11

Effects of Weightlessness on Human Fluid and Electrolyte Physiology

CAROLYN S. LEACH AND PHILIP C. JOHNSON, JR.

Introduction

The fluid-regulating systems of the body have been of interest to space medicine researchers since results from the earliest flights indicated significant changes in this area (Berry et al. 1966; Dietlein and Harris 1966; Lutwak et al. 1969). The virtual absence of gravity causes a decrease in posturally induced hydrostatic force in the extremities, which leads to cephalad redistribution of blood. This redistribution is thought to be responsible for most of the spaceflight-induced changes in fluid and electrolyte metabolism. Plasma volume decreases (Johnson 1979) and water and electrolyte balances become negative (Leach 1979) in space travelers. In addition to these clear-cut effects, more complex and subtle changes in renal and circulatory dynamics, endocrine function, body biochemistry, and metabolism occur during spaceflight.

Two Phases of the Adaptation Process

Studies in which weightlessness is simulated by decreasing lower-extremity hydrostatic forces (as by bed rest or water immersion) have indicated the presence of at least two phases in the adaptation of the fluid and electrolyte homeostatic systems to microgravity (Leach et al. 1983). The "acute" phase is believed to occur within a few hours of attaining weightlessness. Since it has been difficult for astronauts to perform experiments early in a flight, most of the evidence for existence of this phase has come from simulation studies. Bed-rest studies (Leach et al. 1983; Nixon et al. 1979) have shown that central venous pressure (CVP) increases as early as 5 min after bed rest begins (Nixon et al. 1979). This is followed by an increase in the size of the left ventricle, but there is no change in cardiac output or arterial pressures (Nixon et al. 1979). The increased CVP is thought to be interpreted physiologically as an increase in total blood volume. Glomerular filtration rate (GFR) decreases by about 2 hr and effective renal plasma flow (ERPF) by 4 hr, but both return to pre-bed-rest levels by 8 hr. Plasma aldosterone and antidiuretic

From PHYSIOLOGICAL FUNCTION IN SPECIAL ENVIRONMENTS, edited by C.V. Paganelli and L.E. Farhi.

hormone (ADH) decrease between 1 and 6 hr after the beginning of bed rest (Leach et al. 1983; Nixon et al. 1979).

The transient acute phase, found in simulation studies and confirmed by recent Spacelab data to be discussed below, leads to a later "adaptive" phase. Evidence for the existence of the adaptive phase has come from blood and urine samples taken in-flight during Gemini, Apollo, Skylab, and Spacelab missions.

Early Spaceflight Findings

Data from limited in-flight samples, along with preflight and postflight measurements of many physiological parameters, provided evidence that mass is lost, water balance becomes negative, electrolytes and certain minerals are depleted, and cardiovascular deconditioning occurs as a result of weightlessness (Berry et al. 1966; Hoffler 1977; Leach et al. 1975). Fluid, potassium, and nitrogenous compounds were apparently lost from cells as well as from blood (Leach et al. 1975). Levels of some of the hormones involved in regulating fluid and electrolyte balance were altered; for example, urinary ADH and aldosterone and plasma angiotensin were increased postflight. Plasma volume and red cell mass decreased, and orthostatic tolerance and exercise capacity were reduced (Hoffler and Johnson 1975).

Skylab

Experiments for Skylab were planned to document the time course of known physiological changes and to measure additional parameters during long flights. Intake of fluid and nutrients during flight was carefully monitored.

The first in-flight measurements of body mass were performed on Skylab (Thornton and Ord 1977). The crew members lost an average of 2.8 kg, 3.8% of preflight body mass, during flight (Leach and Rambaut 1977). About half the loss of body mass occurred during the first 2 days of flight, with the rest of the loss being more gradual but continuing throughout the missions. Depletion of water was thought to be responsible for the rapid phase of mass loss and depletion of fat and protein for the slow phase (Leach and Rambaut 1977).

Increased urinary excretion of water was expected to account for the water deficit. Surprisingly, urinary excretion decreased during the first 10 days of the missions, and free water clearance decreased slightly (Leach and Rambaut 1977). Water balance studies showed that the main cause of the net body water reduction during the first 2 days of flight was a decrease in fluid intake.

To investigate the postulated shift of fluid away from the lower extremities, the leg volume of Skylab crew members was measured by plethysmography (Thornton et al. 1977). It was estimated that in the first few days of flight, 1.8 l of fluid disappeared from the legs (Hoffler 1977), an amount considerably greater than the 600 to 800 ml redistributed by a change in body position (upright to supine or vice versa) (Sjöstrand 1953). The amount of fluid lost from the legs was almost equal to the total body fluid decrement.

The loss of so much body fluid implies that levels of other blood and tissue components are reduced also. Plasma osmolality and levels of sodium and chloride were decreased during flight, and the amounts of sodium, potassium, calcium, phosphate, and magnesium were increased in 24-hr urine pools collected in-flight. Leach and Rambaut (1977) calculated that approximately 100 meq of sodium were lost from the extracellular space. Electrolytes and other cell constituents may have been translocated from cells to blood. Plasma levels of potassium, calcium, and phosphate increased during flight.

Plasma angiotensin and urinary aldosterone and cortisol were increased over their preflight levels during the whole flight but were particularly increased at the beginning of each flight (Leach and Rambaut 1977). These hormones are released in response to stress and to changes in plasma osmolality and electrolytes. Increased angiotensin and aldosterone may have caused at least part of the increased urinary excretion of potassium, but it is unusual for high levels of aldosterone to be associated with increased sodium excretion. Urinary excretion of antidiuretic hormone (ADH) was decreased during flight, another unexpected finding because the loss of fluid would normally stimulate ADH secretion, and hyponatremia persisted in spite of the apparent reduction in ADH.

Renal function was not measured directly during the Skylab flights. Slight increases in creatinine clearance (Leach 1981), decreased urinary and plasma uric acid, and increased plasma angiotensin indicated that renal function may be affected by weightlessness.

Recent Findings from the Space Shuttle

Several experiments involving fluid and electrolyte physiology have now been performed aboard the space shuttle. Venous pressure was measured for the first time on *Spacelab 1*, 22 hr after launch (Kirsch et al. 1984). At that time venous pressure was lower than it was on the day before launch. Measurement of central and peripheral venous pressures 1 and 12 hr after landing indicated that fluid redistribution after reexposure to gravity was completed between these times. If redistribution caused by microgravity takes about the same amount of time, it is probably complete before 22 hr.

Studies of body fluid changes during spaceflight have been hampered by lack of knowledge about changes in circadian rhythm and by flight-related

problems such as space adaptation syndrome or crew members being on different work/rest cycles or being unable to draw blood very soon after reaching orbit or at the same time each day.

In one experiment a mission specialist collected his urine as pools representing 5 to 26 hr, and the excretion rates of electrolytes and selected hormones were determined. The earliest change detected in this study was a transient increase in the excretion rate of ADH in the first in-flight sample. This was closely followed by a transient increase in the excretion rate of cortisol. Sodium excretion decreased on the day after the peak in cortisol excretion occurred, but later in the flight it increased. Potassium excretion increased at the same time as cortisol excretion on the first day of flight, with smaller peaks on later flight days. Some of these changes may have been caused or affected by the presence of space adaptation syndrome. On the sixth and last day of the flight, aldosterone excretion rate tripled, and cortisol and ADH excretion rates increased by lesser amounts. The excretion rates of fluid, potassium, chloride, calcium, and magnesium increased at the same time. The loss of sodium, which might be expected to result in increased aldosterone secretion, was no greater late in the flight than it had been during the preflight period.

On the Spacelab flights, blood samples were drawn 22 or more hours after launch. Aldosterone, cortisol, and ADH were measured in blood samples from Spacelab 1 by Dr. K.A. Kirsch (personal communication), and our laboratory has measured these and other hormones as well as serum osmolality, sodium, and potassium in other Spacelab experiments. The four crew members on Spacelab 1 who participated in experiments were on two different work/rest cycles, but their blood samples were taken at the same clock time, and studies of the circadian rhythms of several urinary variables showed that the circadian rhythm of metabolic functions did not change (Leach, Johnson, & Cintrón 1985). Blood samples were obtained from four mission and payload specialists on Spacelab 2 and two mission specialists on Spacelab 3. The crew members on Spacelab 2 were on two different work/rest cycles, and during flight they collected blood samples during the postsleep activity period. This was 6:30 or 7:00 a.m. Houston time for two crew members and 5:00 or 6:00 p.m. for the other two. Because of differences in sample collection times, one must be cautious in interpreting the results, but the small number of subjects and time points in any one experiment makes it desirable to examine the results of these three experiments together.

The combined results for all three Spacelab studies (Leach et al. 1985) showed that hyponatremia developed within 20 hr after the onset of weightlessness and continued throughout the flights, and hypokalemia developed by 40 hr. Serum potassium returned to preflight levels later and then increased. Serum chloride was decreased on most in-flight days on which it was measured, but it immediately returned to preflight levels on landing day.

Antidiuretic hormone, which increased transiently in urine in the

shuttle experiment described above and decreased in urine during Skylab flights (Leach and Rambaut 1977) and in plasma during bed rest (Nixon et al. 1979), was increased in plasma throughout the Spacelab flights. Aldosterone decreased by 40 hr, but after 7 days it had reached preflight levels. Angiotensin I was elevated after 2 days in flight. Cortisol increased early but decreased later in the flight. Adrenocorticotrophic hormone was increased until the seventh day, when levels of cortisol and aldosterone returned to or surpassed baseline.

Current Problems

The changes that occur in human fluid and electrolyte physiology during the acute and adaptive phases of adaptation to spaceflight are summarized in Tables 11.1 and 11.2. A number of questions remain to be answered.

At a time when plasma volume and extracellular fluid volume are contracted and salt and water intake is unrestricted, ADH does not correct the volume deficit and serum sodium decreases. Change in secretion or activity of a natriuretic factor during spaceflight is one possible explanation.

Recent identification of a polypeptide hormone produced in cardiac muscle cells which is natriuretic, is hypotensive, and has an inhibitory effect on renin and aldosterone secretion (Atarashi et al. 1984; Palluk et al. 1985) has renewed interest in the role of a natriuretic factor. The role of this atrial natriuretic factor (ANF) in both long- and short-term variation in extracellular volumes and in the inability of the kidney to bring about an escape from the sodium-retaining state accompanying chronic cardiac dysfunction makes it reasonable to look for a role of ANF in the regulation of sodium during exposure to microgravity. Prostaglandin E is another hormone that may antagonize the action of ADH (Anderson et al. 1976). Assays of these hormones will be performed on samples from crew members in the future.

TABLE 11.1. Acute phase of actual or simulated microgravity effects on fluid and electrolyte physiology

Cardiovascular effects (bed rest)
Increased central venous pressure
Increased size of left ventricle
Renal effects (bed rest)
Decreased GFR
Decreased ERPF
Endocrine system changes (Spacelab)
Increased plasma cortisol
Decreased plasma angiotensin I

TABLE 11.2. Adaptive phase of microgravity effects on fluid and electrolyte physiology, compared with preflight.

Mass loss
Water
Protein
Fat
Changes in fluid volumes in major body compartments
Decrease in lower body
Increase in upper body
Decrease in intracellular water
Decrease in extracellular fluid
Negative fluid balance
Decreased fluid intake
Increased evaporative water loss
Decreased renal excretion of water
Slightly decreased free water clearance
Decreased total body water
Electrolyte balance
Decreased exchangeable body potassium
Decreased sodium in extracellular space
Increased excretion of sodium
Increased excretion of potassium
Blood levels of electrolytes
Increased potassium
Decreased sodium
Decreased chloride
Decreased osmolality
Endocrine system changes
Increased plasma angiotensin I
Increased urinary aldosterone
Increased urinary cortisol
Increased plasma ADH
Decreased urinary ADH
Renal function
Decreased plasma and urinary uric acid
Increased creatinine clearance

Cardiovascular intolerance to standing, found to occur immediately after landing in many astronauts, is thought to be related to loss of fluid and electrolytes during weightlessness. In the space shuttle, reentry acceleration is experienced in the head-to-foot direction because the crew members are sitting upright. The gravitational force in that direction is usually about 1.2 times the normal 1.0 *G* (Nicogossian and Parker 1982). The rapid increase in accleration forces during reentry would be expected to pull body fluids toward the legs. If there has been substantial loss of body fluid, fluid volume in the upper part of the body may decrease enough to cause cardiovascular symptoms. Some of these symptoms might be alleviated if fluid and electrolyte metabolism were fully re-

adapted to earth's gravity before landing. Attempts have been made, with some success, by investigators in the United States and Soviet space programs to prevent or ameliorate orthostatic intolerance.

One method that has been used to counter the orthostatic intolerance is fluid and electrolyte loading. If fluid and electrolytes are replaced, blood volume should begin to increase and blood pressure should approach preflight levels. This should be done before exposure to the increased acceleration during the deorbit period. It is now standard practice for U.S. astronauts to consume the equivalent of a liter of physiological saline solution in the form of water and salt tablets before landing is initiated. This practice has been shown to be effective in reducing the severity of symptoms of cardiovascular deconditioning (Bungo et al. 1985). Similar countermeasures have been used by cosmonauts on Soyuz missions (Grigoriev 1983).

Another approach to prevention of postflight orthostatic intolerance is the use of lower-body negative pressure (LBNP) during flight to bring more fluid into the legs; this has been used with some success in the Soviet space program (Grigoriev 1983).

There is now considerable indirect evidence that renal function is altered during weightlessness (Leach, Johnson, & Cintrón 1985), but direct measurements of renal function have been done only in bed-rest studies. Renal function tests will be performed in conjunction with measurement of hormones, electrolytes, plasma volume, and other factors on Spacelab missions in the future. Intake of food and water will be measured throughout the mission, and urine will be collected void by void. Blood samples will be taken at intervals, beginning at 3 hr after launch, and the first renal function test will start at 3.5 hr. A catheter to measure central venous pressure will be inserted before launch and removed 12 hr into the flight. Plasma volume and extracellular fluid will be measured on the second and sixth days of flight. These integrated experiments are expected to provide information important for understanding what happens in both phases of the fluid and electrolyte response to weightlessness.

Acknowledgements. The authors thank Dr. Jane Krauhs and Mrs. Sharon Jackson for assistance with preparation of the manuscript.

References

Anderson RJ, Berl T, McDonald KM, Schrier RW (1976). Prostaglandins: Effects on blood pressure, renal blood flow, sodium and water excretion. *Kidney Int* 10: 205–215

Atarashi K, Mulrow PJ, Franco-Saenz R, Snajdar R, Rapp J (1984). Inhibition of aldosterone production by an atrial extract. *Science* 224: 992–994

Berry CA, Coons DO, Catterson AD, Kelly GF (1966). Man's response to long-duration flight in the Gemini spacecraft. In: *Gemini Midprogram Conference,* February 23–25, 1966. Johnson Space Center, Houston, TX, pp 235–261

Bungo MW, Charles JB, Johnson PC Jr. (1985). Cardiovascular deconditioning during space flight and the use of saline as a countermeasure to orthostatic intolerance. *Aviat Space Environ Med* 56: 985–990

Dietlein LF, Harris E (1966). Experiment M-5, bioassays of body fluids. In: *Gemini Midprogram Conference,* February 23–25, 1966. Johnson Space Center, Houston, TX, pp 403–406

Grigoriev AI (1983). Correction of changes in fluid-electrolyte metabolism in manned space flights. *Aviat Space Environ Med* 54: 318–323

Hoffler GW (1977). Cardiovascular studies of U.S. space crews: An overview and perspective. In: Hwang NHC, Normann NA (eds) *Cardiovascular Flow Dynamics and Measurements.* University Park Press, Baltimore, MD, pp 335–363

Hoffler GW, Johnson RL (1975). Apollo flight crew cardiovascular evaluations. In: Johnston RS, Dietlein LF, Berry CA (eds) *Biomedical Results of Apollo,* NASA SP-368. National Aeronautics and Space Administration, Washington, DC, pp 227–264

Johnson PC (1979). Fluid volumes changes induced by spaceflight. *Acta Astronaut* 6: 1335–1341

Kirsch KA, Röcker L, Gauer OH, Krause R, Leach C, Wicke HJ, Landry R (1984). Venous pressure in man during weightlessness. *Science* 225: 218–219

Leach CS (1979). A review of the consequences of fluid and electrolyte shifts in weightlessness. *Acta Astronaut* 6: 1123–1135

Leach CS (1981). An overview of the endocrine and metabolic changes in manned space flight. *Acta Astronaut* 8: 977–986

Leach CS, Alexander WC, Johnson PC (1975). Endocrine, electrolyte, and fluid volume changes associated with Apollo missions. In: Johnston RS, Dietlein LF, Berry CA (eds) *Biomedical Results of Apollo,* NASA SP-368. National Aeronautics and Space Administration, Washington, DC, pp 163–184

Leach CS, Chen JP, Crosby W, Johnson PC, Lange RD, Larkin E, Tavassoli M (1985). *Spacelab 1 Hematology Experiment (1NS103): Influence of Space Flight on Erythrokinetics in Man,* NASA TM 58268. Johnson Space Center, Houston, TX

Leach CS, Johnson PC, Cintron NM (1986). The regulation of fluid and electrolyte metabolism in weightlessness. In: Hunt J (ed) *Proceedings of the 2nd International Conference on Space Physiology,* Toulouse, France, November 20–22, 1985, ESA SP-237. European Space Agency, Paris, France, pp 31–36

Leach CS, Johnson PC, Suki WN (1983). Current concepts of space flight induced changes in hormonal control of fluid and electrolyte metabolism. *Physiologist* 26: S-24–S-27

Leach CS, Rambaut PC (1977). Biochemical responses of the Skylab crewmen: An overview. In: Johnston RS, Dietlein LF (eds) *Biomedical Results from Skylab,* NASA SP-377. National Aeronautics and Space Administration, Washington, DC, pp 204–216

Lutwak L, Whedon GD, Lachance PH, Reid JM, Lipscomb HS (1969). Mineral, electrolyte and nitrogen balance studies of the Gemini VII fourteen-day orbital space flight. *J Clin Endocrinol* 29: 1140–1156

Nicogossian AE, Parker JF Jr (1982). *Space Physiology and Medicine,* NASA SP-447. National Aeronautics and Space Administration, Washington, DC, p 40

Nixon JV, Murray RG, Bryant C, Johnson, RL Jr, Mitchell JH, Holland OB, Gomez-Sanchez C, Vergne-Marini P, Blomqvist CG (1979). Early cardiovascular adaptation to simulated zero gravity. *J Appl Physiol: Respirat Environ Exercise Physiol* 46: 541–548

Palluk R, Gaida W, Hoefke W (1985). Atrial natriuretic factor. *Life Sci* 36: 1415–1425

Sjöstrand T (1953). Volume and distribution of blood and their significance in regulating the circulation. *Physiol Rev* 33: 202–228

Thornton WE, Hoffler GW, Rummel JA (1977). Anthropometric changes and fluid shifts. In: Johnston RS, Dietlein LF (eds) *Biomedical Results from Skylab,* NASA SP-377. National Aeronautics and Space Administration, Washington, DC, pp 330–338

Thornton WE, Ord J (1977). Physiological mass measurements in Skylab. In: Johnston RS, Dietlein LF (eds) *Biomedical Results from Skylab,* NASA SP-377. National Aeronautics and Space Administration, Washington, DC, pp 175–182