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HEMODYNAMIC STUDIES OF THE LEGS UNDER WEIGHTLESSNESS

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ABSTRACT

Following exposure to weightlessness, alterations in the return of blood from the legs play a crucial role in orthostatic tolerance and may be an important factor in work tolerance. To investigate some of the hemodynamic mechanisms involved, an experiment was performed on the Skylab 3 and Skylab 4 missions to study arterial blood flow, venous compliance, and muscle pumping of blood. Skylab 4 results are presented.

Venous compliance and arterial blood flow were determined by occluding venous flow with a pressure cuff above the knee and recording the resulting change in volume from a midcalf segment by means of a capacitance volume transducer. For flow measurements, the cuff was inflated to 30 mm Hg pressure for three 10-second periods. This sequence was repeated at 50 mm Hg cuff pressure. Flow was calculated from the initial rate of volume change. Compliance curves at 30 mm Hg pressure were obtained by inflating the cuff to this pressure for 3 minutes and recording the volume change as outlined previously; two such determinations were made at each recording. Compliance (differential volume/ differential pressure) was calculated from the known pressure point on the curve.

Muscle pumping action was studied by placing the subject in lower body negative pressure at -30 mm Hg and recording volume change from a calf segment as before. After 3 minutes, the crewman made 10 maximum effort isometric contractions of the leg, waited one minute, and repeated the procedure. The amount of blood collected in the segment from the negative pressure and the amount remaining after pumping were determined.

This entire sequence of studies was performed three times before flight, seven times during flight, and three times after flight. Blood flow showed a marked average increase in all crewmen throughout the inflight phase; wide variations were seen but no clear trend. After flight, an immediate sharp reduction, virtually to preflight values, occurred. Venous compliance demonstrated a slowly increasing compliance which reached a fivefold increase in two of the three crewmen by mission day 15, a slowly decreasing trend in all three crewmen after mission day 40, and a precipitous drop to less than preflight

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values at recovery. The values for the Commander of Skylab 4 showed little change. After muscle pumping, the relative amount of blood remaining in leg veins was approximately the same during flight as before flight, but the absolute amount collected and remaining was increased several times.

It was concluded that the most likely cause of increased blood flow was an increase in cardiac output secondary to increased central venous pressure caused by blood redistribution. Changes in venous compliance are thought to be primarily changes in somatic musculature which is postulated to primarily determine venous compliance of the legs. This was also thought to be demonstrated by the changes in muscle pumping. It is thought that these compliance changes, when taken with the decreased blood volume; provide a basis for the changes seen in orthostatic tolerance, work capacity and lower body negative pressure response.

INTRODUCTION

In the next two reports I shall describe experiments which were added to the original Skylab experiment protocol long after the schedule had been fixed. Only those of you familiar with space flight scheduling and operations can appreciate the problems this causes. At the same time, the scheduling flexibility which was developed as the mission progressed produced far more valuable data than was originally hoped for. These changes became a tribute to the flight crews and management team and again illustrated the outstanding characteristic of manned space flight, the flexibility to optimize returns from an experiment or from a mission. Scheduling under such situations was critical, and if there are recognized holes in the data or crucial data points missing, it was not due to the investigators oversight but to a matter of mission priorities.

Significant among the medical findings following prolonged space flight have been reduced orthostatic tolerance and ergometric work capacity. Changes in hemodynamics of the legs with increased blood pooling and reduction in cardiac output must be considered one of the most probable causes of these effects. Concern for the above plus the observed marked tissue changes occurring in the legs during flight prompted the addition of several procedures to evaluate hemodynamic changes in the leg; resting arterial blood flow, venous compliance and muscle pumping were investigated.

The Lower Body Negative Pressure experiment recorded leg volume changes and this inherently contains compliance information. However in measuring such changes, stress is applied to a considerable portion of the body and affects many body systems capable of altering the primary leg volume response. In so far as possible, we looked at the initial reaction to pressure in the smallest possible vein segment.

Impromptu studies were implemented during the latter portion of the Skylab 3 mission. Results were of sufficient value to include more comprehensive studies on Skylab 4 which will be subsequently described fully; for convenience, each aspect of the experiment will be completely discussed in turn, except for conclusions.

The entire series of procedures was actually performed three times preflight, seven times in-flight, and three times postflight. The minimal original in-flight schedule was further reduced by other scheduling requirements during periods critical to the experiment. Several trials were lost or severely compromised by artifacts which appeared to be electrical. Other than these problems, the data were collected without difficulty.

PROCEDURE

If an occlusive cuff placed around a limb segment is inflated somewhat above venous pressure, arterial flow will be little affected, but venous flow will be stopped until its pressure exceeds cuff pressure. If volume change is also measured, its initial rate of change with time, before appreciable back pressure develops, approximates arterial inflow (fig. 1).

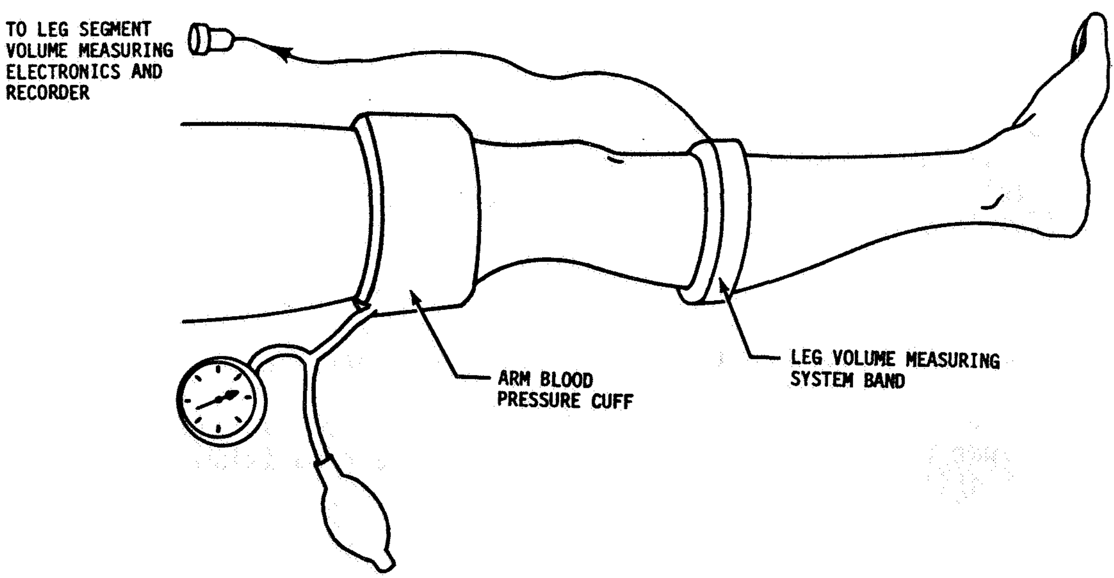

Figure 1. Arterial flow - measurement experimental arrangement.

There are several assumptions and sources of potential error in this measurement.

By waiting until the volume reaches a plateau, *i.e.*, until venous pressure equals cuff pressure and venous flow resumes, a single known value of compliance can be determined, figure 2.

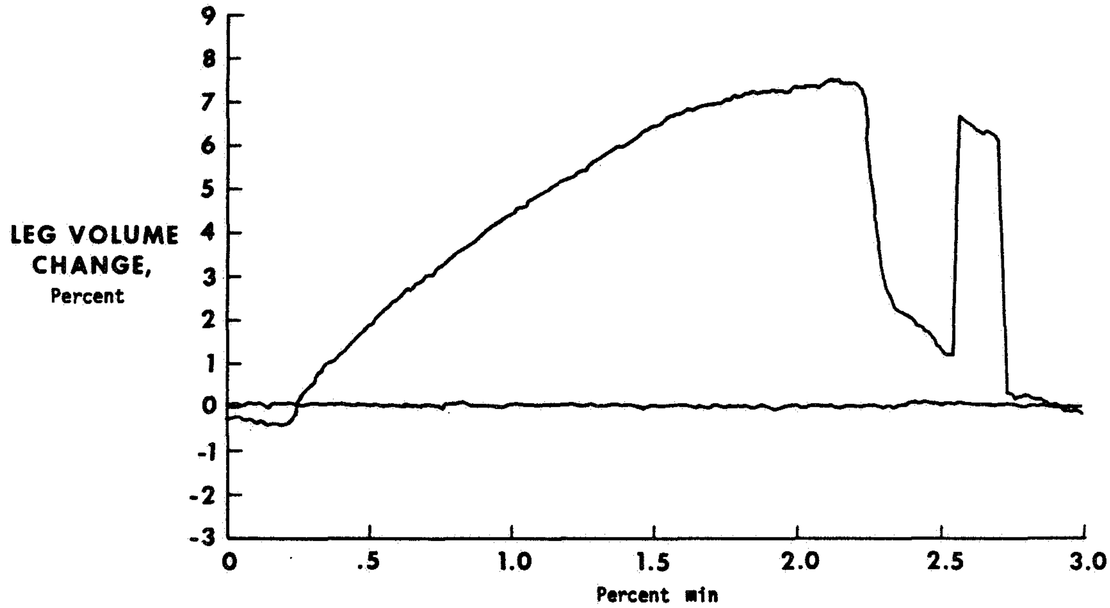

Figure 2. Venous compliance record.

Data for these two studies were obtained, as shown here, with an arm blood pressure cuff above the left knee and a capacitance limb volume measuring system band around the maximum girth of the calf. Volume changes actually measured are only those in the segment directly beneath the cuff. Volume changes of the entire leg or even calf cannot be inferred from this measurement.

Blood flow was recorded by rapidly inflating the cuff to 30 mm Hg for 20 seconds for three trials. This sequence was repeated at 50 mm Hg cuff pressure. Subjects are supine when measured under one-g.

In-flight curves from such a series at 30 mm Hg are shown in figure 3. The first volume change probably caused a small sensor position artifact which in turn shifted the baseline slightly.

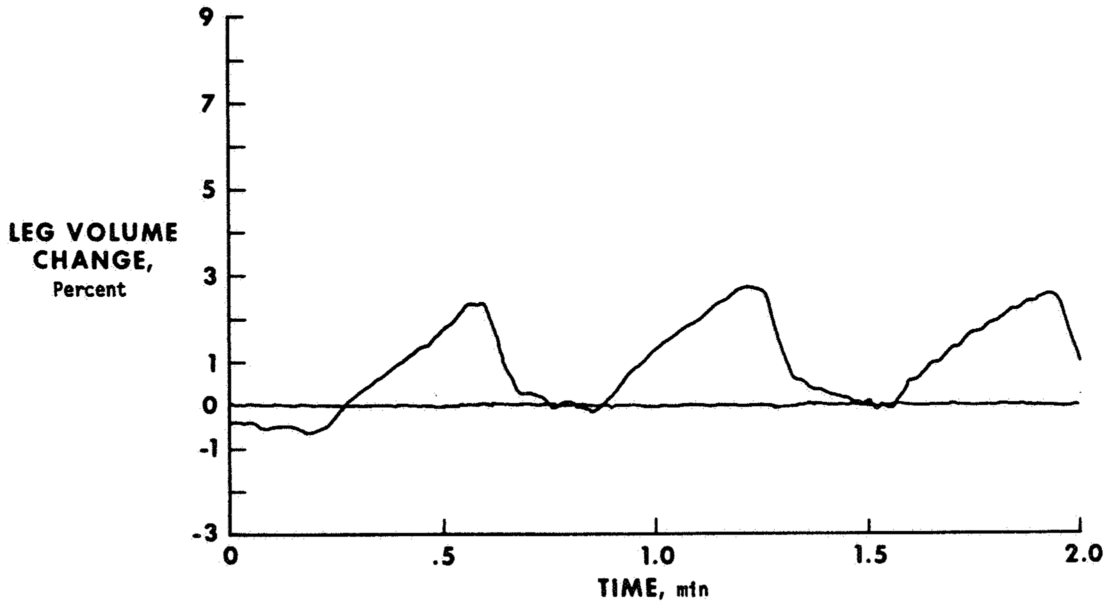

Figure 3. Arterial flow record.

Blood flow was calculated by manually drawing a tangent to the slope and measuring this slope in terms of changed volume/changed time. Usually there was an unexpected increase in volume change during cuff inflation which, in spite of the distance between plethysmograph segment and cuff, must be venous reflux. This initial slope and artifact were avoided during measurement. Another possible but unavoidable error was flow of blood from or into areas not typical of the segment under measurement, *e.g.*, the foot. Blood and fluid flows were calculated in terms of 100 milliliters of tissue under the capacitance band.

Measurements were made at both 30 and 50 mm Hg pressure (figs. 4a and 4b) to indicate the effectiveness of occlusion of the leg vessels by an arm cuff (a leg pressure cuff was not available in-flight) and which was used in all measurements. The curves generally correspond well except for the last two postflight tests from the Scientist Pilot.

DISCUSSION OF DATA

There is great variability in the in-flight data, some of which probably resulted from changes in temperature and in relationship of the time of measurement to ingestion of food and exercise. None of these

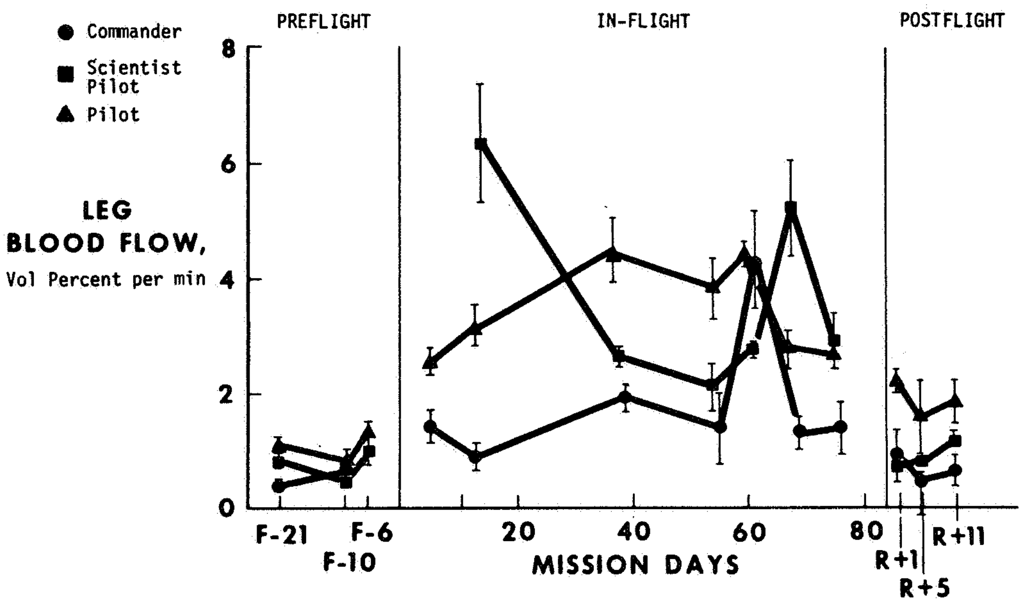

Figure 4a. Skylab 4 leg blood flow, 30 mm Hg pressure.

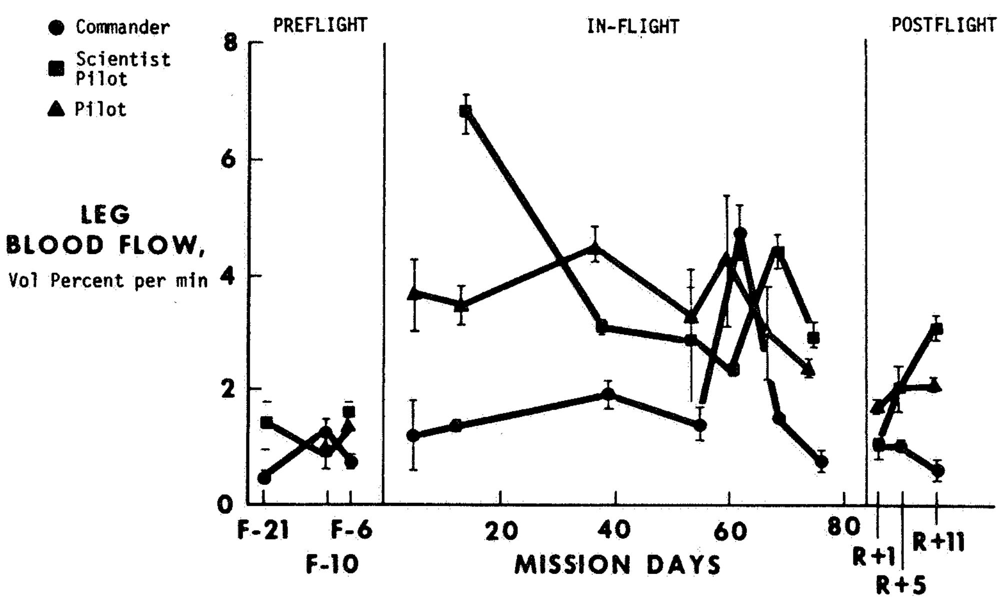

Figure 4b. Skylab 4 leg blood flow, 50 mm Hg pressure.

factors were controlled or adequately known to be properly accounted for. In spite of the variability, it seems safe to say that blood flow was elevated above preflight and postflight levels throughout the flight, and probably remained slightly elevated in the Scientist Pilot postflight.

Several possibilities should be considered for this increase in blood flow. Under one-g, an increase in muscle blood flow is seen in elevation of the legs while supine, or in other maneuvers which increased intrathoracic venous pressure, a mechanism which apparently releases sympathetic vasoconstrictor action. It will be shown in our next report (Anthropometric Changes and Fluid Shifts) that fluid and blood from the legs were shifted cephalad on exposure to weightlessness and this must have produced transient increase in venous pressures which may not have been completely restored to "normal" throughout the flight. Decreases in transmural pressure could have allowed increase in vessel size and flow, but the changes required to do this in the legs are too large to be considered under the circustances.

My own hypothesis is that cardiac output is increased secondary to an increase in the central venous pressure. While there is no hard supporting evidence for this hypothesis, several observations indicated that it may have happened.

In-flight variation was too large to allow any statements about trends. Note, however, a marked difference between the Commander of Skylab 4 and the other two crewmen. This difference was rather obvious in lower body negative pressure testing and it will be seen again in several experiments. Postflight there was an abrupt drop to just above preflight levels. This is consistent with any of the possible causes of increased blood flow which were mentioned.

Compliance is the change in volume for a given change in pressure and, in this case, it is assumed to be a change in venous volume produced by cuff pressure of 30 mm Hg or more simply stated, how much blood will be pooled in the veins at any one pressure. Let me emphasize that the compliance curve is alinear, and that this measurement is only one point on the curve from a vessel which was not completely empty at the start. Further, the exact starting pressure is not known.

Compliance for the three Skylab 4 crewmen are plotted in figure 5 in terms of volume percent change (milliliters/100 milliliters of tissue). It is obvious that more points are needed on these curves, especially in the 2 to 3 week period. It should be noted in all crewmen there was an increase in compliance that required *10 days or more* to reach a maximum. It then appeared to decrease slowly, possibly cyclically in two crewmen, until recovery, when there was an immediate fall to or

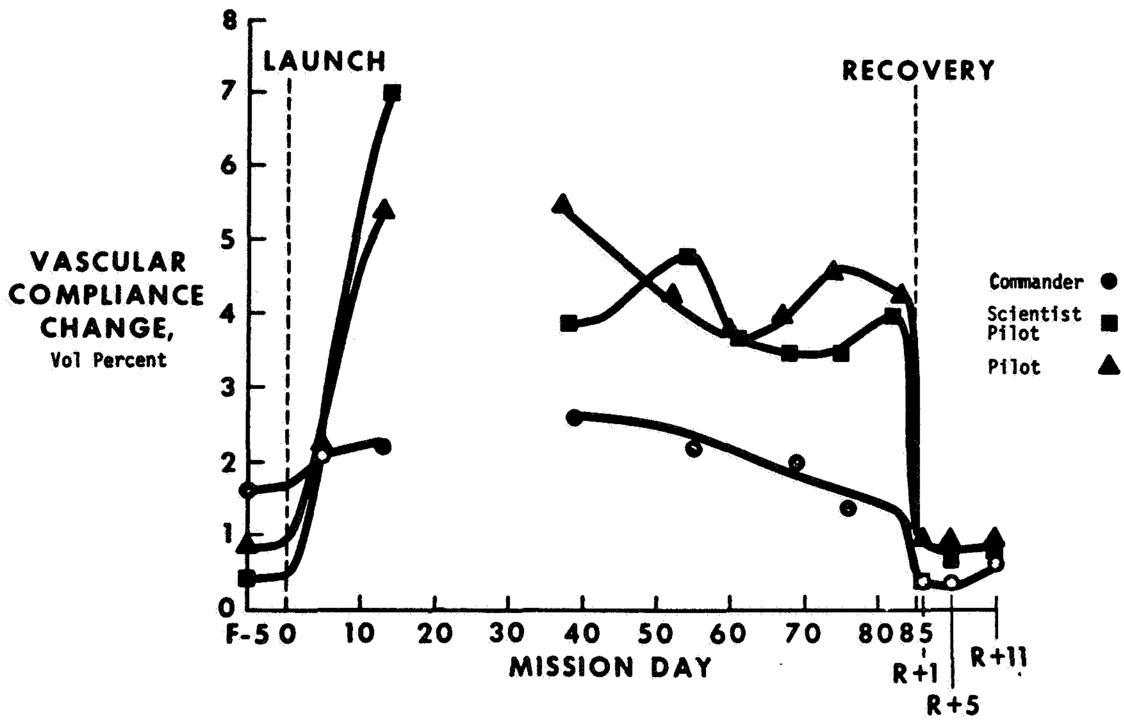

Figure 5. Skylab 4 crew vascular compliance.

even below preflight levels, with again a marked difference in Commander's response.

Before attempting to explain these results, let me give you my views of veins in the leg -- veins which may differ and behave differently from those encountered elsewhere in the body.

Figure 6 is an obviously exaggerated schematic of leg anatomy. The foot and skin of the leg are drained by unsupported veins with thick muscular walls, walls that will even go into spasm when irritated. The leg muscles are drained by much larger thin-walled conduits with little muscle or innervation; in some areas they are described as sinuses and are little more than a sac attached to the surrounding muscles. Response of such vessels should be more dependent upon the surrounding somatic muscles than upon its wall. These deep veins comprise the major venous volume - 85 percent is a commonly used value - the response that we see from the mid-calf is predominantly the response of these deep veins. There is no evidence for an increase in superficial venous volume in-flight.

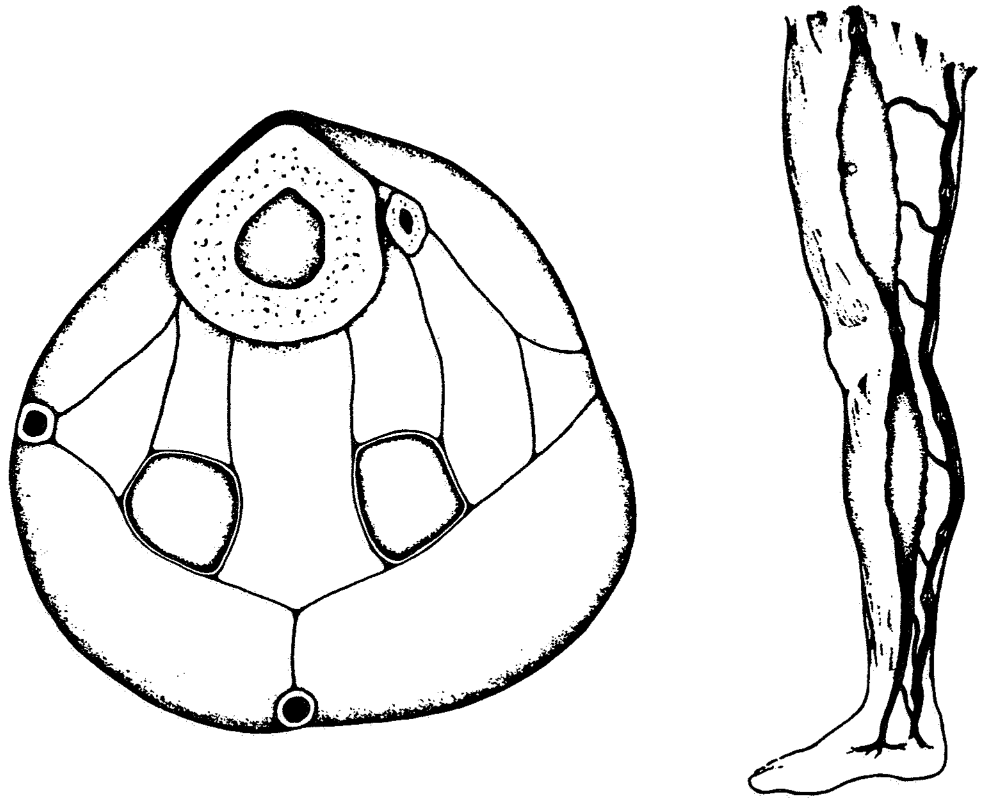

Figure 6. Distorted schematic of leg anatomy. Veins are in black.

Referring back to the responses measured, my interpretation of the changes lie in the condition of the surrounding muscles. There was a slow loss in volume of the calf segment during the first 20 days of weightlessness in contrast to the sudden loss of volume of the legs as a whole. A part of this loss was in the muscle itself. Further, with the unloading of external forces, there must have been some atrophy and a loss in muscle tone.* As the mission progressed, I suspect the body, as it always seems to do, tended to reestablish equilibrium, or "take up the slack" if you will, such that effective tone was increased in-flight and very sharply increased on being resubjected to one-g. Working a muscle, as it was experienced on recovery, causes an increase in fluid volume which may have been effective here.

Additional hemodynamic information was obtained by having the crewmen perform muscle pumping under negative pressure (fig. 7). After an experiment M092 test, the subject was left in the lower body negative pressure device and -30 mm Hg pressure was applied for three minutes causing blood to pool, again assumed to be primarily in the deep veins.

*It may be coincidence but work on the treadmill with heavy calf loading did not start until mission days 8 to 10.

At the end of this time, the subject made ten maximum effort isometric contractions of his legs. These contractions caused large pressure forces to develop against the blood in the deep veins which forced it into the central circulation through one-way vein valves. Time was allowed for an additional pooling to occur and the procedure was repeated.

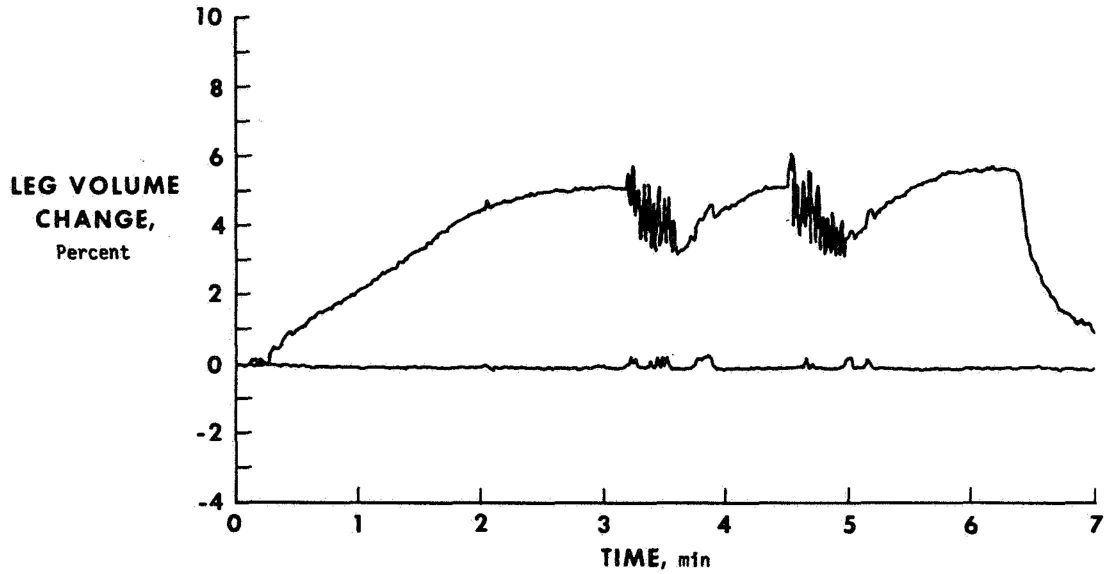

Figure 7. Muscle pumping record.

The volumes of blood accumulated and the amount remaining are plotted in figure 8, for two subjects in-flight - the Scientist Pilot and Commander. The Pilot's responses, which are not shown, were generally similar to those of the Scientist Pilot. The amount of blood pooled was generally comparable to that pooled by cuff occlusion at 30 mm Hg pressure (figs. 4a, 5). The one "wild point" of the Scientist Pilot bothers me; try as I might, I cannot discredit it, so it remains. Again, the amount of blood pooled by the Scientist Pilot is roughly two times that of the Commander; however, after muscle pumping both have the same volume remaining. While this may be sheer coincidence, I suspect there is an anatomical difference in the Commander's deep venous structure. Postflight there was a marked and immediate decrease in the amount of blood pooled while effective pumping action was still present.

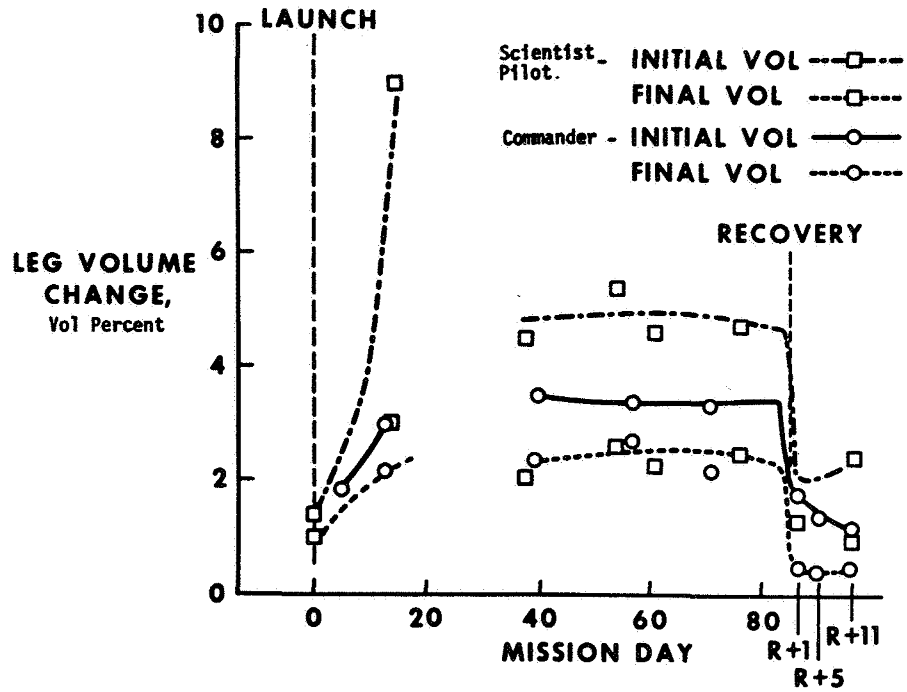

Figure 8. Skylab 4 crew leg volume changes from muscle pumping.

Under one-g, a subject typically removes about 50 percent of pooled volume from his calf, while thigh pumping is relatively less effective. About the same percentage is removed in-flight. The Commander's post-flight pumping was less effective than his preflight average, and preflight and postflight efforts were relatively less effective than his in-flight pumping, which suggests that he has less deep venous volume capacity. This variance is further supported by blood volume studies and is discussed under anthropometry.

How do these findings relate to crewmen in space flight? The Skylab 4 crew confirmed the prompt postflight return to baseline seen in the measurements of this experiment by standing and walking easily for long periods on the day after recovery. The deficiencies were only detectable by the lower body negative pressure and ergometric tests and these also quickly returned to normal.

It would appear that the general shape of the compliance curve for this flight (fig. 5) agreed with the experience of the crew and with the number of times the runs were prematurely ended. The crew felt that the test became increasingly stressful and then the stress declined. Abortion of lower body negative pressure tests also appeared to cluster within this one four-week period. The effects of a decreasing blood volume and red cell mass and increased compliance are probably the two fundamental parameters in lower body negative pressure response.

However, there are a host of factors, even and especially psychological factors, that can affect the compliance curve, to say nothing of final systemic responses.

While it was gratifying to have the importance of venous changes and especially compliance so impressively recognized in the paper on lower body negative pressure, compliance and fluid volumes should not be over-emphasized at the expense of other mechanisms. Although I consider these fundamental, a great host of others remain to be explored.

I would question the concept of significant changes in compliance being caused by empty and flattened veins. As I will show in the next report on Anthropometry, leg veins were not empty, at least the superficial leg veins were not.

Secondly, I question the concept of compliance or potential volume spaces being changed by sleep in weightlessness which seems counter to common experience and to measurements done during Skylab, when muscular activity was shown to increase muscle volume. This activity would reduce potential venous volumes, especially of the deep veins enclosed with the muscles in fascial compartments. Muscle pumping is a very transient phenomena and removes only a portion of the blood. Thus I would look elsewhere for the short term variations in response to lower body negative pressure.

CONCLUSION

In summation: Changes in blood flow were demonstrated, which I think make the problem of obtaining cardiac output data in space even more imperative.

Venous compliance changes were demonstrated which, with blood volume changes, should provide an initial and primary point of departure for investigation of the complete response to lower body negative pressure. Time course of the compliance changes should be considered by mission planners. Shuttle reentry, for example, will fall within the zone of increased sensitivity to orthostatic stress. There was a demonstration of a marked difference in individual response on Skylab 4, which might also be considered in some flight operations. Since compliance of the leg vessels appears to be intimately related to leg muscle, this relationship should be properly investigated. Muscle condition may have played a major role in the slower return to normal of the crews of Skylab 2 and 3. In the future, proper cognizance should be given to such venous studies in bed rest, especially of the deep veins as both the medical community and NASA stand to benefit by such studies.

In conclusion, another portion of man's body has been demonstrated to be capable of making adaptations to weightlessness, which produces both stability under weightlessness and rapid re-adaptation on return to one-g. This bodes well for future manned flights.

ACKNOWLEDGEMENTS

Great appreciation is due the Skylab 3 and 4 crews on this experiment for they performed the in-flight measurements in an excellent fashion with little training on Skylab 4 and no training at all on Skylab 3. Col. Richard Gowen gave a good deal of aid in insuring accurate calibration of the leg bands. Without the support of Bill Schneider and others in the flight management team this work could not have been scheduled.