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EVALUATION OF THE ELECTROMECHANICAL PROPERTIES OF THE CARDIOVASCULAR SYSTEM

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ABSTRACT

Cardiovascular electromechanical measurements were collected on returning Skylab crewmembers at rest and during both lower body negative pressure and exercise stress testing. These data were compared with averaged responses from multiple preflight tests. Systolic time intervals and first heart sound amplitude changes were measured. Clinical cardiovascular examinations and clinical phonocardiograms were evaluated.

Postflight, in all crewmen there were significant changes in ejection time index, in pre-ejection period, and in the ratio, pre-ejection period/ejection time. These changes were present at supine rest as well as during lower body negative pressure stress testing. All systolic time intervals had returned to preflight values within one month. There were decreases in first heart sound amplitude responses to lower body negative pressure by all Skylab 4 crewmen. This response was markedly depressed in one crewman who had a presyncopal episode during the lower body negative pressure test on recovery day.

Two of the three crewmen exhibited depressed first heart sound amplitude responses to submaximal exercise on the day after recovery. Skylab 4 crewmen had altered systolic time intervals during upright rest and during exercise compared with preflight values. The systolic time intervals data were consistent with a reduced stroke volume and possibly a reduction in contractility and/or Frank-Starling effect.

Clinical cardiovascular examinations revealed a reduction in all heart sounds, reduction in precordial movement, and a marked reduction in arterial pulsations. Trace to one plus pretibial edema was noted in the Skylab 3 and Skylab 4 crewmen in the early postflight period. The causes for this transient edema are complex.

The persistent alterations in the systolic time intervals in the face of a replenished blood volume and no consistent correlation with afterload or with change in leg volume during lower body negative pressure suggest that there is a functional impairment to venous return and

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perhaps a myocardial factor in the overall decreased tolerance to this stress in the postflight period. Systolic time intervals data collected during exercise support the above hypothesis and are consistent with decreased stroke volume. Clinical studies also support the contention. All changes noted returned to normal within 30 days postflight so that the processes appear to be transient and self limited. The cardiovascular system seems to adapt quite readily to zero-g, and more importantly it is capable of readaptation to one-g after long duration space flight. Repeated exposures to zero-g also appear to have no detrimental effects on the cardiovascular system.

INTRODUCTION

It is well known that after short duration space flights, such as the Apollo flights, crewmen exhibited cardiovascular instability in response to orthostatic and exercise stresses (1, 2). Although through preflight and postflight stress testing several other physiologic variables associated with the decreased tolerance were documented, in-flight timing of the changes were impossible. The measurements were simple, *e.g.*, electrocardiograph and blood pressure. There were wide unexplained interindividual variations between crewmen of the same flight and different flights in their responses to the tests.

The Skylab program offered an opportunity to study man during long duration space flight. The medical test protocols were an established part of this program in the preflight, in-flight and postflight periods. Because payload and flight qualified hardware were and are a high-cost portion of the NASA programs, there had to be a limit to the number of devices allowed for in-flight biomedical experiments. Devices and techniques which enhanced or embellished the core experiments in-flight were encouraged instead to be a part of the preflight and postflight evaluations. Therefore, most of these items were designed for testing in the Skylab Mobile Laboratories and became an item on the preflight and postflight schedules.

Devices and techniques for measuring and analyzing systolic time intervals and quantitative phonocardiograms were initiated during Apollo 17, the last lunar mission. This first generation hardware was utilized as well for the Skylab 2 mission as part of the lower body negative pressure experiment. The data show that the systolic time interval from Apollo 17 crewmen remained elevated longer postflight than the response criteria of heart rate, blood pressure, and percent change in leg volume all of which had returned to preflight levels by the second postflight. Although the systolic time interval values were only slightly outside the preflight fiducial ($P<0.05$) limits, this finding suggested that: the analysis of systolic time interval may help to identify the mechanisms of postflight orthostatic intolerance by virtue of measuring ventricular function more directly and, the non-invasive technique may prove useful in determining the extent and duration of cardiovascular instability after long duration space flight.

The systolic time intervals obtained on the Apollo 17 crewmen during lower body negative pressure were similar to those noted in patients with significant heart disease.* Although similar changes in systolic time intervals occur with a decreased ventricular filling secondary to a decreased venous return in normal young subjects (3) and although a decreased blood volume was noted in the Apollo crewmen, a progressive myocardial deterioration during long exposure to zero-g could not be ruled out. Based on Apollo and Gemini experience, a firm stance was taken by the biomedical scientists that during flight daily exercise sessions would be provided for Skylab astronauts - the excerise was to be provided by an in-flight cycle ergometer.

Postflight evaluations of systolic time intervals were accomplished after all Skylab missions. During Skylab 4 additional noninvasive techniques were allowed so that after this mission echocardiography, semi-bloodless (radioisotopically determined) circulation times and resting cardiac outputs, and peripheral venous pressure were performed. Results from these techniques are presented in other papers of this symposium (4, 5).

METHODS

General

Preflight examinations for the lower body negative pressure experiment (M092) were conducted over a four to ten month period prior to launch. The last three preflight tests were accomplished at F-30, F-15, and F-5 days, respectively. During these final baseline tests full data collections were performed including the systolic time intervals and absolute amplitude measurements.

Postflight lower body negative pressure test were performed with the few hours of splashdown (recovery day tests). Both lower body negative pressure and the vectorcardiograph exercise tests were done on the day after and on eleven days after recovery. Lower body negative pressure tests were done on several subsequent days after each Skylab flight up to two months postflight on Skylab 4.

*(Unpublished results)

The lower body negative pressure protocol consisted of five minutes supine rest, 15 minutes of incrementally applied negative pressure to -50 mm Hg and a five minute recovery period. The Exercise-Vectorcardiograph test included a five minute rest period in the upright position, a two minute exercise period at 150 watts and a ten minute upright recovery period. The data presented in this paper will include only the control and end of maximal stress periods.

Systolic time intervals were calculated from the vectorcardiograph X-lead, phonocardiogram, carotid pulse trace, and pneumogram during all three missions (fig. 1). However, data acquisition problems in the preflight period of Skylab 2 made the systolic time intervals data difficult to inerpret, and therefore these data are not presented. Also, for similar reasons quantitative phonocardiographic data from Skylab 2 and Skylab 3 are not available for this document. Amplitude of the first heart sound (S_1 Amp) data during exercise and during lower body negative pressure stresses (preflight and postflight) are presented for Skylab 4 only. Systolic time intervals information is presented from Skylab 3 and Skylab 4 for lower body negative pressure and exercise stress tests.

Equipment

The following list of transducers, signals, and types of analyses are provided for a clearer understanding of the data. A more comprehensive description of the system used will be made available at a later date.

Phonocardiographic System. The system used for phonocardiograms included a 20 gram Elema EMT-25C piezo-electric crystal accelerometer transducer which is coupled with a high pass filter network of 25, 50, 100, 200 and 400 Hz central frequencies (-12 dB roll off). The raw output from the transducer which has a high pass characteristic was recorded onto analog tape and subsequently played back through a NASA-designed filter system for analysis. The analyzed signals were reproduced upon light sensitive paper at 100 mm/second using a Brush (Mark 2300) light beam recorder.

Vectorcardiogram. The X-lead of a vectorcardiograph system was used for timing of electrical events of the heart and the characteristics of this system are described elsewhere (5). Tattoos on the crewmen insured reproducible placement of the electrodes.

Pneumogram. A mercury-in-silastic strain gage was used to measure quantitative rate and qualitative depth of respiration. Used mainly to determine the phase of respiration the output was used in determining other measurements such as systolic time intervals.

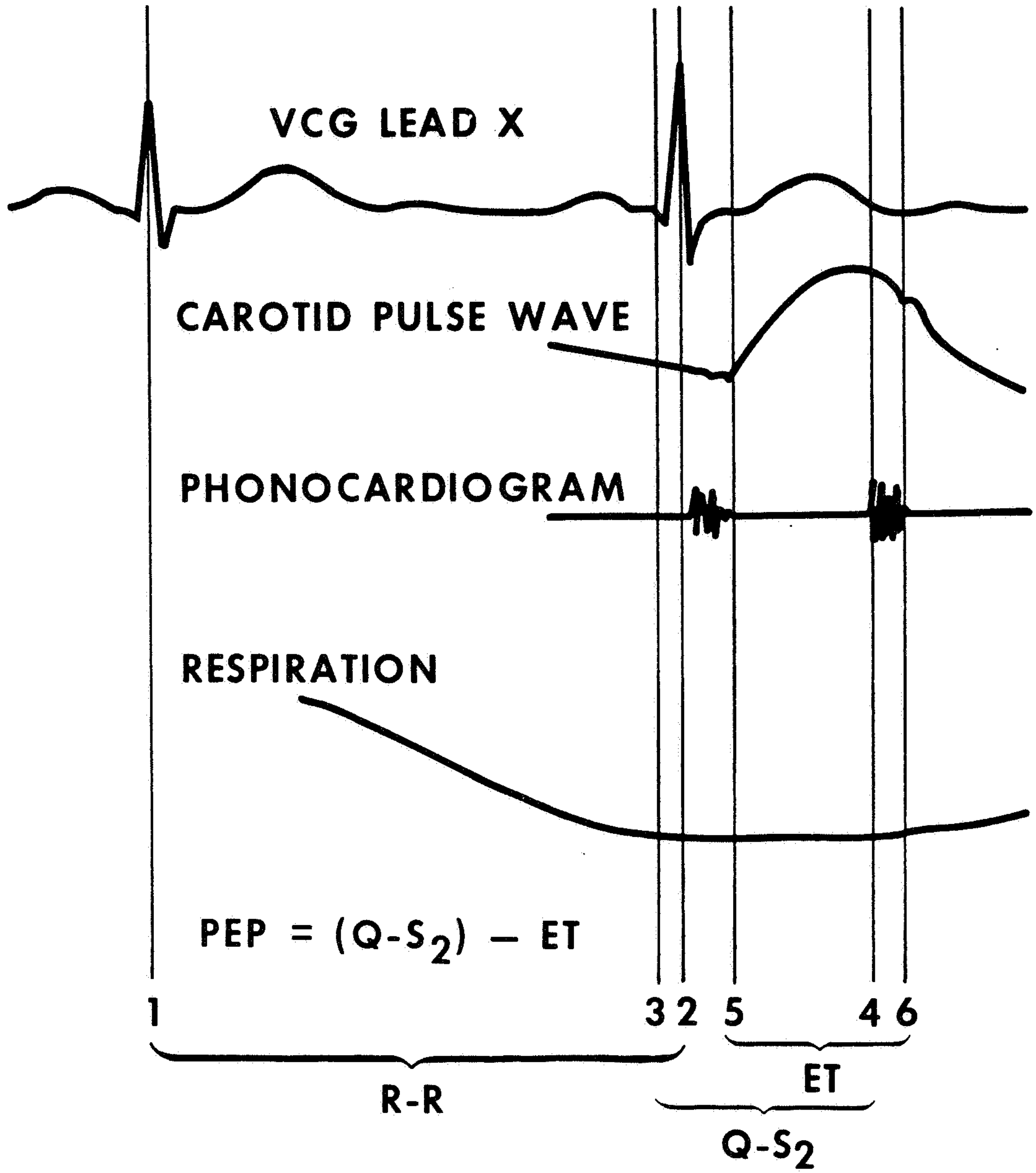

Figure 1. Signals used to measure systolic time intervals. Note that PEP is calculated from the Q-S_2 and ET measurements.

Carotid Pulse. A Sanborn/Hewlett-Packard APT-16 displacement transducer was used to measure carotid pulsations. This transducer had a flat frequency response from d.c. to approximately 60 Hz and has been shown to reproduce arterial pulses faithfully at high and low heart rates (7).

Apexcardiogram. Apexcardiograms were collected on the Skylab 4 crewmen only. The same displacement transducer used for the carotid pulsations was used for the apex cardiogram.

Other Equipment. The Skylab blood pressure measuring system, Lower Body Negative Pressure Device, leg volume measuring system, the cycle ergometer, vectorcardiograph, experiment support system, analog tape recorders, and the various other Skylab equipment are included in other documents or in other papers of this symposium.

TECHNIQUES

Systolic Time Intervals

Systolic time intervals were measured in the following manner: signals from the vectorcardiograph (X-lead), carotid pulse, phonocardiogram, and pneumogram were recorded during the tests on analog tape (Ampex, Model 1260). Replay and analysis of all signals were accomplished via a small computer with software developed jointly between the Cardiovascular Laboratory at the Johnson Space Center and the Massachusetts Institute of Technology. Corrections for heart rate were employed after Weissler, *et al.* (6). Basically, the program user scanned the four data channels which had been digitized at 200 to 1000 samples per second, and chose samples which met predetermined criteria (8). By use of movable cursors the systolic time intervals were determined semiautomatically. Computations were performed according to the program and the entire summary was stored.

First Heart Sound Amplitude

Absolute amplitude of the first heart sound was measured manually from the phonocardiographic signals. Because there is no standard reference such as voltage for phonocardiograms (as there is for electrocardiogram and vectorcardiogram) the stressed S_1 Amp was always compared with the control resting amplitude of the first heart sound of each individual for each test. Each individual served as his own control, both preflight and postflight. The microphone was placed in the fourth left intercostal space just to the left of the sternum in all crewmen, during all tests. Amplitude of the first heart sound was expressed as a percent change from control state. In general, 20 consecutive beats were chosen in the control period of the exercise or Lower Body Negative Pressure test protocols, and the amplitudes of the first heart sound (S_1) were measured in millimeters. At maximal steady state stress, ten consecutive beats were measured and compared with the control mean S_1 Amp. Comparison of the S_1 Amp at maximal stress was expressed as percentage change in amplitude from control.

Clinical Evaluations

In addition to systolic time intervals and S_1 Amp measurements clinical cardiovascular examinations which included phonocardiography, apexcardiography, and carotid pulse analyses were performed. The results of these clinical evaluations are given in order to add more information about the postflight cardiovascular condition of the Skylab astronauts.

RESULTS

Reports on the data from in-flight cardiovascular tests for the Skylab crewmen are contained in the papers being presented by Drs. R. L. Johnson, G. W. Hoffler, and R. Smith at this symposium. The following results reflect only information from preflight and postflight studies which were conducted during the lower body negative pressure, and exercise-vectorcardiograph experiment (M093) experiments. Because the most extensive measurements were made on the Skylab 4 crewmen, these data dominate the results and discussion. However, comparisons are made with the other Skylab missions and with Apollo.

Lower Body Negative Pressure

Figures 2 through 4 show the postflight systolic time intervals responses of the Skylab 4 (84 days) crewmen to lower body negative pressure over time. Heart rate was elevated postflight.

In general, the results of the postflight tests show that there was no change in total electromechanical systole ($Q\text{-}S_2$), ejection time index was decreased at rest and during lower body negative pressure, and pre-ejection period and the ratio of pre-ejection period to uncorrected ejection time (PEP/ET) were both increased significantly. Table I shows the percent change in systolic time intervals postflight for Skylab 4 and Skylab 3 crewmen. It is clear from this table that Skylab 3 crewmen had greater increases in pre-ejection period and pre-ejection/ejection time than did the Skylab 4 crewmen. This finding was present at rest, at -50 mm Hg lower body negative pressure and for a longer duration postflight at rest and during maximal stress.

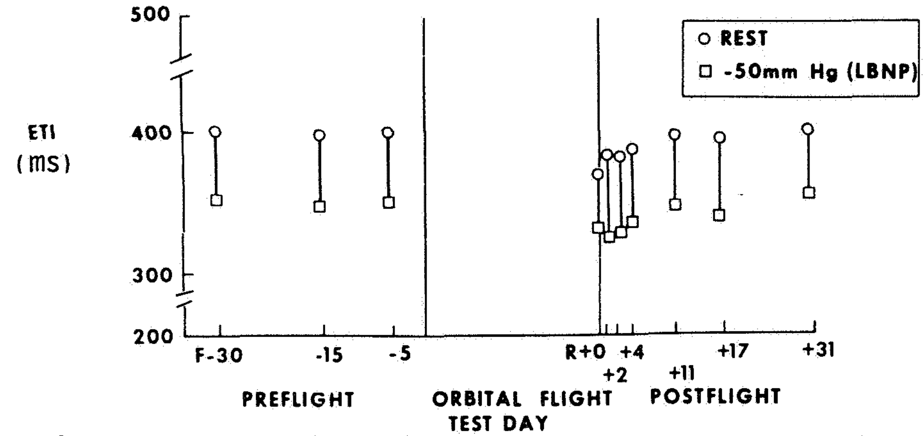

Figure 2. Resting and lower body negative pressure (LBNP) stressed mean ejection time index (ETI) for all Skylab 4 Crewmen.

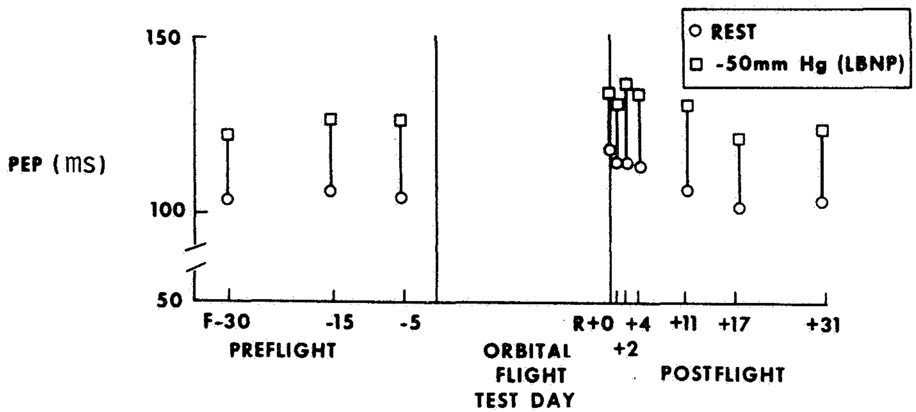

Figure 3. Resting and lower body negative pressure (LBNP) mean pre-ejection period (PEP) for all Skylab 4 crewmen.

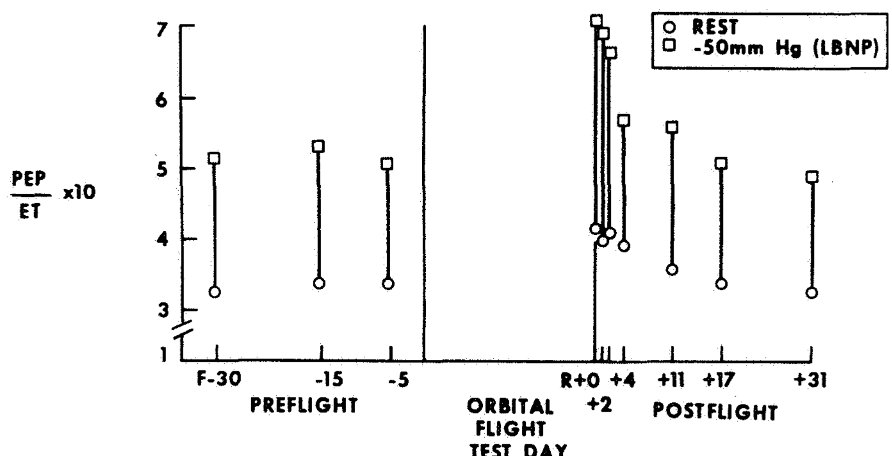

Figure 4. Resting and lower body negative pressure (LBNP) stressed pre-ejection period/ejection time (PEP/ET) - mean values for Skylab 4 crewmen.

TABLE I. PERCENT CHANGE IN SYSTOLIC TIME INTERVALS DURING LOWER BODY NEGATIVE PRESSURE - SKYLAB 3 AND SKYLAB 4 CREWMEN

Recovery Day, Percent Change From Preflight

SKYLAB MISSION	TEST	$(Q - S_2)$ INDEX	EJECTION TIME INDEX %	PRE-EJECTION PERIOD %	PRE-EJECTION PERIOD / EJECTION TIME %
3	REST	NO CHANGE	↓ 7	↑ 18	↑ 28
	LBNP	NO CHANGE	↓ 10	↑ 14	↑ 33
4	REST	NO CHANGE	↓ 7	↑ 15	↑ 20
	LBNP	NO CHANGE	↓ 7	↑ 10	↑ 28

All systolic time interval changes were back within preflight values by two to four weeks in all crewmen. Most resting systolic time intervals had returned within a week to 11 days. Most systolic time intervals at -50 mm Hg had returned by 9 to 16 days on Skylab 4. However, all three of the Skylab 3 crewmen had abnormal pre-ejection period/ejection time until the tests 31 days after recovery because of both abnormal ejection time interval and borderline high pre-ejection period during stress.

Mean of the diastolic pressures (one determinant of systolic time intervals) for the Skylab 3 and Skylab 4 crewmen are shown in figure 5. Diastolic pressure tended to be elevated during the first or second day after splashdown and then returned to preflight values; the Commander on Skylab 4 maintained an elevated diastolic pressure until 11 days after recovery. Also, the Pilot on Skylab 3 had an elevated diastolic pressure until 4 days after recovery. No crewman exhibited frank pathologic blood pressures during supine rest (control) phase of the lower body negative pressure tests. Stress heart rates had returned to preflight levels by the fourth day after recovery.

Percent change in leg volume (fig. 6) during lower body negative pressure was within preflight values on recovery day. With the exception of the Commander's test on the fourth day postflight, the Skylab 3 crewmen's response remained within baseline limits. The percent change in leg volume for two Skylab 4 crewmen (Scientist Pilot and Pilot) appeared to be elevated on days one to four after recovery, while the Commander's response was within preflight levels during this period. In spite of these findings the Skylab 4 crewmen regained their preflight systolic time intervals more quickly than did the Skylab 3 crewmen; these findings will be addressed again in the discussion.

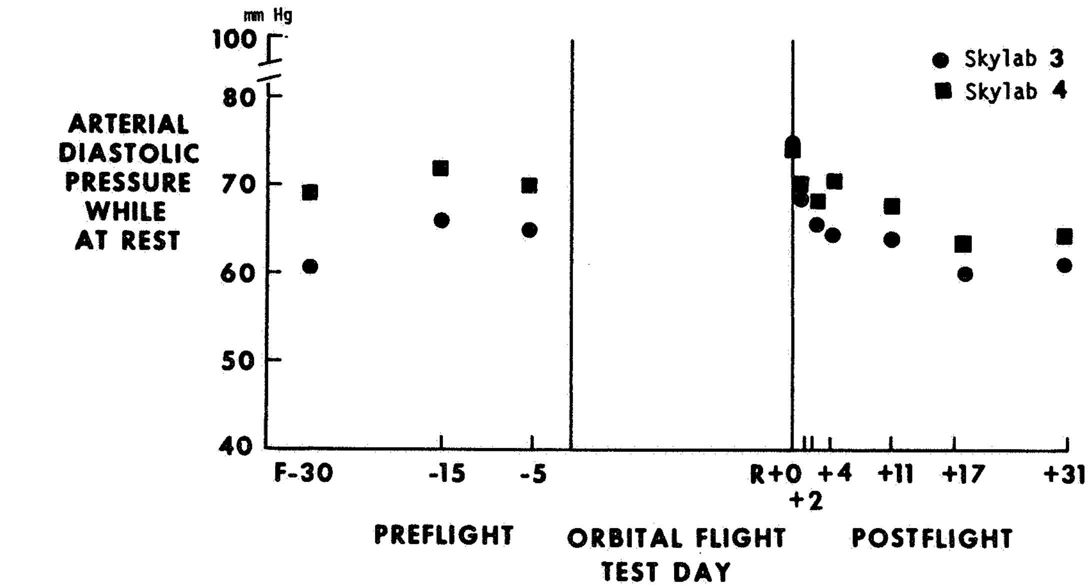

Figure 5. Resting diastolic pressures, mean values for Skylab 3 and Skylab 4 crewmen.

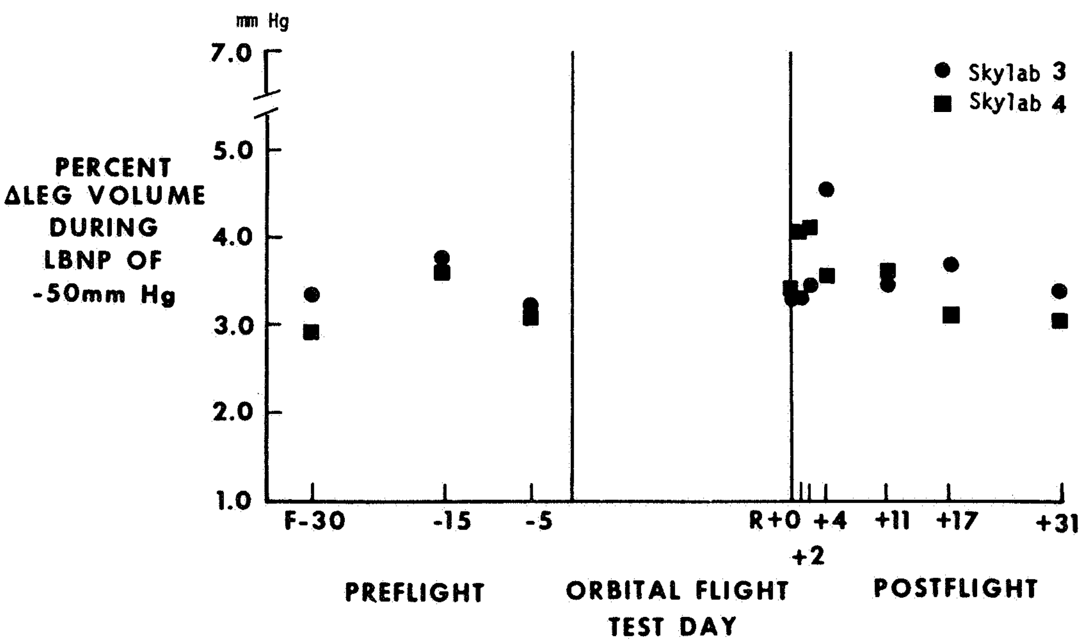

Figure 6. Mean percent change in leg volume during preflight and postflight lower body negative pressure (LBNP) tests at -50 mm Hg negative pressure.

The S_1 Amplitude responses of all Skylab 4 crewmen were depressed post flight as shown in figure 7. Figure 8 shows a typical S_1 Amp response by the Skylab 4 Pilot preflight versus the day after recovery. Notice the progressive reduction in S_1 Amp with increase in negative pressure in the first postflight day test as compared to a preflight test. Heart rates are also shown in figure 8.

During his recovery day lower body negative pressure test the Pilot's S_1 Amp response fell to 30 percent, a value which during Apollo was uniformly associated with syncope (9). The Pilot exhibited presyncope during this recovery day test at approximately one minute into the maximal stress level. His S_1 Amp response to lower body negative pressure was back to preflight limits only by 31 days postflight compared to 11 days postflight for the Commander and Scientist Pilot.

Exercise Results

Preflight systolic time interval responses to the two minute bout of exercise at 150 watts were typical of those reported by other workers (8, 10). Figures 9, 10, 11, and 12 reflect the Skylab 4 mean systolic time interval responses on the first and eleventh days postflight, compared with three preflight tests. Supine resting values were obtained from the lower body negative pressure test data which were collected approximately one hour before exercise. Compared to preflight responses the first day postflight test can be summarized as follows: Total electromechanical systole (Q-S_2) corrected for heart rate (Q-S_2)I increased and ejection time index decreased during upright rest and exercise by four percent in the Scientist Pilot and Pilot with the Commander showing no significant change in (Q-S_2)I or in ejection time index. Mean pre-ejection period increased 15 percent at rest and increased 14 percent during excerise. The pre-ejection period/ejection time increased by 22 percent at rest and 26 percent during exercise compared with the preflight values. Table II shows individual crewmen results.

TABLE II. PERCENT CHANGE IN STI - REST AND EXERCISE - POSTFLIGHT COMPARED WITH PREFLIGHT IN SKYLAB 4

CREWMAN	STATE	(Q-S_2)I	ETI	PEP	$\frac{PEP}{ET}$
Commander	Rest	↑ (NC)	↓ (NC)	↑ 6	↑ 19
	Exercise	↑ (NC)	↓ (NC)	↑ 5	↑ 18
Scientist Pilot	Rest	↑ 4	↓ 4	↑ 22	↑ 24
	Exercise	↑ 4	↓ 4	↑ 16	↑ 31
Pilot	Rest	↑ 4	↓ 4	↑ 18	↑ 22
	Exercise	↑ 4	↓ 4	↑ 22	↑ 30

NC = No significant change

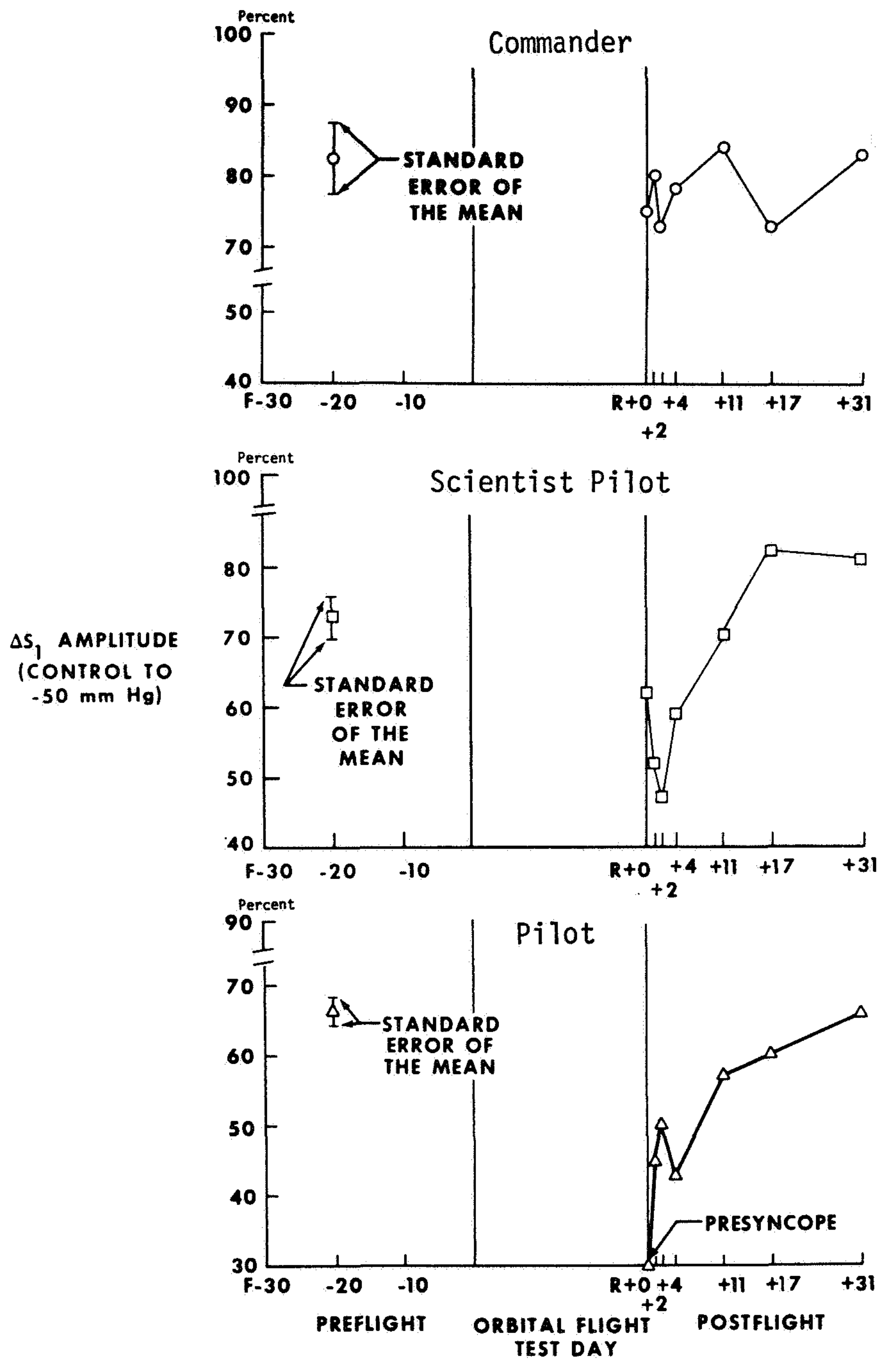

Figure 7. Percent change in first heart sound amplitude from control to -50 mm Hg lower body negative pressure for Skylab 4 crewmen.

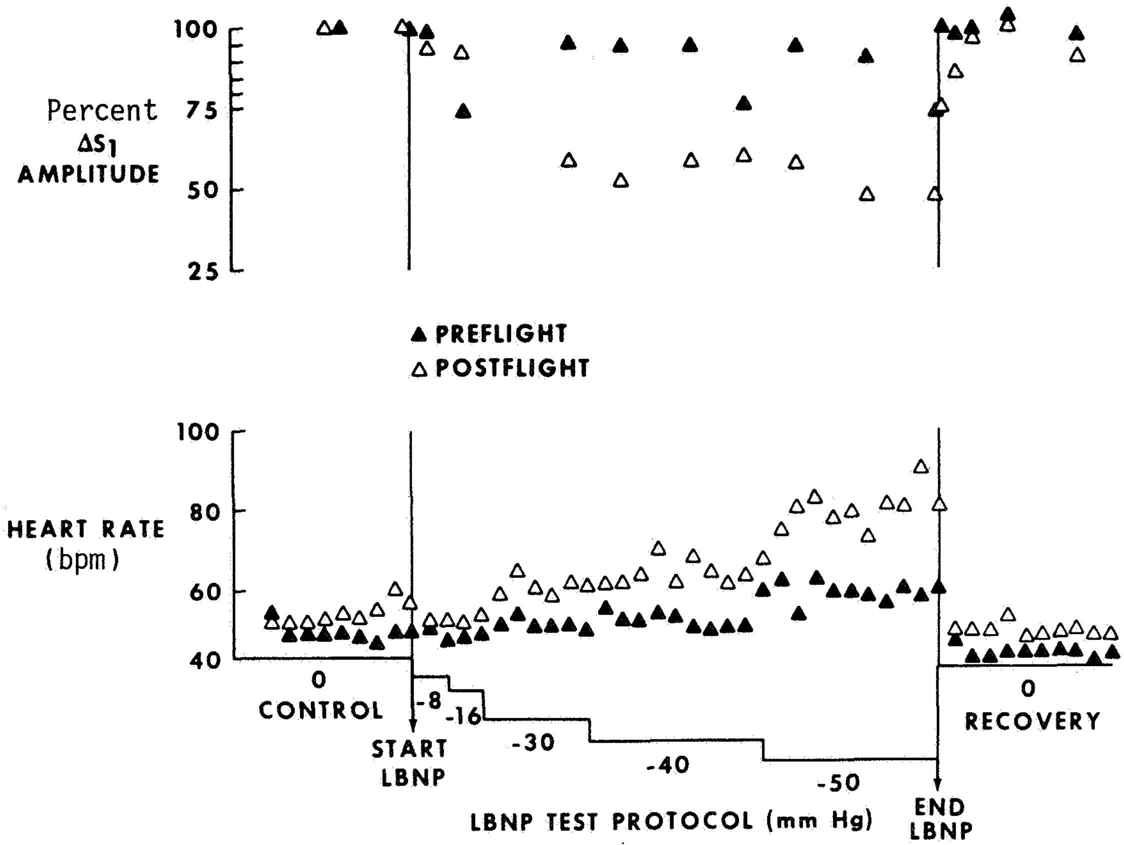

Figure 8. Heart rate and first heart sound amplitude response to lower body negative pressure (LBNP) by Pilot of Skylab 4 - preflight versus day 1 postflight.

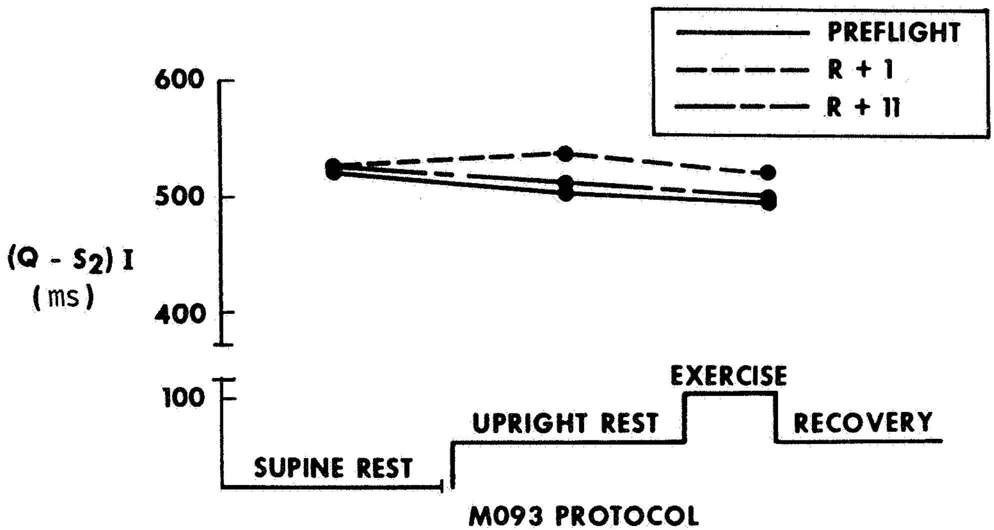

Figure 9. Response of all Skylab 4 crewmen to exercise - total electromechanical systole. Mean $(Q\text{-}S_2)I$ at rest and after 150 watts exercise.

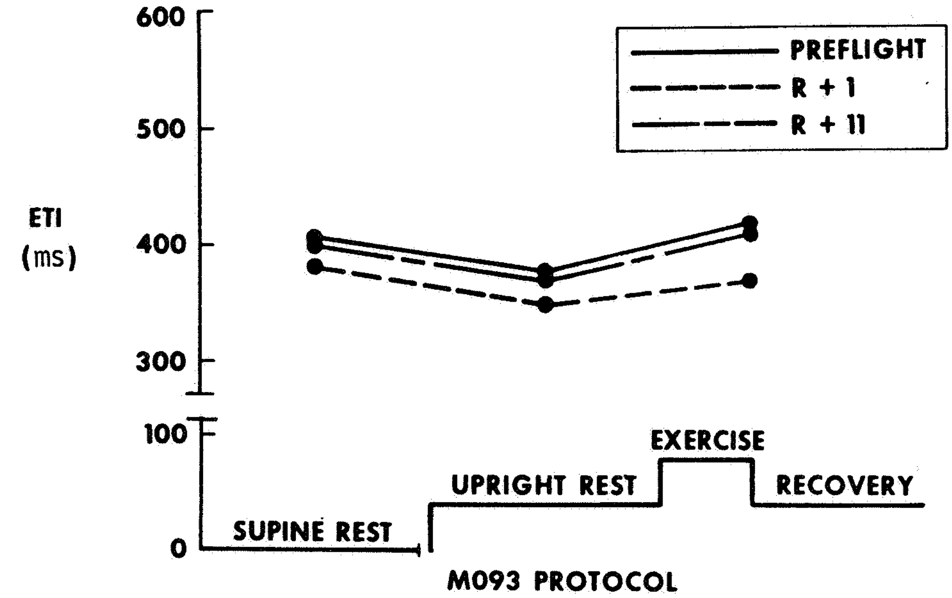

Figure 10. Response of all Skylab 4 crewmen to exercise - mean ejection time index (ETI) at rest and after 150 watts exercise.

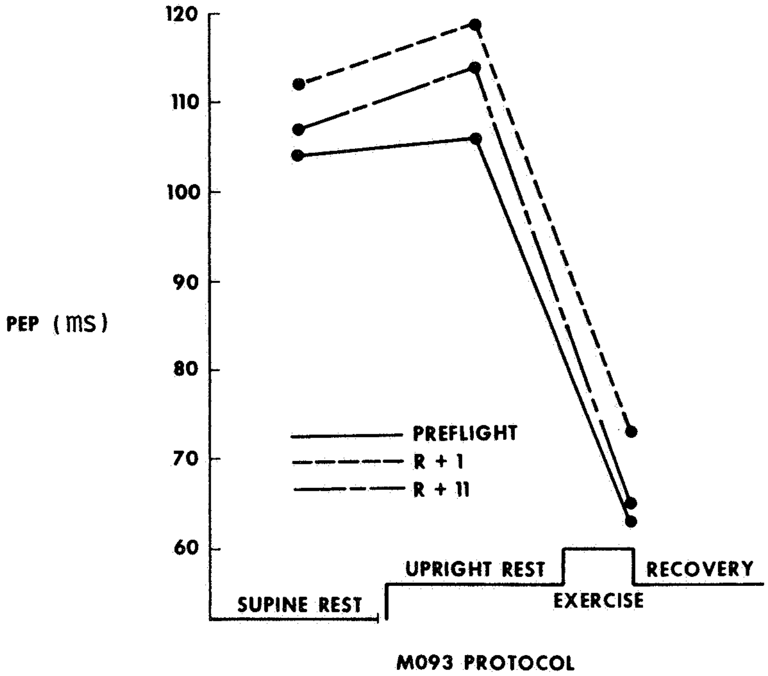

Figure 11. Response of all Skylab 4 crewmen to exercise - mean pre-ejection period (PEP) at rest and after 150 watts exercise.

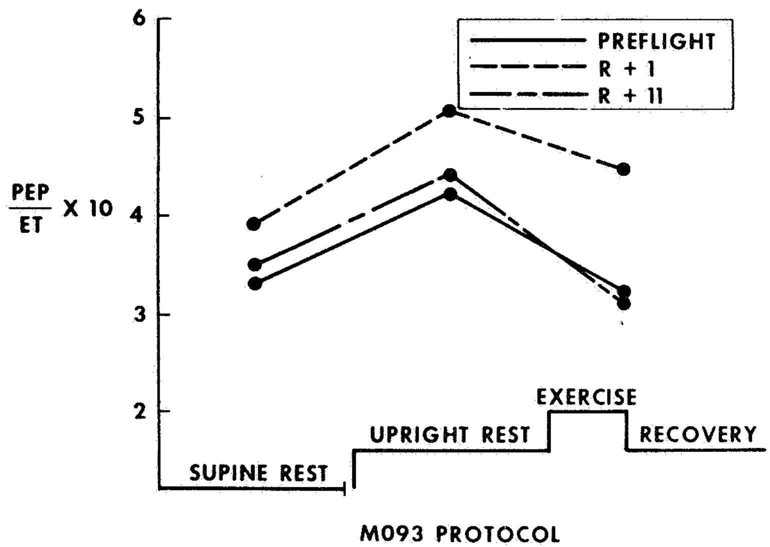

Figure 12. Response of all Skylab 4 crewmen to exercise - mean pre-ejection period/ejection time (PEP/ET) at rest and after 150 watts exercise.

First heart sound amplitude responses to exercise of the individual Skylab 4 crewmen are shown in figure 13. The Commander had very little if any change in the S_1 Amp for given heart rate at 150 watts postflight. The Scientist Pilot had a depressed S_1 Amp response on the first day postflight, but an apparently normal one on the eleventh day postflight. The Pilot's S_1 Amp response was low compared with the other crewmen on two of the three preflight tests. His response appeared to be depressed further postflight with no differences between the first and eleventh day postflight tests. These data have not been analyzed statistically as of the writing of this paper so that full interpretation of this data is not possible at this time. No evidence for a training effect was apparent.

Clinical Findings, Phonocardiography and Apexcardiography

The crewmen of Skylab 3 and Skylab 4 were given thorough cardiovascular examinations which included phonocardiograms. Apexcardiograms were done on Skylab 4 crewmen only. Although fourth heart sounds (S_4) were present on some crewmen preflight these sounds are not abnormal (11). All heart sounds were diminished postflight. Several crewmen had prominent S_4 with exercise (12). However, even heart sounds and arterial pulsations obtained during exercise were attenuated in the immediate postflight period. By 11 day postflight these findings disappeared. Apexcardiography was normal preflight. Postflight the point of maximal impulse was not palpable and no apexcardiograms could be obtained. This was true as late as the eleventh day postflight on Skylab 4 crewmen. This finding is consistent with the other data and probably reflects diminished ventricular action.

One finding which was of concern at first, but which is now accepted as not being of clinical importance was trace to one plus pretibial edema in all crewmen. This finding appears to begin on day 1 or day 2 postflight. The edema is usually "trace" after one or two hours of ambulation. In Skylab 3 the edema lasted to day 16 postflight On Skylab 4 it was absent on day 18 postflight. Although the systolic time intervals data were abnormal and it is known that usually edema is a common sign of a compromised left ventricle, the causes for this postflight edema are probably more complex than those of pure cardiac dysfunction.

The facies caused by cephalad fluid shifts, seen on television and in photographs which are so obvious during flight, are peculiarly absent within an hour after splashdown. It is interesting that the in-flight facies, described elsewhere appear quite similar to subjects who are studied in the head down tilt position (1).

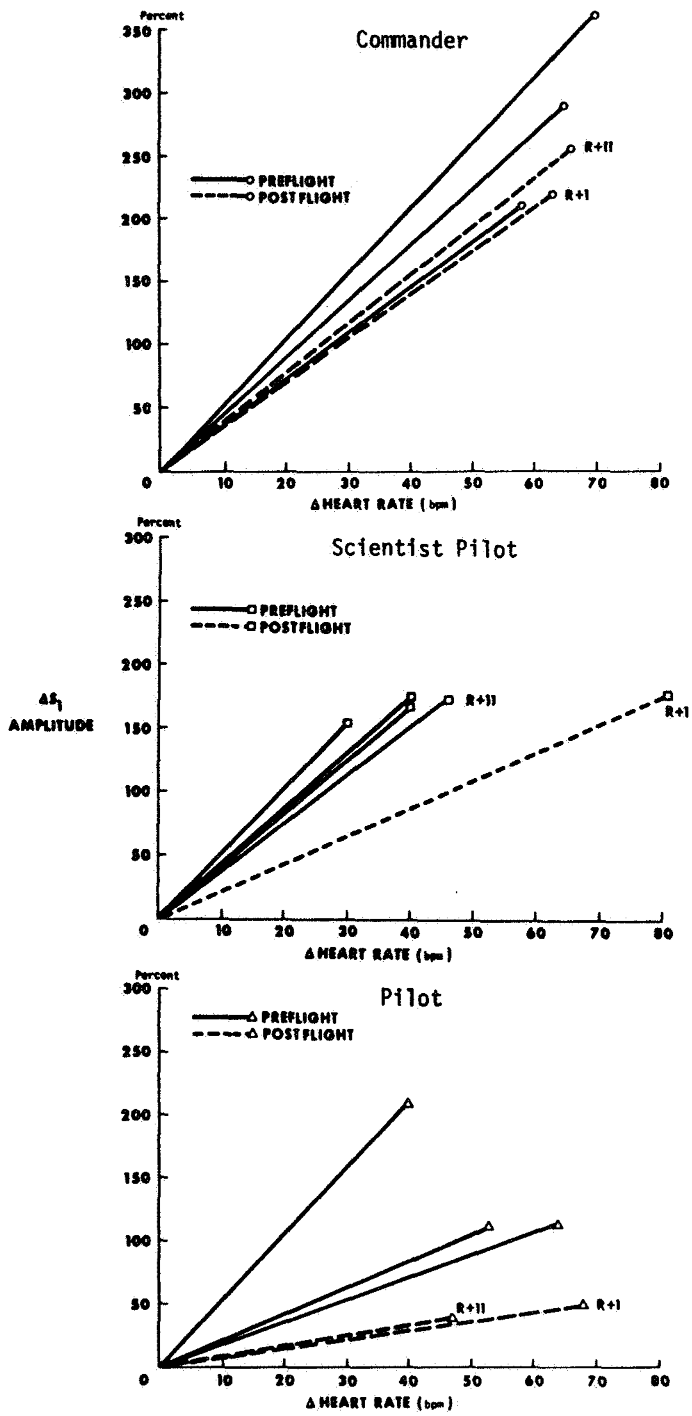

Figure 13. First heart sound amplitude response to exercise - Skylab 4 Crewmen.

Immediately postflight, the Skylab crewmen appeared to be relatively dehydrated and the skin on the face was wrinkled rather than being puffy and fluid filled. Clinically, it appears that the fluid is redistributed rapidly postflight, but the pattern of distribution is such that plasma volume (and blood volume) is not replaced immediately. This decreased blood volume is probably a major cause for abnormal systolic time intervals during the recovery day testing at rest and during lower body negative pressure stress (as is afterload). The Skylab 4 crewmen did not appear to be as dehydrated upon recovery as were the Skylab 3 crewmen.

DISCUSSION

Sytolic time intervals and S_1 Amp data are difficult to interpret in man. Interpretation is even more difficult when some of the hemodynamic variables are possibly unknown. However, a better interpretation of these data is possible if one knows the hemodynamic events which occur in response to a known stress (13, 14). The intervals of systole have been described and interpreted for certain stresses such as lower body negative pressure (3, 15, 16); and exercise (10, 8). The availability of additional information such as blood volume, diastolic or mean blood pressure, and posture are needed when one attempts to interpret systolic time interval information (8). The externally measured intervals have been shown to correlate quite well with those measured directly (17).

Actually there are two problems to the analysis of systolic time intervals and S_1 Amp data. One problem involves accuracy of measuring the various parameters. Another, more difficult problem, is interpretation of the obtained results. The data presented in this paper is subject to both of these problems. However, every attempt has been made to choose the proper transducers and recording equipment and to measure as accurately as possible the intervals and amplitudes.

The systolic time interval data obtained from the Skylab astronauts during the preflight period reflect good reproducibility of these measurements. During this controlled period the intervals do not vary a great deal as can be seen in figures 1 through 7 which present the results of the three preflight tests. Conversely, one recognizes that the postflight, as well as in-flight, period is not nearly as controlled (18). However, the reproducibility of postflight from several missions allows some confidence that these data do represent the responses of individuals after space flight.

The preflight (control) rest and lower body negative pressure data obtained from the Skylab astronauts are quite similar to the systolic time interval data obtained from younger men (3). The postflight systolic time interval data at rest and during lower body negative pressure (especially on recovery day and days 1 and 2 post recovery) reflect changes one would expect from a decrease in total blood volume, but also from myocardial dysfunction (19, 20, 13, 21). In the face of a constant total electromechanical systole (corrected for heart rate) with a decreased ejection time index and an increased pre-ejection period one is presented with three possibilities, or combinations, to explain the results:

- a decrease in preload,
- an decrease in contractility, and/or
- an increase in afterload (22).

A decrease in preload was suggested by measurements of significant decreases in blood volume on all Skylab crewmen (5). There were deficits in both red blood cell mass and plasma volume. The blood volume is reportedly back to preflight levels by one week with some fluctuations in plasma volume although the red blood cell mass remains depressed for a longer duration (23). The decrease in preload associated with lower body negative pressure stress or with upright posture is well established (14, 16, 24).

If decrease in absolute blood volume were the only factor influencing the systolic time interval findings after space flight one would expect the systolic time intervals to return to preflight values along with the blood volume repletion (24). However, this is not the case. The systolic time intervals remain abnormal for a longer period. Skylab 3 crewmen took longer to return to baseline systolic time intervals than did the Skylab 4 crew although the decreased blood volume and the duration of this decrement were similar. The differences between the crews may be related to activities of the crewmen in-flight, *e.g.*, the amount of exercise performed; or they may be related to postflight activities as well.

The systolic time interval during lower body negative pressure stress remains abnormal longer than did the systolic time intervals at rest. This finding is not surprising since one goal of stress testing is to elicit cardiac malfunction when none is apparent at rest. Additionally, because the stressed systolic time intervals remained depressed after blood volume repletion, it could be argued that perhaps more blood is pooled at -50 mm Hg postflight than is pooled preflight. Therefore, a decreased preload by virtue of increased pooling could account for the results of postflight lower body negative pressure induced changes in systolic time intervals. The percent change in leg volume does not support this hypothesis. The Skylab 3 crewmen exhibited abnormal systolic time intervals for one month after return although there was little deviation in percent change in leg volume during lower body negative pressure between preflight and postflight periods. No consistent pattern of percent change in leg volume and systolic time interval response was noted for the Skylab 4 crewmen either (fig. 6).

Afterload, a potent determinant of the intervals of systole, if consistently elevated could cause the systolic time interval changes noted in the astronauts' postflight tests (22). The Commander of Skylab 4 had significant elevation in diastolic pressure through day 11 postflight. The Pilot demonstrated a similar picture after Skylab 3. However, these crewmen did not differ in their systolic time interval responses to lower body negative pressure, or at rest, from the other crewmen of their respective missions. The systolic time interval response appears to be only partially accounted for by changes in afterload with the exception of recovery day testing. A summary of these data are given in figure 5.

Contractility, the other independent determinant of systolic time intervals (in particular pre-ejection period) (25, 22, 26) could be considered as a cause for the changes in systolic time intervals observed postflight. Patients with primary myocardial disease, as well as patients with other forms of chronic heart disease whose ventricles are abnormal, exhibit changes in systolic time intervals which are identical to those noted in Skylab crewmen postflight (22, 6, 13). However, these patients' hearts are usually enlarged, *i.e.*, increased preload is a sign of the problem. Ejection fraction is quite low in these patients (20, 28). The total electromechanical systole (corrected for heart rate) of these patients are either normal or slightly prolonged. Although preload is more than adequate, a condition which would be reflected by an abbreviated pre-ejection period, contractility is decreased and pre-ejection period is markedly prolonged. The stroke volume is decreased as is the ejection fraction, the ejection time index is shortened. Consequently, pre-ejection period/ejection time is elevated in these patients. In compromised hearts, administration of a positive inotropic drug such as digitalis shortens the total electromechanical systole (corrected for heart rate) mainly by virtue of a decreased pre-ejection period. Ejection time index is either unchanged or prolonged. These systolic time intervals reflect the increase in contractility, stroke volume, and ejection fraction. No exact causal relationship can be applied to ventricular function, given a set of systolic time interval alone, because of the complex variables. However, ancillary information makes their interpretation a valuable method for the evaluation of cardiac function.

The above example of how systolic time interval reflects cardiac function, although not directly applicable to the Skylab results does point out the kind of reasoning one must go through in order to intrepret a set of systolic time intervals. However, the astronauts could have had a slight decrease in contractility in addition to the decrease in preload. The systolic time interval responses to the exercise-vectorcardiograph test postflight reflect possible decreases in stroke volume which may be due to decreased left ventricular function (28, 21, 29). Significant increases in total electromechanical systole (corrected for heart rate) and pre-ejection period with decreases in ejection time index are consistent with myocardial decrements in the Skylab 4 crewmen in response to a 150 watt exercise challenge on day 1 postflight. Also, the systolic time intervals and first heart sound amplitude data obtained during post flight lower body negative pressure tests are suggestive of myocardial dysfunction, *e.g.*, the recovery day test on the Pilot. This data is also suggestive of a bedrest response, where significant losses of blood volume exist and a myocardial factor could not be ruled out as a cause for cardiovascular decrements (30). We are confronted with the fact of a true decrement in performance without a clear indication that the decrement is due to a decrease in preload or to a mixture of decreased preload and decreased heart muscle function. Neurohumoral factors are also possible.

Note

Studies on the amplitude of the first heart sound during lower body negative pressure and exercise stresses provide analysis of ventricular function from a slightly differenct view. It had been shown as with systolic time intervals that during stress testing patients or animals with cardiac dysfuction show a lower increment in first heart sound amplitude than do normal organisms (31, 27, 29, 23, 33). First heart sound amplitude can be used as an index of cardiac performance, expecially during stress testing.

In reviewing the data from Skylab 4 astronauts certain correlations are apparent between the systolic time interval and first heart sound amplitude data. For example, the first heart sound amplitude responses of the Pilot to lower body negative pressure and to exercise are quite similar. Of the Skylab 4 crewmen the Pilot exhibited the lowest increment in first heart sound amplitude per increment in heart rate during the exercise tests on days 1 and 11 postflight. His first heart sound amplitude responses to lower body negative pressure was lowest and its return to preflight took longer than did the other two crewmen's responses. Resting value of ejection time index, an index of stroke volume, took longest to return of the Skylab 4 crewmen (day 11 postflight). Lower body negative pressure stressed pre-ejection

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period/ejection time was above preflight limits until day 18 postflight (the same, however, as the Commander). During postflight exercise on day one postflight, pre-ejection period was 17 percent and 6 percent higher than the Commander and Scientist Pilot, respectively. Lengthening of total electromechanical systole (corrected for heart rate) and pre-ejection period/ejection time during this exercise stress was equal to that of the Scientist Pilot, but greater than these values in the Commander (4 percent and 12 percent). Also, on recovery day, when he exhibited a presyncopal episode during lower body negative pressure, the Pilot's first heart sound amplitude fell to 30 percent (25). His percent change in ejection time index was lowest and pre-ejection period highest of the crewmen during this test.

These close correlations of systolic time interval and first heart sound amplitude responses to postflight stress testing add assurance that these techniques, each proven by direct methods to reflect ventricular function, point to a decrease in ventricular function as being a definite cause for the observed decrements in post flight orthostatic and exercise tolerance, whether or not peripheral mechanisms are responsible for the decreased ventricular performance. It is unfortunate that noninvasive methods are not available which can allow one to give an exact accounting of the specific roles played by the heart, the peripheral circulatory system, and neurohumoral systems in causing these decrements. Such techniques would certainly allow us to develop *definite* dose-response curves for cardiovascular countermeasures during longer duration space flight.

The postflight noninvasive measurements including echocardiography (4), which were accomplished at rest and during stress testing on Skylab 4, present as near complete a picture of cardiovascular status as was possible to obtain. Furthermore, the additional accuracy which might have been provided by invasive methods may well have lead to less conclusive results on several experiments if complications of these invasive procedures had occurred. To our knowledge, no measurements made on any of the Skylab crewmen including stress testing had any affect on the natural course of readaptation to one-g.

CONCLUSIONS

Although much of the decrement in cardiovascular functioning seen postflight is due to decreased blood volume, there is evidence in the systolic time interval, first heart sound amplitude, and clinical data to suggest that there was at least a functional impediment to venous return and possibly a myocardial factor as well. Whatever the causes, the impairments were not of gross pathologic porportions. If ability to take care of oneself is considered, the astronauts appeared to be quite capable of this task postflight.

Systolic time intervals and phonocardiographic data, at rest and during stress, indicate that decrements in cardiovascular function are not related necessarily to mission duration. However, this statement must be interpreted with the knowledge that each crew was handled slightly different. For example, on the longest mission much more time was alloted to various exercises than on the 28 or 59 day missions.

Functional impairment of the cardiovascular system as a result of space flight appears to be self limited. Readaptation to one-g is complete and probably requires one to two months. Many readaptations including systolic time interval and first heart sound amplitude responses to lower body negative pressure and submaximal exercise require less time.

The use of noninvasive techniques to study the cardiovascular responses after space flight is useful in determining hemodynamic changes quantitatively over time. Such techniques would definitely be worthwhile during zero-g exposure of future missions in order to define cardiovascular status from first exposure to steady state adaptations. Sensitive noninvasive techniques coupled with ground based analogs of weightlessness would serve to establish dose-response curves for the cardiovascular system so that exact countermeasures could be used operationally during the Space Shuttle era and beyond.

Supplemental Comments Regarding Cardiovascular Adaptations

It is difficult to discuss the preflight and postflight finding of Skylab without speculating on what happens to the body upon exposure to zero gravity and upon the ensuing adaptations the body makes to this environment. It is equally difficult to discuss the postflight findings without speculating on the condition of the body during long duration space flight just prior to, during, and upon entry into the Earth's gravitational field. Comments in this section will be limited to cardiovascular responses.

Upon entry into the zero-gravity environment the right heart is provided with an increased venous return by virtue of the lack of a gravity field and the relatively abundant capacity of the upper body vasculature. The abundance of blood available to the heart under these circumstances must lead to an increase in cardiac output as the healthy heart ejects as much blood as it is presented. The increased right ventricular filling may be partially compensated for by an increase in pulmonary blood volume, but at some filling pressure is channeled directly to the left ventricle, creating an increase in Starling Effect (increased preload). If *no* exercise is performed, the oxygen needs of the body are easily satisfied by the increased cardiac output compared with one-g and heart rate decreases as the adrenergic stimuli subside in the wake of a daily routine, which is established after launch. It is of interest that a progressive decrease in heart rate was noted during Apollo missions.

During exercise as on the Skylab cycle ergometer the first few trials are likely to be awkward secondary to lack of zero-g experience. There is probably a decreased mechanical efficiency until the crewman learns how to master the zero-g induced difficulties of holding on and pedaling. Once these mechanical problems are mastered, however, the zero-g environment allows one to accomplish higher workloads than was possible during one-g cycle ergometry because the venous return is increased and the problems of supine exercise in one-g are absent. Oxygen consumption is increased also because the arms play a more active role during zero-g exercise on the ergometer as the crewman begins to work against his arms.

An increase in $\dot{V}_{O_2}$ Max is recognized generally as reflecting a training effect. However, in zero-g an increased $\dot{V}_{O_2}$ Max must be interpreted with caution. Use of the arms contributes to $\dot{V}_{O_2}$. Also, the increase in cardiac output caused by the increased availability of blood in zero-g will cause the appearance of a training effect by causing an increased $\dot{V}_{O_2}$ and allowing greater work capacity.

Fixed submaximal work loads (from one-g testing) present less of a challenge in zero-g (once learning has occurred) by the above mechanisms, which mimic a training effect, so that such parameters as heart rate and blood pressure are decreased compared with one-g testing. The recovery heart rate is also decreased since blood from the working muscles is returned more quickly in zero-g and does not stagnate as happens in one-g in the upright position. The rapid return of heart rate after exercise is a common finding after a training effect, and one could reach this latter conclusion if not aware of the possible behavior of body fluids, and especially blood, in zero-g.

Exercise induced increases in blood pressure apparently do not significantly effect any symptoms of increases in intercranial pressure. Crewmen failed to recognize any differences in head fullness during isometric as opposed to dynamic exercise although both were used frequently during each in-flight day. It is known, however, that by comparison with dynamic exercise, isometric exercise causes a much greater increase in both systolic and diastolic pressure with only small increments in heart rate. The dynamic exercise, rather than causing an increase in the symptom of head fullness, actually caused relief of this symptom. Additionally, the secondary effects of the cephalad fluid shifts, *i.e.,* nasal and sinus congestion were also abated by strenous dynamic exercise. The mechanisms for relief of these symptoms are probably related to redistribution of the cardiac output to the exercising muscles (arms and legs) and to an outpouring of vasoactive catecholamines which constrict mucosal blood vessels and reduce mucosal tissue swelling.

In contrast to exercise responses, the lower body negative pressure test is more stressful in zero-g than in one-g (1). Blood volume may be decreased, plus the crewman is forced deeper into the Lower Body Negative Pressure Device by lack of gravity. Crewmen quickly discover this discrepancy and learn how to make the stress more comparable to the one-g tests (1). Although of no clinical importance several crewmen noticed the recoil from the heart's contractions. This sensation is more apparent in the head and neck during complete relaxation. Ballistocardiography could be more useful in zero-g.

Postflight, there are definite decrements in the ability of the cardiovascular system to withstand orthostatic and metabolic stresses. These decrements can be measured (24, 34, 19). There is an immediate decrement in exercise performance to a given workload (35, 36, 2). Maximal aerobic capacity was not evaluated postflight although the M171 experiment utilizes moderate to heavy workloads. Decreases in ability to perform heavy exercise such as jogging may be depressed for several weeks postflight. At least part of this lag time is due to postflight schedules and to weakened musculoskeletal structures. Orthostatic intolerance has already been discussed (1). The crewmen are usually surprised by the decreased stress of this test postflight compared to in-flight sensations.

In the postflight period readjustment to one-g probably begins with the opening of the parachutes. The cardiovascular decrements noted shortly after this time probably are related to a decrease in absolute blood volume, a functional impairment to venous return (which lasts beyond the volume deficit) and possibly to a transient primary myocardial dysfunction. Fortunately, the decrements appear to be transient and self-limited.

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