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CHAPTER 1
ENDOCRINE, ELECTROLYTE, AND FLUID VOLUME CHANGES ASSOCIATED WITH APOLLO MISSIONS

by

Carolyn S. Leach, Ph.D.
W. Carter Alexander, Ph.D.
Lyndon B. Johnson Space Center
P.C. Johnson, M.D.
Baylor College of Medicine

Introduction

As a result of medical observations during the American and Soviet manned space flight programs, it is now known that complex physiological changes occurred in crewmen returning from space missions (Berry & Catterson, 1967; Kakurin, 1971). These changes have been associated with severe operational demands coupled with exacting mechanical tasks, acceleration, weightlessness, sleep loss, changing circadian rhythms, confinement, periods of relative inactivity alternating with strenuous physical activity, and a cabin atmosphere which is both hyperoxic and hypobaric. The urgent need to study the physiological changes in exact mechanistic terms led to the development of the endocrine/metabolic program in support of manned space flight.

Before the Apollo 7 mission, considerable knowledge had been accumulated concerning the fluid and endocrine changes associated with Mercury and Gemini Earth-orbital missions (Leach, 1971; Dietlein & Harris, 1966). It was known that astronauts always weighed less after a mission than they did before the mission. This decrease in weight was associated with modest decreases in plasma volume. These results showed that, although cardiovascular deconditioning resulting from space flight was similar in extent to that found after bed rest, the weight changes after space flight were greater but the plasma volume changes were smaller. There is evidence from Gemini

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studies that the reentry sequence is associated with a sudden increase in epinephrine release as shown by a short-lived granulocytosis. This finding indicated that reentry for Gemini crewmen was a stressful experience. Before Project Mercury, certain segments of the scientific community were apprehensive that certain aspects of weightlessness might produce life-threatening conditions including hypercalcemia and hypercalciuria. This apprehension subsided when no evidence of a calcium abnormality was found. Even after the 14-day Gemini 7 mission, X-ray bone densitometry showed absent to slight loss of bone mineral (Mack et al., 1967).

Using this background, more extensive endocrine and metabolic studies were planned for the Apollo Program. As with other portions of the medical program, these studies were designed to provide data relative to the maintenance of flight crew health and well-being during a mission. The purpose of this chapter is to summarize and discuss the endocrine and metabolic results obtained before and after the Apollo missions and the results of the limited inflight sampling. From these studies, it is possible to obtain an idea of the nature and the extent of endocrine responses by the crewmen who flew the Apollo missions.

As part of the overall operational medical program, the endocrinological and metabolic studies were designed to evaluate the biochemical changes in the returning Apollo crewmembers. The areas studied were balance of fluids and electrolytes, regulation of calcium metabolism, adaptation to the environment, and regulation of metabolic processes.

Methods

The same general protocol was followed for most of the Apollo missions. Deviations from the procedures occurred when the quarantine program was imposed upon the Apollo 11,12, and 14 missions.

With the crewmembers reclining for 30 minutes, approximately 45 ml of peripheral venous blood were drawn three times (thirty, fifteen, and five days) before space flight. Blood was drawn approximately two hours after recovery (as soon as possible) and one, seven, and fourteen days later. All blood samples were drawn with the subject fasting from midnight until 7:00 a.m. except for the postrecovery sample, which was drawn regardless of the time of day or prior food intake by the crewmen. Generally, the crewmen had not eaten for six hours before recovery and had been awake for at least eight hours. For the preflight control samples, the crewmen had been awake less than one hour.

The 24-hour urine samples were collected preflight and postflight from each crewman on the same days as were the blood samples. The pooled urine was collected without additive, aliquoted, stablized with acid, and frozen for analysis. Urine samples were collected inflight by means of a biomedical urine sampling system (BUSS). Each BUSS consisted of a large (four liters) pooling bag in which urine was collected. Each contained 10 gm of boric acid for stabilization of certain organic constituents. One entire 24-hour urine sample from each Apollo 16 crewman was returned. For Apollo 17 collections, a sampling bag was used. In this bag a sample of urine (as much as 120 cm^3) was stored for later analysis. The collection bags contained 30 mg of lithium chloride. The final lithium concentration was used to estimate total urine volume.

Ground control subjects were used during each mission to determine the effects of collection and transportation of blood and urine samples. The control results showed that transportation of the endocrine samples to the NASA laboratories produced no change in values. Analyses of the blood samples (plasma or serum) included osmolality, sodium, potassium, chloride, adrenocorticotrophic hormone (ACTH), angiotensin I, cortisol, human growth hormone (HGH), insulin, parathormone thyroxine, and triiodothyronine. The 24-hour urine samples were analyzed for electrolytes, osmolality, volume, aldosterone, cortisol, antidiuretic hormone (ADH), total and fractionated ketosteroids, and amino acids. Procedures for these analyses have been previously reported (Leach et al., 1973; Alexander et al., 1973). Radionuclide studies were performed according to the schedule shown in table 1. The methods used for the radionuclide studies were described by Johnson and co-workers (1973). Table 2 contains the calculated radiation exposures from these radionuclide studies. The data in table 2 indicate that these exposures added only modestly to total radiation exposure of the astronauts and that the exposure levels are well within occupationally prescribed limits. All preflight data were averaged, and the standard error (SE) of the mean was calculated. The data taken immediately postflight were also averaged, and the percent deviation from the preflight level given. Inflight data are presented in figures 1 to 16. Prolonged exposure to increased temperature and to the boric acid preservative made the urine voided inflight unsuitable for catecholamine or ADH analyses.

Table 1

Schedule of Apollo Radionuclide Studies

Test Schedule	Total Body Potassium	Plasma Volume	Extracellular Fluid	Total Body Water
30 days preflight	X			
15 days preflight	X	X	X	X
5 days preflight	X			
As soon as possible after recovery	X	X	X	X
1 day after recovery	X	X	X	X
7 days after recovery	X	X	X	X

Table 2

Calculated Radiation Exposure of Apollo Crewmen

Nuclide and Physical Form		Critical Organ (rem/μCi)	Total Body (rem/μCi)	Total μCi	Total Body (rem)
Iodine-125	Albumin	Thyroid – 0.0625–0.1875	0.00050	8	0.0040
Sulfur-35	Sulfate	Total body – 0.00009	0.00009	100	0.0090
Hydrogen-3	Water	Total body – 0.00017	0.00017	200	0.0340
Potassium-42	Chloride	Muscle – 0.00134	0.00086	300	0.2580
					0.3050

Results

Postmission body fluid losses have been found in both American and Russian space flight crewmen (Webb, 1967). Apollo crewmen showed an average of five percent decrease in body weight after flight when the mean of the preflight results (thirty, fifteen, and five days) was compared to the individual postflight values. The average loss was 3.51 kg, approximately one-third of which was regained within the first 24 hours after recovery. These data are given in table 3.

Table 3

Summary of Apollo Crewmen Body Weight Data

Preflight Mean, kg (lb)	N*	Immediate Postflight Mean kg (lb)	One Day Postflight Mean kg (lb)	Percent Change
75.96 (167.50)	33	72.45 (159.75)	–	–4.6
–		72.45 (159.75)	73.05 (161.08)	+0.8

*Number of crewmen tested.

Body weight changes indicate significant fluid changes among all crewmembers exposed to weightlessness. Loss of fluid does not seem to be related to the duration of the mission. Because of this fact, studies were undertaken to investigate cations and anions, both of which have critical roles in the regulation of fluid volume. Serum electrolyte data from the Apollo crewmen are summarized in table 4. Significant differences were observed in a 7.3 percent decrease in potassium and a 4.5 percent decrease in magnesium immediately after flight. These changes were accompanied by no significant change in serum sodium or chloride.

Table 4

Summary of Apollo Serum Electrolyte Results

Electrolyte	N*	Preflight Mean ± SE	Immediate Postflight Mean ± SE	Percent Change
Sodium (mEq/l)	33	141 ± 0.1	141 ± 0.3	0
Potassium (mEq/l)	33	4.1 ± 0.03	3.8 ± 0.05	–7.3
Chloride (mEq/l)	32	104 ± 0.3	104 ± 0.5	0
Magnesium (mg/100 ml)	32	2.2 ± 0.04	2.1 ± 0.05	–4.5

*Number of crewmen tested.

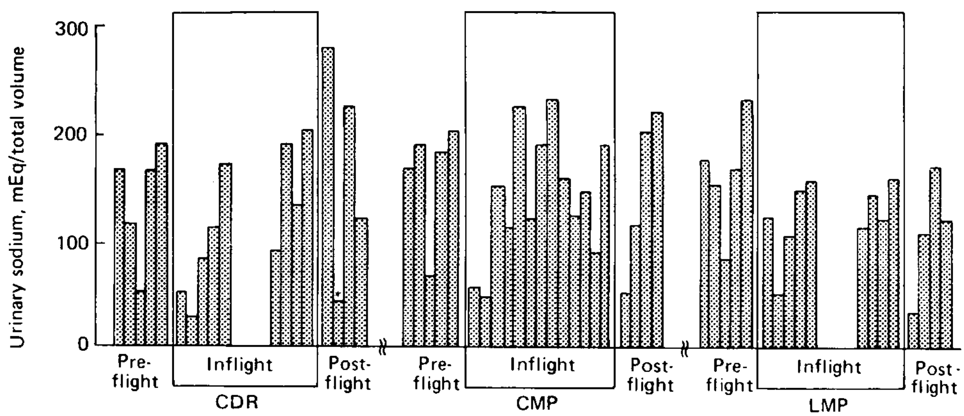
The 24-hour urine electrolyte results are given in table 5. These samples exhibited significant decreases in sodium, potassium, chloride, and magnesium values. The results from Apollo 17 inflight collections are shown in figures 1 to 4.

Table 5

Apollo Twenty-Four Hour Urine Electrolyte Results

Electrolyte	N*	Preflight Mean ± SE	First 24 Hours Postflight Mean ± SE	Percent Change
Sodium (mEq/vol)	30	169 ± 15	87 ± 12	−49
Potassium (mEq/vol)	30	79 ± 4	42 ± 3	−47
Chloride (mEq/vol)	30	155 ± 7	60 ± 7	−61
Magnesium (mg/vol)	23	9 ± 0.5	6 ± 0.5	−36

*Number of crewmen tested.



Note: CDR = Commander
CMP = Command Module Pilot
LMP = Lunar Module Pilot

* Indicates one 12-hour sample

Figure 1. Apollo 17 urinary sodium results.

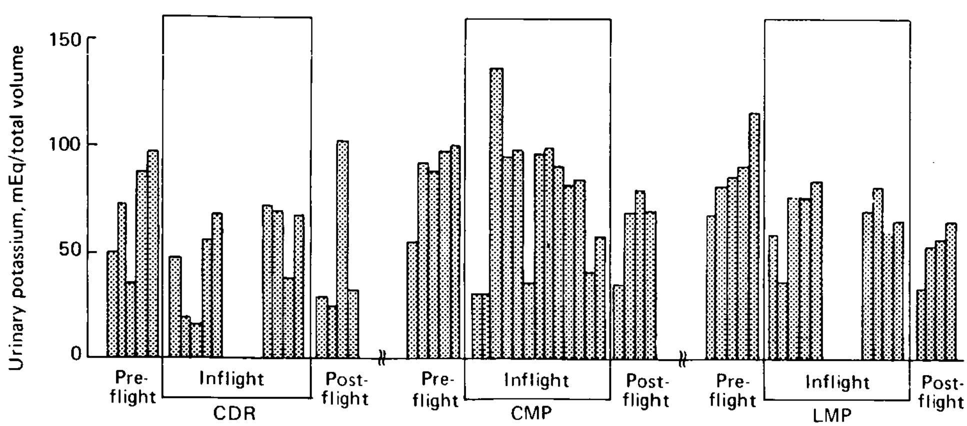


Figure 2. Apollo 17 urinary potassium results.

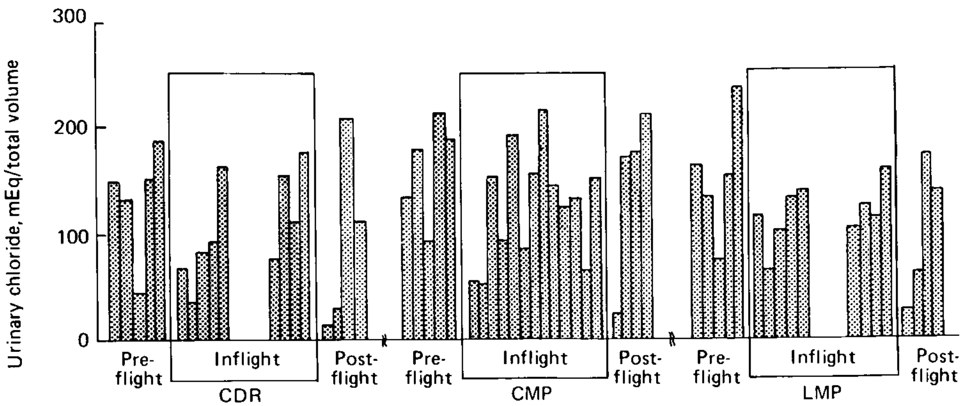


Figure 3. Apollo 17 urinary chloride results.

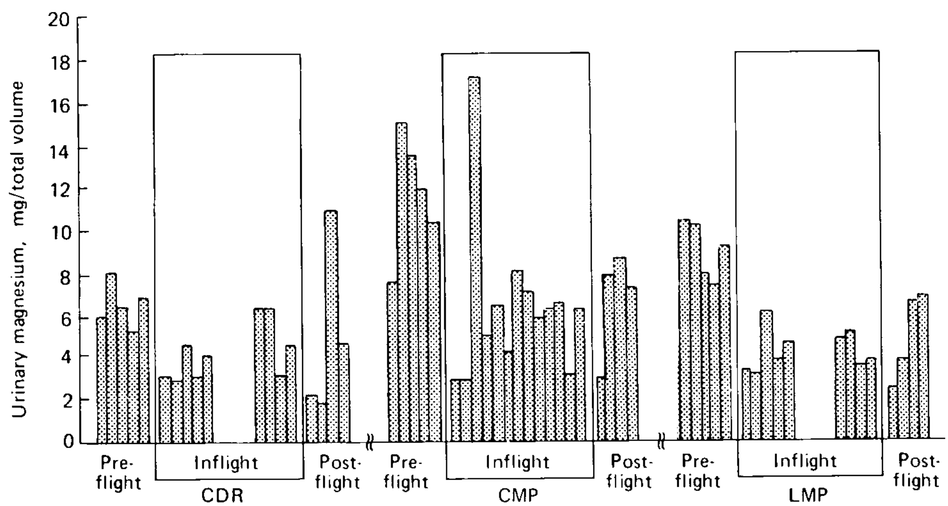


Figure 4. Apollo 17 urinary magnesium results.

To aid in the understanding of water and electrolyte balance and of renal function, renin activity was measured as angiotensin I in blood samples, and aldosterone was measured in urine. Table 6 contains these results. The plasma angiotensin I values show a 488 percent increase in the crewmen tested on the day of recovery. This elevation was followed by a significant increase (57 percent) in urinary aldosterone during the first day following recovery. In figures 5 and 6, the inflight aldosterone results for the Apollo 16 and 17 missions, respectively, are shown.

Table 7 contains summary data on urinary volume, ADH, and osmolality. These results indicate a 32 percent decrease in urine volume after flight with significant increases in osmolality (20 percent) and ADH (152 percent). The inflight volume and

Table 6

Apollo Sodium Retaining Hormone Results

Hormone	N*	Preflight Mean ± SE	First Postflight Examination ± SE	Percent Change
Plasma Angiotensin I (mμg/ml/hr)	21	1.7 ± 0.2	9.9 ± 2.0	+488
Urinary Aldosterone (μg/volume)	28	12.2 ± 0.8	19.9 ± 2.0	+ 57

* Number of crewmen tested.

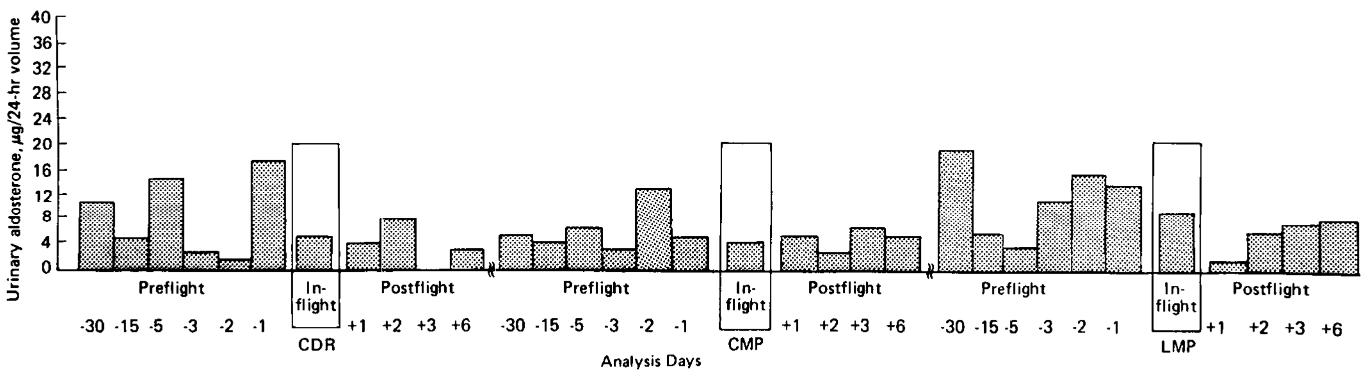
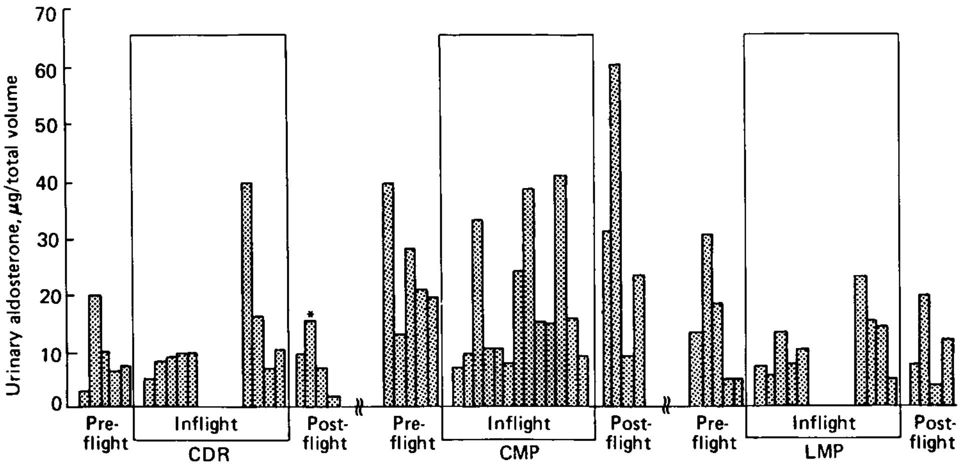


Figure 5. Apollo 16 urinary aldosterone results.



*Indicates one 12-hour sample

Figure 6. Apollo 17 urinary aldosterone results.

Table 7

Apollo Urine Volume Data

Test	N*	Preflight Mean ± SE	First 24 hours Postflight Mean ± SE	Percent Change
Urine Volume (ml)	30	1602 ± 77	1089 ± 109	− 32
Osmolality (milliosmols)	30	696 ± 24	833 ± 45	+ 20
ADH (milliunits/vol)	26	28 ± 3	72 ± 17	+152

*Number of crewmen tested.

osmolality values for the Apollo 17 mission are shown in figures 7 and 8, respectively. A summary of the measured body fluid volumes is given in table 8. These same data are also expressed as milliliters per kilogram of body weight. Table 9 contains the total body exchangeable potassium data as measured by potassium-42. Table 10 contains blood urea nitrogen (BUN) and creatinine clearance data. The creatinine clearance results show no significant change in renal function after flight as indicated by this test. A slight but significant increase in BUN was found. Apollo 17 inflight creatinine values are shown in figure 9.

The calcium, phosphorus, and parathormone (PTH) changes are summarized in table 11. It is believed that the calcium, phosphorus, and PTH results not only reflect normal bone metabolism but would seem to reflect normal renal function. These results are in agreement with the results of photon absorptiometry studies performed on several Apollo flights which s showed small to insignificant losses of bone calcium after flight (Vogel, 1971).

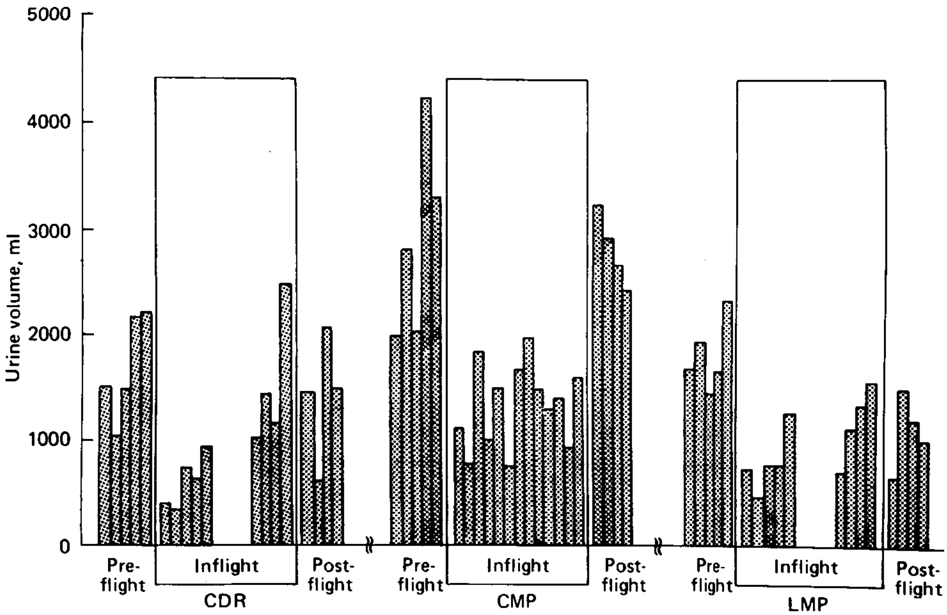


Figure 7. Apollo 17 urine volume data.

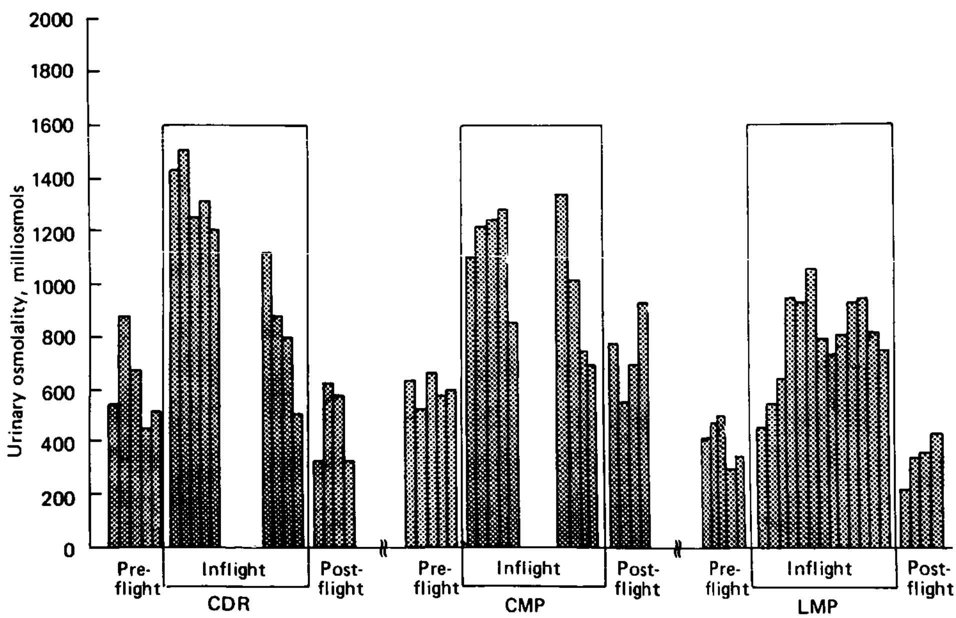


Figure 8. Apollo 17 urinary osmolality.

Table 8

Apollo Body Fluid Compartment Data
Mean Percent Change ± SE

	Volume			ml/kg		
	Immediately Postflight	One Day After Recovery	>7 Days After Recovery	Immediately Postflight	One Day After Recovery*	>7 Days After Recovery
Plasma volume	−4.4 ± 1.7	+4.8 ± 2.2	+3.4 ± 1.4	−0.1 ± 1.4	+8.2 ± 1.9	+5.3 ± 1.6
Total body water	−2.4 ± 0.4	−0.1 ± 0.6	−0.5 ± 0.3	+1.6 ± 0.4	+2.9 ± 0.8	+1.2 ± 0.6
Extracellular fluid	−2.7 ± 1.0	+0.2 ± 1.3	−0.5 ± 0.8	+1.1 ± 0.9	+2.8 ± 1.5	+1.5 ± 1.4
Intracellular fluid	−2.1 ± 0.8	+0.2 ± 1.1	−0.6 ± 0.9	+1.9 ± 0.9	+3.2 ± 1.2	+0.8 ± 0.7
Interstitial fluid	−2.2 ± 1.0	−1.3 ± 1.6	−1.5 ± 1.1	+1.7 ± 1.0	+1.6 ± 1.8	+0.3 ± 1.6

* Used R +2 values for Apollo 15.

Table 9

Apollo Total Body Exchangeable Potassium

Mean Percent Change in Total mEq Potassium		
Dilution Time in Hours	24	48
Apollo 15	−15.3	−13.8
Apollo 16	+ 3.8	+ 2.3
Apollo 17	−16.3	− 5.2
Mean Percent Change in mEq Potassium/kg Body Weight		
Dilution Time in Hours	24	48
Apollo 15	−12.7	−12.6
Apollo 16	+ 7.7	+ 7.0
Apollo 17	−13.5	− 0.3

Table 10

Index of Apollo Renal Function

Test	N*	Preflight Mean ± SE	Immediate Postflight Mean	Percent Change
BUN (mg/100 ml)	33	18.5 ± 0.6	20.7 ± 0.7	+ 12
Creatinine clearance (liters/24 hr)	29	151 ± 8	133 ± 8	−12

*Number of crewmen tested.

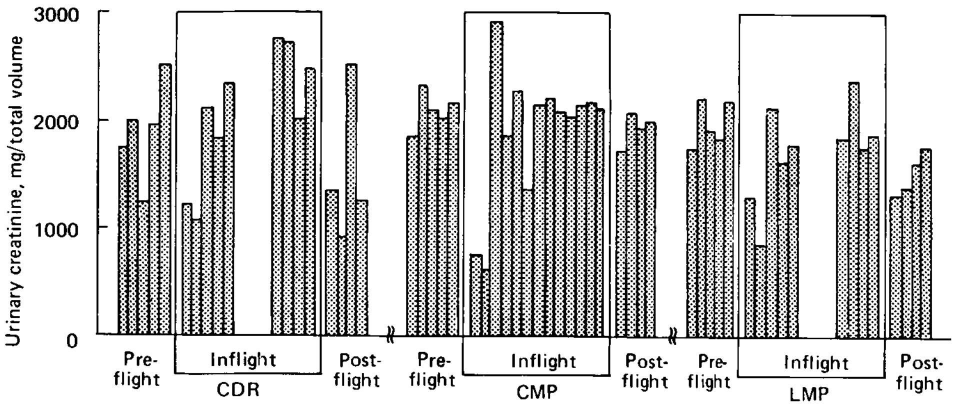


Figure 9. Apollo 17 urinary creatinine results.

Table 11

Apollo Calcium Metabolism Results

Test	N*	Preflight Mean ± SE	First Postflight Examination ± SE	Percent Change
Calcium serum (mg/100 ml)	33	9.6 ± 0.05	9.7 ± 0.05	+ 1.0
Urine (mEq/vol)	30	9.3 ± 0.8	7.8 ± 0.8	−15
Phosphorus serum (mg/100 ml)	33	3.5 ± 0.07	3.6 ± 0.1	+ 3
Urine (mg/vol)	30	966 ± 64	956 ± 67	− 4
Parathormone serum (pg/ml)	12	0.44 ± 0.03	0.42 ± 0.05	− 5

*Number of crewmen tested.

Plasma cortisol and ACTH results are given in table 12. Although no significant change was found, a mean decrease was demonstrated in both hormones. The urinary hormonal data indicating adrenal activity are also given in table 12. Cortisol demonstrated a 24 percent increase, whereas the total 17-hydroxycorticosteroid excretion was decreased 30 percent. The inflight values for these measurements for Apollo 17 crewmen are shown in figures 10 and 11. Both catecholamine compounds show decreases after flight when the data from all crewmen are grouped for analysis. Some individual preflight values are often elevated. This is believed to be due to premission stress. The total and fractionated ketosteroid data are given in table 13. These results demonstrate a 30 percent decrease in the total component, which is spread over four fractions: androsterone, etiocholanolone, dehydroepiandrosterone (DHEA), and 11 = OH etiocholanolone. A slight increase was observed in pregnanediol and 11 = O etiocholanolone. Figures 12 and 13 demonstrate the typical inflight component of these results for Apollo 17 crewmen.

Table 12

Apollo Adrenal-Pituitary Hormone Concentration

Test	Sample	N*	Preflight Mean ± SE	First Postflight Examination ± SE	Percent Change
Cortisol (µg/100 ml)	Plasma	30	16.7 ± 0.5	12.2 ± 2.0	−27
ACTH (pg/ml)	Plasma	12	37 ± 5	28 ± 5	−24
Cortisol (µg/vol)	Urine	27	60.3 ± 3.0	74.7 ± 7.0	+24
Epinephrine (µg/vol)	Urine	24	26.3 ± 2.0	24.1 ± 4.0	− 8
Norepinephrine (µg/vol)	Urine	24	55.5 ± 3.0	55.8 ± 8.4	+ 0.5
Total 17-Hydroxycorticosteroids (mg/vol)	Urine	6	6.1 ± 0.5	4.3 ± 1.2	−30

*Number of crewmen tested.

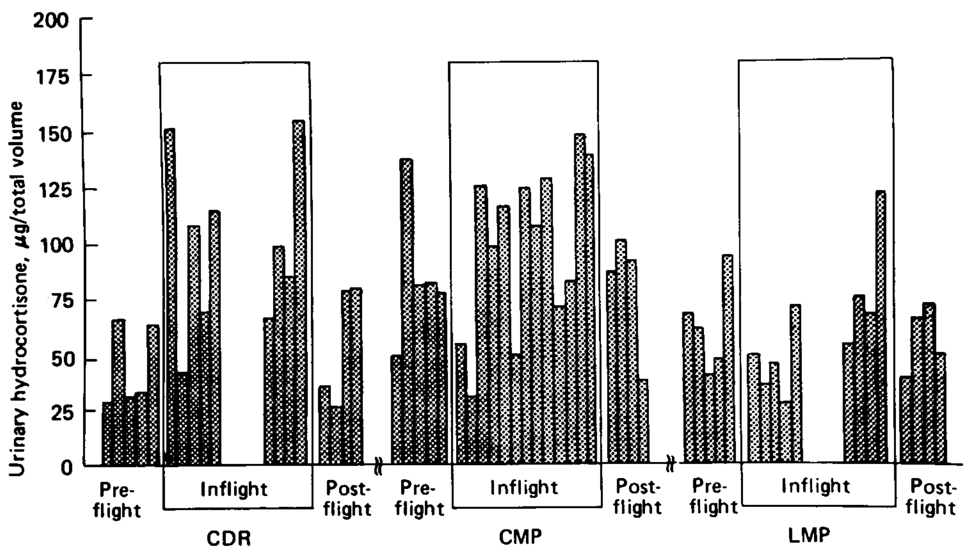


Figure 10. Apollo 17 urinary hydrocortisone results.

The serum and plasma values for various hormones and related parameters are summarized in table 14. Glucose showed a 10 percent increase after flight, and insulin increased 32 percent after flight. Human growth hormone demonstrated a 304 percent increase after flight. The postflight increase in thyroxine was statistically significant, whereas slight change was noted in percentage of triiodothyronine binding.

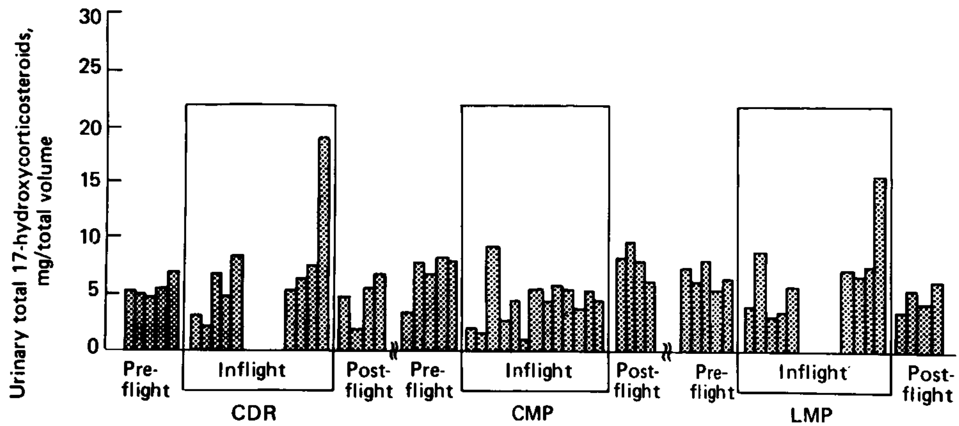


Figure 11. Apollo 17 urinary total 17-hydroxycorticosteroids.

Table 13
Apollo Total and Fractionated
17-Ketosteroid Excretion Results

	mg/Total Volume			
Compound	N*	Preflight Mean ± SE	First Day Postflight Mean ± SE	Percent Change
Pregnanodiol	9	0.33 ± 0.05	0.38 ± 0.08	+ 14
Androsterone	9	2.28 ± 0.53	1.57 ± 0.13	−49
Etiocholanolone	9	3.47 ± 0.51	2.25 ± 0.27	−35
Dehydroepiandrosterone	9	1.15 ± 0.46	1.10 ± 0.29	− 5
11-Ketoetiocholanolone	9	0.34 ± 0.13	0.38 ± 0.09	+ 10
11-Hydroxy Androsterone	9	0.15 ± 0.05	0.15 ± 0.06	0
11-Hydroxyetiocholanolone	9	0.33 ± 0.19	0.18 ± 0.06	−44
TOTAL mg/TV	9	8.66 ± 1.54	6.05 ± 0.72	−30

* Number of crewmen tested.

Table 15 is a summary of the urinary amino acid results for six representative amino acids from a total of 39 analyzed. The comparison of postflight to preflight control levels has been variable. However, taurine has been consistently elevated after flight (140 percent). The inflight data for Apollo 17 crewmen are presented in figures 14 to 16.

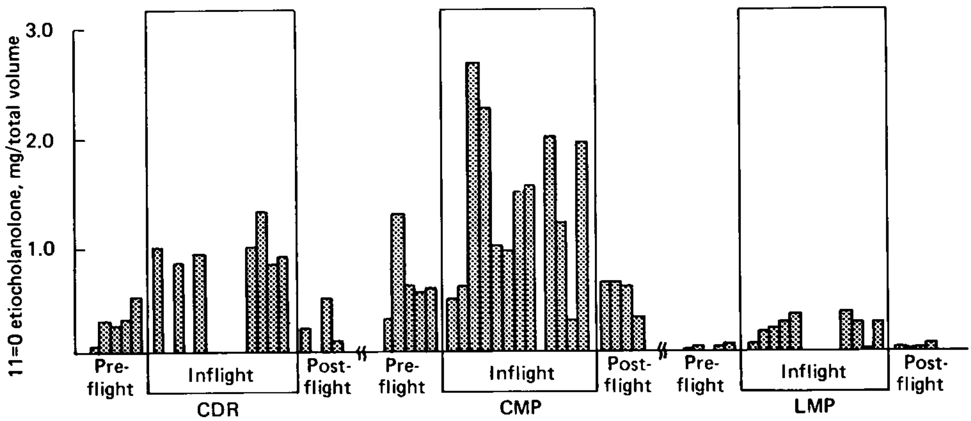


Figure 12. Apollo 17 urinalysis of 11 = 0 etiocholanolone.

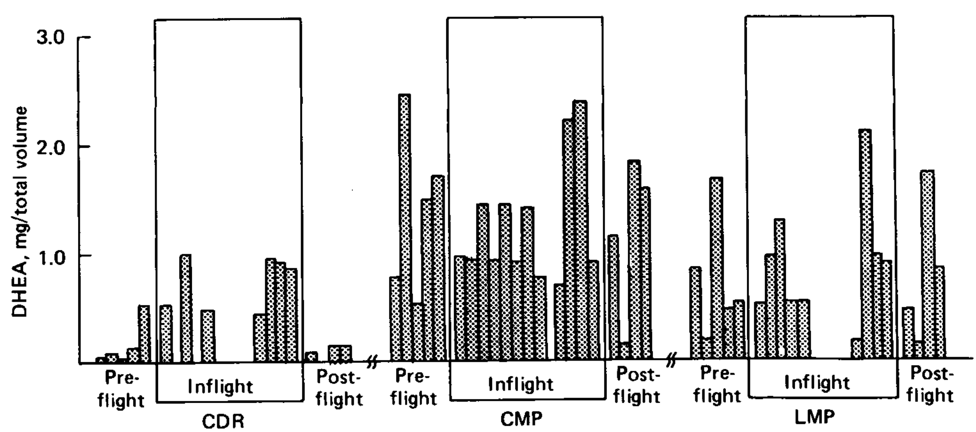


Figure 13. Apollo 17 urinalysis of dehydroepiandrosterone (DHEA).

Table 14

Summary of Plasma Hormones and Related Parameters for Apollo Crewmen

Hormone	N*	Preflight ± SE	Postflight ± SE	Percent Change
Thyroxine (T_4) (μg/100 ml)	30	6.8 ± 0.1	7.6 ± 0.5	+ 12
Tri-iodothyronine (T_3) (% uptake)	30	32.4 ± 0.1	32.1 ± 0.1	− 1
Insulin (μU/ml)	22	6.8 ± 1.2	9. 0 ± 1.4	+ 32
Glucose (mg/100 ml)	33	95.7 ± 1.3	105.1 ± 2.2	+ 10
Human Growth Hormone (ng/ml)	10	2.6 ± 0.2	10.5 ± 3.1	+304

*Number of crewmen tested.

Table 15

Summary of Apollo Amino Acid Excretion Results

		mg/Volume		
Amino Acid	N*	Preflight Mean ± SE	First Day Postflight Mean	Percent Change
Phosphoethanolamine	12	6.1 ± 0.4	7.2 ± 2.6	+ 18
Taurine	12	126.2 ± 18.5	304.0 ± 89.5	+140
Glycine	12	53.7 ± 6.8	45.7 ± 11.2	− 15
Alanine	12	30.2 ± 6.8	25.3 ± 3.2	− 15
Tyrosine	12	18.4 ± 1.8	16.8 ± 2.1	− 9
β-Alanine	12	5.25 ± 2.0	5.8 ± 1.8	+ 13

*Number of crewmen tested.

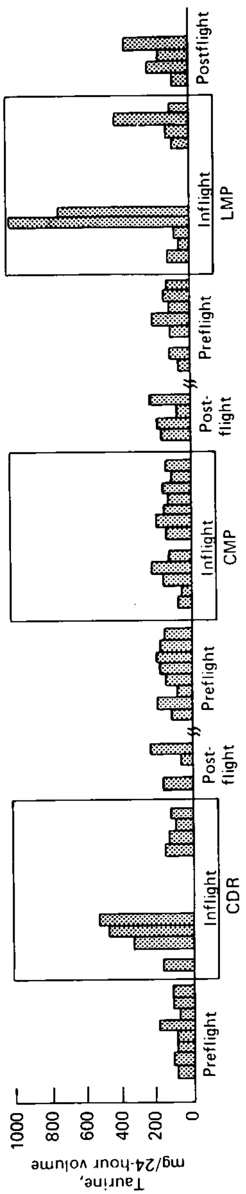


Figure 14. Apollo 17 urinalysis of taurine.

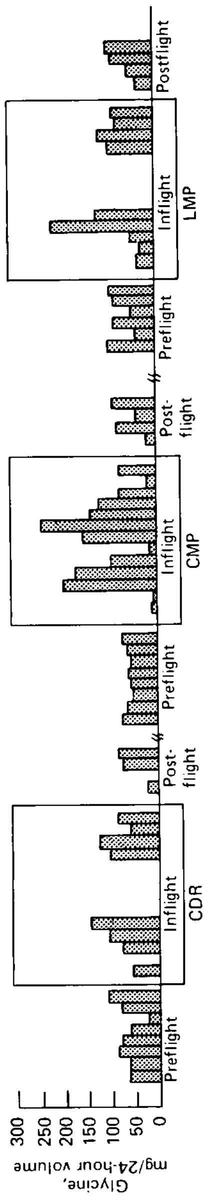


Figure 15. Apollo 17 urinalysis of glycine.

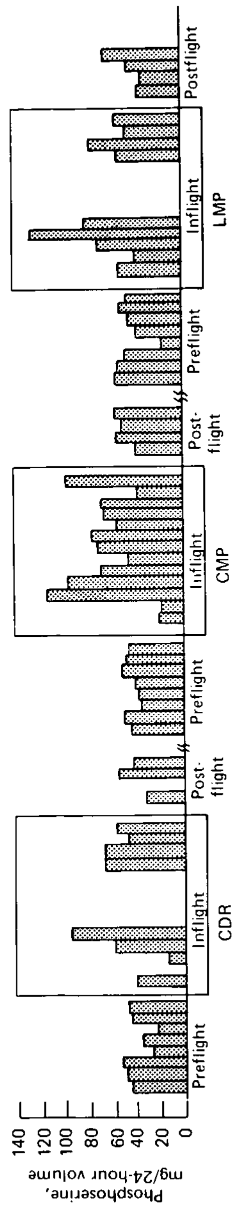


Figure 16. Apollo 17 urinalysis of phosphoserine.

Discussion

After considering all previously mentioned data together with the clinical condition of the returning Apollo crewmen, the following hypothesis was proposed to explain the changes. As a crewman enters the weightless environment, his circulating blood volume and extracellular fluid shift from the extremities and the lower abdomen and are redistributed equally throughout the vascular space. This alteration of the blood volume is interpreted as a relative volume expansion. The fluid redistribution necessitates a compensatory change in water balance with a net loss of fluid and electrolytes. The extent of the fluid and electrolyte loss is related also to food consumption, which has been variable and generally below basal requirements during the first 24 hours of a mission. The changes in water balance are believed to occur principally in the first or second day of flight just as they do in bed rest (Hyatt et al., 1970). This theory explains why crewmembers showed weight decreases even after short duration Mercury and Gemini missions (Webb, 1967). On return to Earth and the one-g environment, a portion of the weight loss is regained within the first 24 hours. A rapid weight gain of this magnitude indicates a renal and endocrine response to the new environment. The remainder of the weight loss could be attributed to tissue loss. Consistently measured decreases in red cell mass and decreases in individual cell electrolyte content, determined by the electron microprobe, add support to this hypothesis. Furthermore, significant decreases in serum magnesium during the postflight period suggest previous losses of intracellular electrolyte, since magnesium is concentrated in the intracellular space along with potassium.

Postflight decreases in total body potassium of the Apollo 12 to 14 crewmen were determined by gamma spectrometric measurement of the total body potassium-40. Seven of the nine men showed a significant decrease (three to ten percent) for this measurement (Benson & Bailey, 1971). Beginning with the Apollo 15 mission, total body exchangeable potassium was measured (Leach et al., 1972). The results are expected to differ from total body potassium because slow-to-equilibrate pools may not be completely exchanged in the 24- and 48-hour periods analyzed. However, because comparisons of measurements before and after space flight of the same individuals are being made, the relative changes are meaningful. Crewmembers of the Gemini 7 mission demonstrated positive potassium balance before and after the flight and negative balance during the flight. Results from Gemini missions and data available from Apollo crewmen confirm that aldosterone is elevated during space flight. This elevation could have been produced by decreases in renal blood flow or in carotid artery or right-heart pressures: the specific etiology must await further experimentation.

All Apollo missions were followed by a change in the plasma volume of returning crewmen. The overall mean of the crewmen's plasma volume decrease for the Apollo missions was considerably less than the 10 percent mean decrease associated with an equivalent period of bed rest. Only three of the twenty-one crewmembers tested showed losses greater than the average bed rest results. A smaller decrease in plasma volume could be one manifestation of an inflight increase in adrenal activity, particularly aldosterone secretion. Because no plasma volume measurements for Apollo missions were taken during flight, it was not known whether plasma volume was actually lower during flight and increased slightly before being recorded immediately after flight or whether plasma volume remained essentially stable after the 4.4 percent decrease (table 8) had occurred.

Even with adequate calories available, most crewmen showed a weight loss after flight. Part of this weight loss was made up during the first 24 hours after recovery, but it took from several days to weeks for crewmen to return fully to their premission weight. This fact suggests that part of the weight loss during a mission is tissue and another part fluid. Only fluid loss could be made up in the first 24 hours; recovery of tissue losses takes considerably longer. Weight loss from short term dieting is generally followed by an increase in extracellular fluid, which compensates for the tissues lost. This extra fluid is ordinarily lost by diuresis at irregular intervals of several days to several weeks. The increased extracellular fluid volume seen after these missions could be explained as a compensation for tissue losses. The water retention associated with weight loss is probably accomplished by increased aldosterone secretion.

During recovery operations, crewmen were exposed to increased ambient temperatures in the spacecraft, in the helicopter, and on the carrier deck because of the tropical location of recovery operations. The crewmen did not eat or drink between the time they left the spacecraft and the time of blood sampling; thereafter, they could eat or drink anything they desired. The postrecovery diet was generally high in salt, protein, and calories. The postrecovery urine generally showed increased osmolality with a decrease in electrolyte content, a combination that indicated increased excretion of nonelectrolyte osmotic substances. Part of this increase in osmolality might have been a result of the increased blood urea nitrogen (BUN) found after recovery. The clinical laboratories found postflight elevations in uric acid. Because of the increased environmental temperatures during the first four hours after recovery, a slight increase in serum sodium was to be expected then, and in osmolality later. However, serum sodium was actually less after flight than before flight, and osmolality was unchanged; therefore, serum sodium may have been even lower before reentry. This discovery, coupled with the BUN change, suggests that renal blood flow is decreased during weightlessness, and this decrease could be partly responsible for the increased aldosterone excretion by way of the renin-angiotensin system.

Balakhovskiy and others (1971) have suggested that the postflight weight loss in American astronauts was due to dehydration caused not by space flight but by environmental temperatures in the tropical recovery zones. Apollo data do not substantiate dehydration as the causative factor for the fluid/electrolyte results because serum sodium and osmolality were not increased at recovery.

Prolonged bed rest is associated with a negative calcium balance beginning in the second week (Deitrick et al., 1948). It was postulated that exposure to weightlessness would produce similar losses of calcium from the skeleton. The results of the Apollo missions did not appear to indicate significant changes in calcium metabolism. First, no change in parathormone was found in recovery specimens; second, urine and serum calcium were elevated; and third, bone densitometry failed to show consistent decreases in bone mass. Therefore, for missions of 14 days or less, it was apparent that significant calcium losses did not occur. Hypercalcemia does not account for the loss of sodium, as has been suggested (Griffith, 1971). However, if changes in calcium dynamics had occurred, they would have probably just begun during the last few days of the missions.

Current data show no evidence of plasma cortisol and adrenocorticotrophic hormone (ACTH) increase after flight. The stress of reentry is assumed to be not great enough to produce a change in these hormones. The time of recovery, however, generally is at a different point in the diurnal cycle of the pituitary-adrenal axis than in the preflight control (Leach & Campbell, 1971). Without stress, higher values were to be expected at the time of the control specimens (8:00 a.m.) than at the time of recovery (between morning and early afternoon). Reentry stress may have elevated these hormones higher than they were 24 hours before recovery.

The Apollo 16 mission was the first after Gemini 7 in which inflight urine samples were returned for analysis. The 17-hydroxycorticosteroids were found to be significantly decreased during the 14-day Gemini 7 mission (Lutwak et al., 1969). Likewise, total 17-hydroxycorticosteroid values were decreased in second-day inflight specimens from Apollo 16 crewmen and were normal to decreased in the more comprehensive sample collection of the Apollo 17 mission. Ordinarily, if total 17-hydroxycorticosteroid excretion decreases, a decrease in cortisol is to be expected; however, cortisol excretion during the inflight phase of both missions was normal to elevated or, stated differently, no value was lower than preflight or postflight values. This divergence of results could be related either to a sample storage program that affected the 17-hydroxycorticosteroid analyses or, possibly, to changes in blood flow to the liver that altered the conjugation rate of the free hormone resulting in decreased excretion of 17-hydroxycorticosteroids.

In several endocrine-related diseases, the determination of urinary 17-ketosteroids, either fractions or total, has been helpful in both diagnosis and understanding the pathophysiology of these diseases. The decrease in the total 17-ketosteroid fraction agrees with the decrease in the total 17-hydroxycorticosteroid data. The mechanism is believed to be related to the liver conjugation of these steroids. The inflight increase in specific fractions reflects the heightened adrenal activity during the flight phase. The dehydroepiandrosterone (DHEA) increases shown on the Apollo 16 and 17 missions inflight are considered significant since they had been shown to occur in potassium-depleted subjects (Leach et al., 1973). The exact function of this steroid is not known, but it appears to be related to stress responses as well as to nitrogen and mineral metabolism.

Bed rest, the most frequently used analog of weightlessness, alters glucose metabolism (Lipman, 1970). Studies have shown that glucose and insulin are elevated after two weeks of absolute bed rest. Apollo results suggest that space flight may have a similar effect with an apparent decrease in the efficiency of insulin to lower plasma glucose concentrations. However, increased growth hormone may be a factor in these observed increases. A significant change in plasma thyroxine (T_4) may represent the thyroid gland's response to increases in plasma proteins.

To assess metabolic responses in the area of nutrient use as well as stress, human growth hormone (HGH) was measured. This hormone was significantly increased (table 14) postflight. Because HGH acts to increase blood sugar and plasma-free fatty acids, and to lower plasma amino acids by incorporating them into proteins, these results after space flight are compatible with the evidence of muscle breakdown discussed previously.

The changes in amino acid excretion patterns are thought to be related to diet as well as to muscle metabolism. However, as in every study of amino acid excretion, renal threshold, glomerular filtration rate, and cellular use enter into the full explanation. Furthermore, the relationship between adrenal steroid activity and amino acid excretion must be considered because adrenal steroids alter urinary excretion patterns of amino acids (Zinneman et al., 1963). Glycine, significantly elevated in the inflight samples, is required by the body for formation of nucleic acid, porphyrins, creatinine, hippuric acid, and bile acid conjugates (Searcy, 1969). Therefore, the increased excretion of this amino acid could be related to cellular mass loss or to the suspected decrease in liver blood flow. The significant increases in taurine after flight could be an indication of a decrease in bile acid formation and hence in liver function. Sarcosine, another amino acid that was increased during flight, is related to muscle protein and is believed to be a further indication of muscle breakdown during flight.

Summary

Biochemical analyses were performed on samples of blood and urine obtained from astronauts at various intervals before and after each Apollo space mission. During the Apollo 16 and 17 missions, urine samples from the inflight phase were also obtained, and a similar series of biochemical analyses was performed.

The observed universal loss in body weight was accompanied by decreases in intracellular water and by increases in extracellular water after flight with a resultant net loss in total body water. Water losses, however, appeared to account for only about one-third of the total mass loss. That losses in cellular mass also occurred was evident from decreases in the body's potassium-40 content and in its exchangeable potassium pool. The loss of tissue was further supported by increases in blood and urinary nitrogenous components after flight as well as in decreases in serum potassium and magnesium.

The observed losses in potassium and retention of fluid were generally reflected in appropriate postflight elevations in renin activity, aldosterone, and antidiuretic hormone (ADH). Changes in excretion patterns inflight were also observed. Elevation of aldosterone during flight supports the concept that the electrolyte changes were hormonally induced. Hydroxycortisone was normal to increased, whereas total 17-hydroxycorticosteroids and total 17-ketosteroids were low normal to decreased during flight. A change in the metabolism of these hormones is suggested by these results.

The following hypothesis is presented to explain the mechanisms underlying the observed electrolyte and fluid compartment changes. In a weightless environment, there is a tendency for plasma volume to be distributed more evenly within the vascular system and away from the gravity-dependent extremities. This shift is interpreted by receptors, probably in the right atrium, to be an increase in vascular volume. The increase in vascular volume is counteracted by an increased water loss, followed by a compensatory, adrenal-pituitary-mediated retention of water and sodium and by a continued loss of potassium. Other hormone changes observed are tentatively ascribed to the stresses associated with the condition of the Apollo space flights, to the well-known consequences of hypokinesis, and to the metabolic effects of hypocaloric nutritional intake.

References

Alexander, W.C.; Leach, C.S.; Fischer, C.L.; Lambertsen, C.J.; and Johnson, P.C.: Hematological, Biochemical, and Immunological Studies During a 14-Day Continuous Exposure to 5.2% O_2 in N_2 at Pressure Equivalent to 100 FSW (4 ata). Aerospace Med., vol. 44, no. 7, July 1973, pp. 850-854.

Balakhovskiy, I.S.; Natochin, U.V.; and Kozyrevskaya, G.I.: Status of Water-Salt Metabolism Under Space Flight Conditions. NASA TT F-14029, 1971.

Benson, R.E.; and Bailey, V.: Personal Communication. March 15, 1971.

Berry, C.A.; and Catterson, A.D.: Pre-Gemini Medical Predictions Versus Gemini Flight Results. Section 16 of Gemini Summary Conference, NASA SP-138, 1967, pp. 210-218.

Deitrick, J.E.; Whedon, G.D.; and Shorr, E.: Effects of Immobilization Upon Various Metabolic and Physiological Functions of Normal Men. Am. J. Med., vol. 41, no. 1, Jan. 1948, pp. 3-36.

Dietlein, L.F.; and Harris, E.: Experiment M-5, Bioassays of the Body Fluids. Section 42 of Gemini Midprogram Conference, NASA SP-121, 1966, pp. 403-406.

Griffith, D.P.: Immobilization Hypercalciuria: Treatment and a Possible Pathophysiologic Mechanism. Aerospace Med., vol. 42, no 12, Dec. 1971, pp. 1322-1324.

Hyatt, K.H.; Smith, W.M.; Vogel, J.M.; Sullivan, R.W.; Vetter, W.R.; Calder, B.E.; Bohnn, B.J.; and Haughton, V.M.: A Study of the Role of Extravehicular Dehydration in the Production of Cardiovascular Deconditioning by Simulated Weightlessness (Bedrest), Part II. Final Report. NASA CR-114809, 1970.

Johnson, P.C.; Driscoll, T.B.; Alexander, W.C.; and Lambertsen, C.J.: Body Fluid Volume Changes During a 14-Day Continuous Exposure to 5.2% O_2 in N_2 at Pressure Equivalent to 100 FSW (4 ata). Aerospace Med., vol. 44, no. 7, July 1973, pp. 860-863.

Kakurin, L.I.: Medical Research Performed on the Flight Program of the Soyuz-Type Spacecraft. NASA TT F-14026, 1971.

Leach, C.S.: Review of Endocrine Results: Project Mercury, Gemini Program, and Apollo Program. Proceedings of the 1970 Manned Spacecraft Center Endocrine Program Conference, NASA TM X-58068, 1971.

Leach, C.S.; Alexander, W.C.; Fischer, C.L.; Lambertsen, C.J.; and Johnson, P.C.: Endocrine Studies During a 14-Day Continuous Exposure to 5.2% O_2 in N_2 at Pressure Equivalent to 100 FSW (4 ata). Aerospace Med., vol. 44, no. 7, July 1973, pp. 855-859.

Leach, C.S.; Alexander, W.C.; and Johnson, P.C.: Adrenal and Pituitary Response to the Apollo XV Crewmembers. J. Clin. Endocrinol. Metab., vol. 35, no. 5, Nov. 1972, pp. 642-645.

Leach, C.S.; and Campbell, B.O.: Hydrocortisone and ACTH Levels in Manned Spaceflight. Rhythms in Special Environments. Proceedings of the International Society for the Study of Biologic Rhythms (Little Rock, Arkansas), Nov. 1971.

Leach, C.S.; Hyatt, K.H.; and Johnson, P.C.: Increased Dehydroepiandrosterone Excretion During a Low Potassium Diet. Clin. Res., vol. 21, no. 1, 1973, p. 87.

Lipman, R.L.: Impairment of Peripheral Glucose Utilization in Normal Subjects by Prolonged Bedrest. J. Lab. Clin. Med., vol. 76, no. 2, Aug. 1970, pp. 221-230.

Lutwak, L.; Whedon, G.D.; LaChance, P.A.; Reid, J.M.; and Lipscomb, H.S.: Mineral, Electrolyte and Nitrogen Balance Studies of the Gemini-7 Fourteen-Day Orbital Space Flight. J. Clin. Endocrinol. Metab., vol. 29, no. 9, Sept. 1969, pp. 1140-1156.

Mack, P.B.; LaChance, P.A.; Vose, G.P.; and Vogt, F.B.: Bone Demineralization of Foot and Hand of Gemini – Titan IV, V, and VII Astronauts During Orbital Flight. Am. J. Roentgenol., vol 100, no. 3, July 1967, pp. 503-511.

Searcy, R.L.: Diagnostic Biochemistry. McGraw-Hill Book Co., Inc., 1969, p. 50.

Vogel, J.M.: Bone Mineral Measurement, Apollo XV. NASA T-93591, 1971.

Webb, Paul: Weight Loss in Men in Space. Sci., vol. 155, no. 3762, Feb. 1967, pp. 558-560.

Zinneman, H.H.; Johnson, J.J.; and Seal, U.S.: Effect of Short-Term Therapy with Cortisol on the Urinary Excretion of Free Amino Acids. J. Clin. Endocrinol., vol. 23, no. 10, Oct. 1963, pp. 996-1000.