these regional shifts of fluid volume, atrial return and cardiac output must transiently increase. Whether atrial distention initiated neurohormonal stimulation of diuresis seems uncertain from available Skylab data at this time. Hemoglobin increases in blood samples taken in-flight suggest that hemoconcentration occurred relatively early in flight (13). Whether plasma volume is reduced chiefly by diuresis or through other mechanisms, is not clear. The low humidity of the Skylab atmosphere and, in the Skylab 2 flight, high environmental temperature, would be expected to lead to large fluid decreases through insensible losses and sweating.

High pressure baroreceptors, especially those of the carotid arteries, should initially sense the absence of hydrostatic forces as an elevated arterial pressure and initiate reflexes to reduce pressure and heart rate. Such an event was not observed in Skylab cardiovascular examinations but it would probably have occurred too early and transiently for detection.

Much of the more dynamic changes of the type discussed must have already taken place before the earliest lower body negative pressure tests could be performed. The results of these tests suggest, however, that profound changes in circulatory dynamics continued to occur throughout much of the flight. Vigorous daily activities must also have impacted temporarily any equilibrium that had been reached.

One can postulate with reasonable certainty, however, that by the time of the first in-flight lower body negative pressure tests, total circulating blood volume had been reduced, some hemoconcentration had occurred, and at least a significant fraction of fluids previously

located in the legs was now accommodated by veins and interstitial tissues of the upper part of the body. Whether these fluids were available to supplement circulating blood volume during lower body negative pressure is an unanswered question of great importance to understanding the lower body negative pressure results.

Lower body negative pressure stresses the cardiovascular system by reducing effective circulating blood volume as blood is segregated in the veins of the lower half of the body. Reduced return of blood to the right heart results in reduced cardiac output comparable to that which occurs during orthostasis in a gravity field (13). The volume of blood thus diverted must be a determining factor in the degree of stress produced.

The measurement of calf volume increases during lower body negative pressure should furnish an index to at least estimate the magnitude of this pooled volume. Calf volume increased by considerably greater percentages during in-flight lower body negative pressure than in pre-flight tests. This change was apparent during the earliest in-flight tests, persisted throughout flight, and diminished again in postflight tests. Moreover, a large fraction of the total volume change in-flight occurred during the first two minutes of lower body negative pressure when negative pressures were least. The most plausible explanation for the latter changes seems to lie in a relatively empty venous system in the legs at the beginning of the tests.

Veins require only low transmural pressures to retain their circular configuration. If lower pressures prevail, they tend to become elliptical or flat (15). In this state, relatively large volumes of blood could be accommodated before any change in venous pressure occurred. This so-called zone of free distensibility, which does not involve stretching of venous wall muscle, probably accounts for the large volume increases in the calf at the slight negative pressure levels as discussed above. The volume of this zone of free distensibility, even during the alterations taking place due to weightlessness, may be expected to vary from time to time under the influence of daily activities. Physical activity in weightlessness requires minimal participation of lower extremity muscles. Such activity might be expected to result in a net loss of venous volume in the lower extremities with venous outflow exceeding arterial inflow. Conversely, due to higher resting venous pressures in the upper body, periods of inactivity such as sleep may allow some filling of leg veins, thus reducing the zone of free distensibility. After periods of inactivity such as sleep, a smaller volume of blood would then be initially displaced by lower body negative pressure than in the former situation.

Pertinent to these considerations is the observation that none of the 13 instances of early termination of tests due to presyncopal symptoms occurred during tests conducted in the morning hours or within seven

hours of arising from sleep, although approximately one-third of all in-flight tests were conducted within that period. These 13 tests were associated with larger than usual calf volume increases during the lowest negative pressure phases of the tests. This suggests that the pooling of large volumes of blood during the first few minutes of the test may so alter the effectiveness of compensatory cardiovascular mechanisms as to render them incapable of adequate responsiveness to the greater stress later in the test.

The higher incidence of presyncopal symptoms in test conducted seven or more hours after arising may be related to the hypothesis mentioned earlier, namely that fluids tend to migrate back to the lower extremities during the inactivity of sleep and that mild activity after sleep tends to empty them again. That this may occur is suggested by the observation of the astronauts that the symptoms of fullness of the head were usually absent on awakening but returned after arising. Similarly, vigorous prolonged exercise on the bicycle ergometer, which should divert a much larger fraction of cardiac output to the muscles of the lower extremities, temporarily relieved these symptoms. If this reasoning is correct, in addition to long-term alterations in fluid volume distributions, fluid volumes in the capacitance vessels and tissues of the lower limbs may be greater in the early hours after arising than later in the day after activity has tended to displace these fluid volumes headward.

Relatively larger proportions of fluid in the lower body early in the day would tend to limit the volume of fluid drawn into the legs and out of the effective circulating blood volume by lower body negative pressure. Other factors being equal, tolerance to lower body negative pressure would then be greater in tests done early than in those conducted late in the day. Among the three astronauts, the Commander of Skylab 2, the Pilot of Skylab 3, and the Commander of Skylab 4, whose in-flight tests were nominally performed in the morning, only one presyncopal episode occurred and this was in the Commander during a test performed in the afternoon over nine hours after arising. In addition, in these three astronauts the heart rate increases induced by -50 mm Hg negative pressure during their 45 in-flight tests, averaged 10.7 beats per minute higher than during preflight tests. The other six astronauts whose tests were nominally scheduled in the afternoons exhibited mean increases of 16.5 beats per minute over preflight stressed values during their 93 in-flight tests. The former difference does not reach statistical significance while the difference between in-flight and preflight stressed heart rates of the six latter astronauts was highly significant ($P < 0.001$). While cardiovascular characteristics of individual astronauts may account for these differences they, along with the presyncopal episodes, may also support the hypothesis that headward shifts of fluids occur during the course of daytime

activities, leading to decreasing orthostatic tolerance during the day, and that fluids tend to reaccumulate in the lower body during the inactivity of sleep in a weightless environment.

Although the greatly expanded calf volume changes during the brief -8 and -16 mm Hg phases of in-flight tests were most striking, larger volume changes during the -30, -40, and -50 mm Hg phases also occurred during in-flight tests. At these levels, transmural pressures across venous walls must result in stretching of venous musculature. Increased capacitance of the veins, reduced tone of supporting muscle in proximity to the veins, and diminished tissue pressure must participate to varying degrees in the greater calf volume changes in weightlessness. The relative change in any one of these factors could not be determined, but our current understanding of the effects of weightlessness suggests that all three should be affected. The larger residual volume at the end of the recovery period that occurred in-flight may reflect a greater outflow during lower body negative pressure of fluid from capillaries into tissues. It may also simply indicate that further venous contraction cannot occur, because the zone of free distensibility has been reached. While variations in calf volume increases and residual volume varied from test to test, a definite trend of change during the flight was not seen in the Skylab 4 crew. In this crew the leg volume increase during lower body negative pressure reached higher levels, particularly in the Scientist Pilot and Pilot, than observed in crewmen of the first two flights. Whether the increased exercise, the slower decreases in calf circumference, and the smaller weight losses in the Skylab 4 crewmen were in some way related is not known.

The volume of blood pooled in the lower extremities during in-flight tests did not seem to correlate from test to test with the magnitude of heart rate or blood pressure change during lower body negative pressure. In general, however, those of the nine Skylab astronauts with the greatest increases in calf volume during the in-flight tests also showed the greatest increases in heart rate and changes in blood pressure. In addition, although correlation of heart rate increases with leg volume increases was not evident in preflight tests, the crewmen whose calf volume increases were greatest in preflight tests usually also showed the largest increases during the in-flight tests.

In-flight resting heart rates of the three Skylab 4 crewmen, like those of Skylab 3, were elevated significantly over preflight resting rates. Elevation of resting systolic blood pressure and pulse pressure along with decreases in diastolic pressure and mean arterial pressure, changes seen in the majority of the Skylab 2 and Skylab 3 crewmen, occurred in all three Skylab 4 crewmen, though not always to a statistically significant degree. Such changes are compatible with increased

stroke volume and lowered peripheral resistance due to increased cross section of the resistance vessels (16). If stroke volume was increased, a significant increase in cardiac output was present at rest. There would appear to be no need for increased cardiac output in terms of higher oxygen requirements under these conditions. A plausible and entirely hypothetical explanation of this apparent paradox postulates an alteration in the distribution of cardiac output secondary to weightlessness and the changed distribution of blood volume. If blood flow to the upper body is increased beyond the requirement for oxygen or thermal regulation, opening up and dilatation of normally closed arteriovenous channels in the upper body would lead to a blood pressure pattern of the type observed in the arms and conceivably shunt blood to venous channels in quantities sufficient to elevate cardiac output. Such a condition would be most apt to obtain during rest.

The in-flight mean increase in heart rate during -50 mm Hg lower body negative pressure over resting rates for all nine Skylab crewmen averaged 20.4 beats per minute, a highly significant difference. The increase in heart rate during orthostatic stress has generally proven to be the best single index in the assessment of orthostatic tolerance. According to reports of the Skylab 4 crewmen, -30 mm Hg lower body negative pressure in-flight produced a stress subjectively similar to the -50 mm Hg level preflight. Comparison of mean heart rates for the three crewmen revealed that in-flight heart rates at -30 mm Hg slightly exceeded those in preflight tests at -50 mm Hg, although the difference from resting values in-flight was slightly less than the difference preflight at these negative pressure levels. Greater reductions of mean in-flight stressed systolic pressure and pulse pressure also indicated that -50 mm Hg negative pressure in-flight represented a considerably greater stress than the same level of lower body negative pressure preflight.

The periodic major fluctuations of resting and stressed heart rates and blood pressures observed in previous flights occurred in the Skylab 4 crewmen also. The pattern of these fluctuations varied for each crewman, but their magnitude and frequency were greater during the first part of the mission than later. Their nature and significance is unknown, but, in the case of the Skylab 4 crewmen, their prominence and duration appeared to decrease as cardiovascular responses to in-flight lower body negative pressure stabilized. Adaptation of physiological systems to repetitive acute stress characteristically involves a series of physiological oscillations between overcompensation and undercompensation which gradually declines in magnitude until an optimal accommodation is reached. Oscillating patterns of less pronounced degree were also seen in the three astronauts receiving lower body negative pressure at 3-day intervals in the 56-day Skylab Medical Experiments Altitude Test (SMEAT) (17).

In tests in which presyncopal symptoms required that the test be discontinued, recovery was prompt and complete. In each instance, the subject pushed the emergency relief valve although by then warning declines in heart rate and systolic pressure were usually apparent to the observer. Early forebodings concerning possible harm to the astronaut had assured provision for adequate monitoring displays and hardware safety features.

Postflight findings for Skylab 4 crewmen were remarkable for the relatively small loss of orthostatic tolerance and the rapid return of related cardiovascular parameters to preflight limits. Loss of calf girth was no greater than had been observed in the 59-day Skylab mission. Losses in volume of the lower limb as measured on Recovery day were slightly smaller than in crewmen of the 59-day Skylab 3 mission.

Blood pressure responses were similar to those seen postflight in previous missions with marked elevations of resting systolic and diastolic pressures and, during negative pressure stress, additional large increases in diastolic pressure. Calf volume increases during lower body negative pressure were small during the recovery day test, but thereafter usually somewhat above preflight levels during several successive tests.

The heart rate and blood pressure responses during lower body negative pressure postflight indicated intense sympathetic activity and an adequate cardiac and peripheral arteriolar response. The intensity of these responses paralleled those seen in the first weeks of flight despite evidence that the volume of blood displaced to the lower body was much smaller postflight than in weightlessness which seems probable that even brief periods of orthostasis initiates the process of shifting fluids footward. Relatively dehydrated tissues in the lower body undoubtedly accept large volumes of fluid when venous pressure in the lower extremities rises for even brief periods of time, creating the effect of a sudden hemorrhage in the face of an already contracted blood volume. Baroreceptor mechanisms, particularly those involving the carotid sinus, long adjusted to the higher pressures than those experienced in weightlessness, may exhibit increased sensitivity for a time to the reduction in pressure associated with the reappearance of hydrostatic pressures in body fluids. Baroreceptor responses may cause intense venoconstriction as well as arteriolar restriction and thus limit both inflow and capacity of the venous system. In addition, during in-flight tests, there was evidence that even though total blood volume was reduced, blood volume in the upper body may actually be expanded and thus furnish a larger available reservoir from which to supply blood to the lower body during lower body negative pressure than in the early postflight period.

The experience of Skylab indicates that protection against orthostatic forces during the first few hours postflight not only serves to prevent orthostatic hypotension but may play an important role in cushioning the cardiovascular effects of return to gravity by preventing sudden large shifts of intravascular fluids to lower extremity vessels and extravascular tissues. Recumbency and the use of external pressure to counteract hydrostatic forces while in the upright position retard these readaptive changes which, if allowed to take place rapidly, can only accentuate the adverse effects of an inadequate circulating blood volume.

The Skylab Missions provided the first American opportunity for detailed studies of the cardiovascular system during the course of prolonged exposure to weightlessness. Basic questions concerning the cardiovascular adaptations to this environment have been answered. For example, a better understanding of the lack of correlation between postflight decrements in orthostatic tolerance and flight exposures of from a few to 14 days was gained. Skylab studies have clearly shown that changes in fluid volume distribution during the first few hours of flight creates profound alterations in cardiovascular functions which in turn, impair orthostatic mechanisms to a marked degree as early as four or five days after entering the weightless environment.

As anticipated, even though the understanding of cardiovascular responses to the conditions of space flight and to stresses resembling orthostasis has been significantly advanced, Skylab studies have raised other questions that have never before been asked; for example, those regarding altered vascular flow and pressure relationships and patterns. Space flight furnishes an environment for cardiovascular study which can be produced in no other way. It is difficult to imagine that increased understanding of cardiovascular function and control mechanisms, as they are altered in weightlessness, will not in the future become relevant to the cardiovascular problems that face us on earth.

CONCLUSIONS

- ° The Skylab lower body negative pressure experiment demonstrated that loss of orthostatic tolerance had already developed by the time of the first tests after four to six days of flight. Cardiovascular responses to lower body negative pressure showed the greatest instability and orthostatic tolerance the greatest decrement during the first three weeks of flight. After approximately five to seven weeks, cardiovascular responses became more stable and evidence of improving orthostatic tolerance appeared.

- In-flight data from the lower body negative pressure experiment proved to be useful not only in predicting the early postflight status of orthostatic tolerance, but also in the in-flight assessment of crew health status.
- The marked increases in calf volume induced by in-flight lower body negative pressure appeared to be secondary to large headward shifts of fluid from the lower body as a result of weightlessness. Judged by objective as well as subjective evidence, in-flight lower body negative pressure presented a much greater stress to the cardiovascular system than the same levels of negative pressure during preflight tests.
- Measurements of calf girth and, in Skylab 4, of the lower limbs confirmed an early, large reduction of lower limb volume. The beginning of this fluid shift appeared to correlate temporally with the onset of signs and symptoms of congestion of the head and neck.
- At rest, in-flight mean resting heart rates, systolic blood pressures and pulse pressures were typically increased while diastolic and mean arterial pressures decreased compared to preflight values in all three Skylab 4 crewmen and in the majority of the other Skylab crewmen. Differences in in-flight responses to lower body negative pressure stress from preflight responses included greater heart rate and leg volume increases in all crewmen and, in most, higher diastolic pressures and mean arterial pressures and lower systolic blood pressures and pulse pressures.

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