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BED-REST STUDIES: FLUID AND ELECTROLYTE RESPONSES

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ABSTRACT

Acute and chronic changes in hydrostatic and osmotic pressures have a major influence on body fluid-electrolyte composition and distribution in humans. Acute changes in body position (e.g., standing) result in a decrease in plasma volume (PV), and subsequent assumption of the horizontal position restores the depleted PV. Long-term confinement in the horizontal position for 2-3 weeks results in a chronic decrease in PV, increased interstitial fluid volume, and unchanged or slightly increased extracellular fluid volume. Concentrations of blood electrolytes, glucose, and nitrogenous constituents remain within normal limits of variability when maintenance levels of isometric or isotonic exercise are performed for 1 hr/day. Hematocrit and plasma osmolality can be elevated significantly throughout bed rest (BR). Significant diuresis occurs on the first day, and increases in urine Na and Ca continue throughout BR, although voluntary fluid intake is unchanged. Urine Na and K are elevated during the second week of BR in spite of stabilization of PV and extracellular volume. The initial diuresis probably arises from the extracellular fluid while subsequent urine loss above control levels must come from the intracellular fluid. Preservation of the extracellular volume takes precedence over maintenance of the intracellular fluid volume. These findings suggest the functioning of a natriuretic factor (hormone) to account for the continued increased loss of Na in the urine.

INTRODUCTION

Although a necessary part of proper medical treatment for many infirmities, enforced bed rest with the patient in the horizontal position has probably been used inappropriately for many others. Normal healthy people spend about one-third of their lifetime in bed (about 8 hr/day). Prolonged bed rest alters at least three major input stimuli: hydrostatic pressure is lowered within the body fluid compartments and cardiovascular system; compression force on the long bones of the skeletal system is essentially eliminated; and there is usually a reduction in the total daily energy expenditure because of the partial confinement to bed. Also, the changed surroundings may induce feelings of anxiety in the patient (20). The sum total of physiological and psychological responses of bed-rest patients has been well described in allegorical terms by Asher (1):

"Look at a patient lying long in bed; what a pathetic picture he makes! The blood clotting in his veins, the lime draining from his bones, the scybala stacking up in his colon, the flesh rotting from his seat, the urine leaking from his distended bladder, and the spirit evaporating from his soul!"

Within the first few days of bed rest the major responses involve contraction of body fluid and electrolyte content, an apparently abnormal carbohydrate (glucose) metabolism, and altered venous compliance (Table 1).

TABLE 1. TIME-COURSE OF PHYSIOLOGICAL CHANGES DURING BED REST

0-3 days	4-7 days	8-14 days	Over 15 days
Urinary diuresis	Creatininuria	Pyrophosphaturia	Peak hypercalciuria
Urinary calcium loss	Hydroxyprolinuria Phosphaturia	Decreased red cell mass	Changed sensitivity to thermal stimuli
Decreased plasma, interstitial, and extracellular fluid volumes	Negative N ₂ balance	Decreased leucocyte phagocytosis ability	Secondary increase in auditory threshold
Decreased secretion of gastric juice	Increased blood fibrinogen and clotting	Increased sweating sensitivity	Decreased +G, tolerance
Decreased calf blood flow	Increased blood fibrinolytic activity	Increased exercise hyperthermia	
Increased venous compliance	Increased auditory thresholds	Decreased tissue heat conductance	
Increased neutrophil digestive function	Decreased near-point of visual acuity		
Glucose intolerance	Lengthened focal point		
Decreased +G, acceleration tolerance	Increased hyperemia of eye conjunctiva and dilation of retinal arteries and veins		
	Decreased neutrophil absorption		
	Tilt-table intolerance		

FLUID COMPARTMENT VOLUME RESPONSES

Acute changes in body position induce abrupt changes in fluid compartment volumes. Assumption of the upright body position, for example on a tilt-table, results in an immediate shift of fluid — within seconds — from the tissues above the hydrostatic indifference point (HIP) and into the tissues (pooling) below the HIP (18). The HIP appears to be located just below the apex of the heart. Some translocated fluid comes from the plasma volume (PV) and some presumably from the interstitial volume (ISV) resulting from increases in hydrostatic pressure below the HIP. If the subjects remain motionless when tilted, the combined effects of reductions in PV (hypovolemia), central venous pressure and flow, and peripheral resistance will culminate in a significant fall in systemic blood pressure and subsequent fainting. At syncope, PV will have decreased by 13%-16%. An excellent, comprehensive discussion of cardiovascular and fluid-shift responses to tilting was presented by Hinghofer-Szalkay at this symposium in 1982 (14).

There are three periods during prolonged bed rest when significant fluid shifts occur: the first day, the end of the second week, and the end of the fourth week (7,10). When the body is placed in the horizontal position, there are essentially opposite responses to those that occur when the body is

placed in the vertical position. Within the first few minutes of bed rest, with the head tilted downward by 5° , there is a shift of fluid from the extremities to the chest. The subjects experience fullness and heaviness in the head, central venous pressure increases from 5.7 to 7.9 cm H₂O, and leg volume decreases from 7.5 to 6.9 l (23). At the same time, PV is decreasing [from 2,895 ml to 2,770 ml (-4.3%) after 6 hr and to 2,742 ml (-5.3%) after 24 hr of head-down bed rest] (23). There are no direct measurements of changes in PV after 30 min of bed rest, but during head-out water immersion there is a definite increase in PV (measured with Evans blue dye) of 8.8% at 30 min, with a progressive decline in PV thereafter (9). Unlike during water immersion where there is graded external pressure on the skin, during bed rest there is uneven pressure on only part of the skin that varies as the subjects change body position. These variable-pressure conditions probably contribute to variable responses of the fluid-electrolyte system. There is a diuresis during the first day (5) and a concomitant loss of PV during the first one or two days of bed rest. Plasma volume appears to reach an equilibrium level at about -10% to -13% by the fourth day (possibly sooner) of horizontal bed rest (Fig. 1, Refs. 6, 17). Test results show that isometric exercise (250 kcal/hr) or isotonic exercise (780 kcal/hr) during 14 days of bed rest appeared to maintain PV at the equilibrium level of about -13% (Fig. 1), whereas PV continued to decrease during bed rest with no remedial exercise (see Figs. 1 and 2). Red cell mass decreased linearly with time by 100 ml (-5.0%) after 14 days and by 300 to 550 ml after 1 month (17,22). Subjects sustaining plasma and red cell volume losses of these magnitudes would very likely be incapacitated if forced to stand erect in a 1-G environment. After 2 weeks of horizontal bed rest, slow-onset head-to-foot (+G_z) acceleration tolerance was reduced by 49% in young women (11), and by 24%-35% in young men (8). About one-half of the loss in acceleration tolerance after bed rest can be accounted for by the hypovolemia during bed rest and the additional hypovolemia during acceleration. The limit of hypovolemia at the point of maximal tolerance during various active (peak exercise) and passive (bed rest and +G_z acceleration) stresses is between -14.9% and -19.5% (Tables 2 and 3).

The other major component of the extracellular fluid volume (ECV) is the ISV. Like PV, the ISV also decreases during the first few days of bed rest (Fig. 1). Between the fourth and fourteenth days the ISV increases to above-normal levels, apparently to compensate for the reduction in PV. Thus, the ECV remains unchanged from pre-bed-rest levels (Fig. 1), or it may be increased by 2.3 l (12%) (21). In this situation, maintenance of the total ECV appears to take precedence over preservation of PV.

Diuretic fluid loss and the associated negative water balance contribute to the reduction in total body water during bed rest (5,24). Total body water is reduced by about 600 ml by the second day of bed rest (15), a volume equal to the reduction in PV. After 12-14 days (possibly sooner) total body water decreases by about 1,500 ml (15) when the ECV is restored and PV remains depressed. With the restored ECV and a constant depressed PV, the loss of total body water must have come from the intracellular fluid compartment; this response is probably due in part to atrophy of muscle cells. Immobilization of the elbow results in a 41% decrease in strength and significant decreases of 33% in the area of fast-twitch fibers and of 25% in the area of slow-twitch fibers (19).

These results strongly suggest that the early loss of fluid via the kidney is derived from the extracellular (plasma and interstitial) fluid compartment. Fluid for subsequent restoration of the ECV and for the continuing decrease of the PV must then come from the intracellular fluid compartment, exclusive of the decreasing red cell mass, because of the different rates of change of the ECV and cell mass. There are insufficient data to determine when or if the PV reaches equilibrium. Both isometric and isotonic exercise

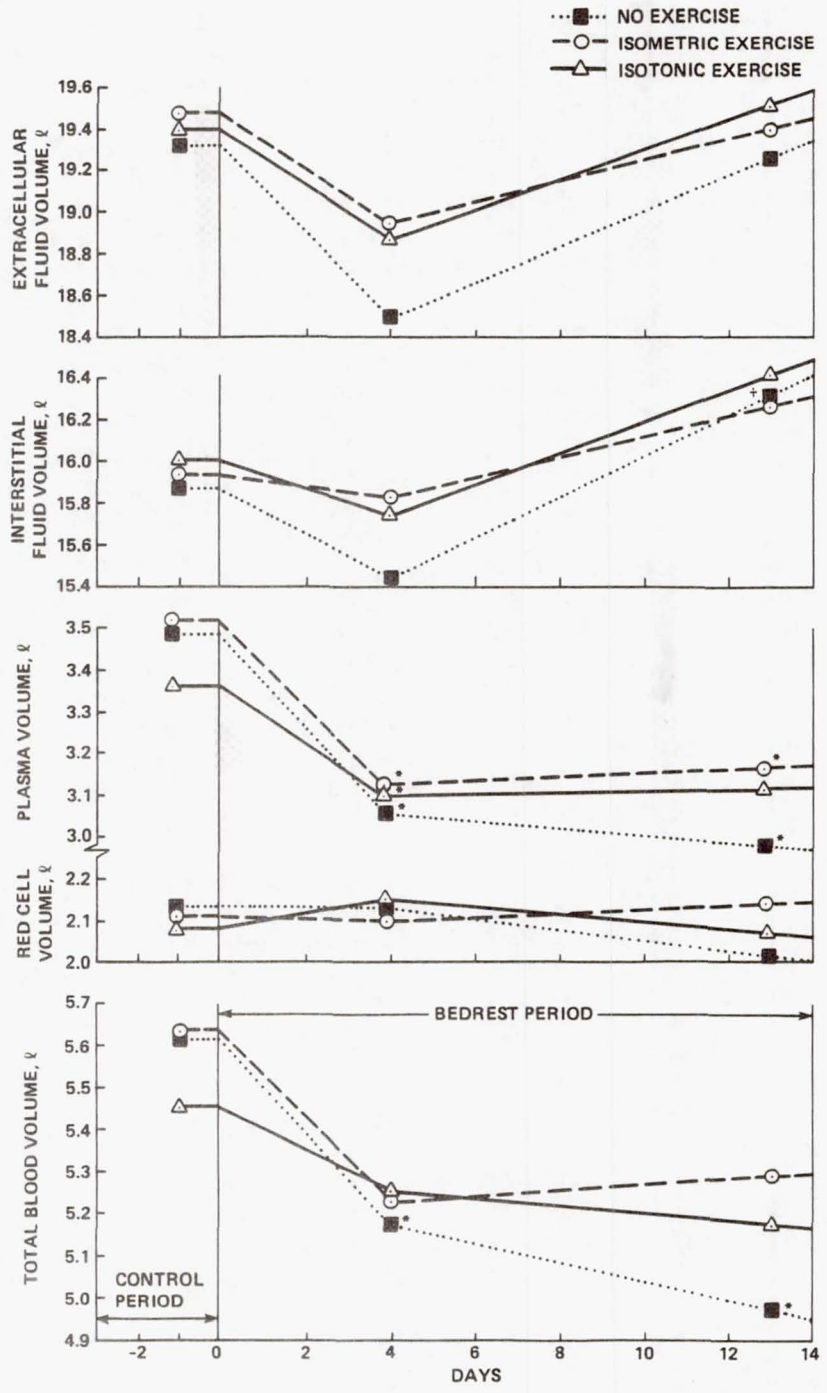


Fig. 1. Mean fluid compartment and red cell volumes from seven men during control and horizontal bed-rest periods. *P < 0.05 from control values. †P < 0.05 from day 4 values. From Ref. 6 with permission.

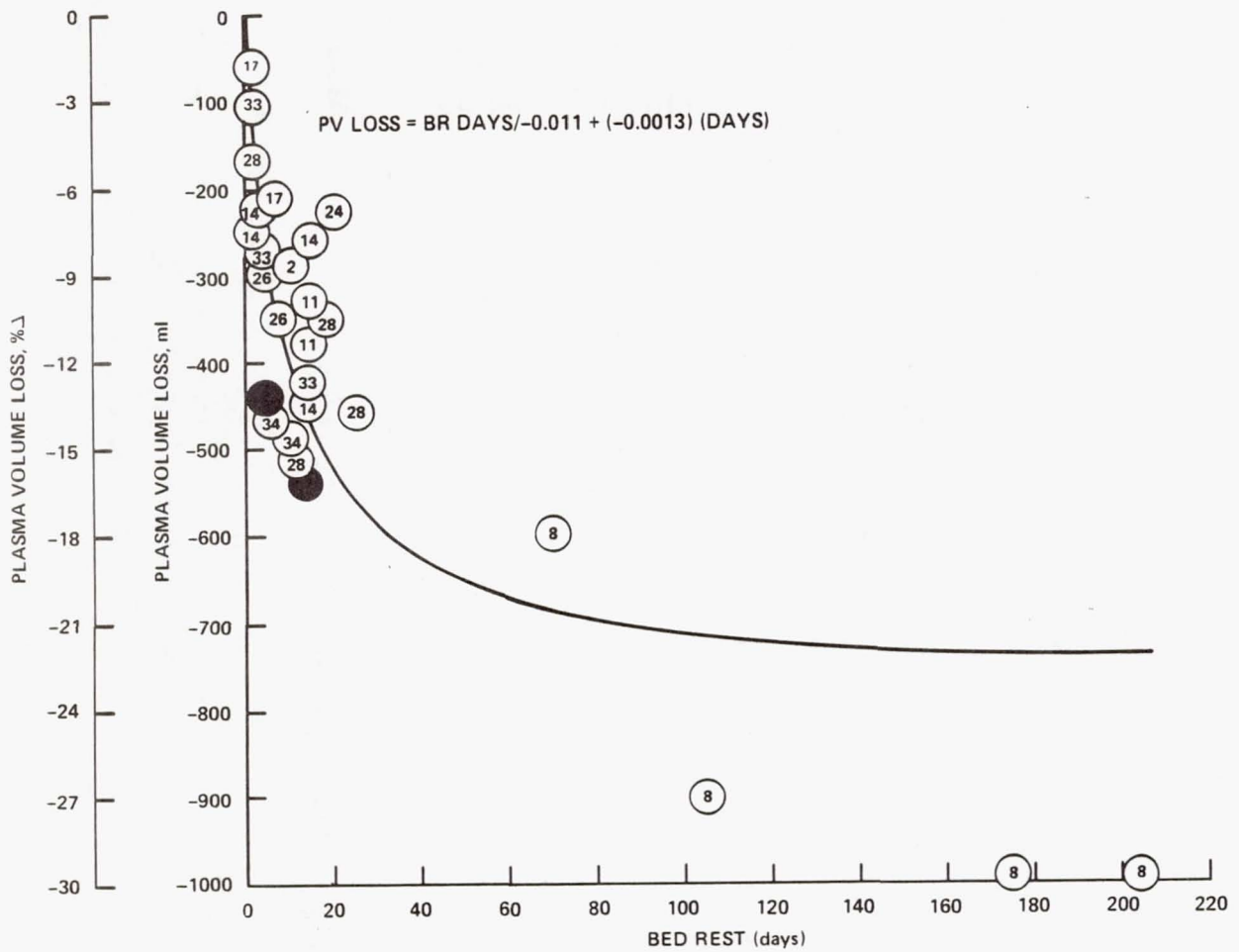


Fig. 2. Plasma volume loss during horizontal bed-rest periods with data from 11 studies that utilized no remedial procedures. Curve fitted with computer analysis. From Ref. 6 with permission.

TABLE 2. CHANGE IN PLASMA VOLUME DURING STRESS: PEAK EXERCISE

Difference	Control period, Peak exercise,		Σ , % Δ
	% Δ	% Δ	
Van Beaumont et al. (25)			
3 δ upright, cycle	--	-14.9	-14.9
3 δ upright, cycle	--	-15.1	-15.1
Van Beaumont et al. (27)			
6 δ upright, cycle	--	-15.6	-15.6
Greenleaf et al. (13)			
4 δ upright, cycle	-3.4%	-16.1	-19.5
4 δ supine, cycle	+0.8%	-17.6	-16.8

TABLE 3. CHANGE IN PLASMA VOLUME DURING STRESS: BED REST AND +G_z ACCELERATION

Reference	Bed rest, %Δ	Acceleration, %Δ	Σ, %Δ
Greenleaf et al. (12)			
3.2 g/min			
8♂ bed rest 1 (ITE)*	-6.8	-10.6	-17.4
8♂ bed rest 2 (ITE)	-6.5	-11.9	-18.4
Van Beaumont et al. (26)			
3.2 g/min			
7♂ bed rest 1 (NOE)*	-12.6	-6.3	-18.9
7♂ bed rest 2 (IME)*	-11.3	-6.3	-17.6
7♂ bed rest 3 (ITE)	-7.8	-7.1	-14.9
Greenleaf et al. (11)			
3.0 g/min			
12♂ bed rest 1 (NOE)	-12.6	-4.1	-16.7

*NOE, no exercise; ITE, isotonic exercise; IME, isometric exercise.

performed during bed rest appear to attenuate the hypovolemia, but they have essentially no effect on restoration of the ISV (Fig. 1). Following 2 weeks of bed rest, maintenance of extracellular (interstitial) volume takes precedence over maintenance of plasma and intracellular volumes. This response is essentially independent of the effects of moderate remedial exercise. Therefore, the mechanism that stabilizes the ECV by increasing ISV appears to respond mainly to the decrease in hydrostatic pressure rather than to the reduction in exercise metabolism.

PLASMA ELECTROLYTE AND PROTEIN RESPONSES

The chronic reduction of PV during prolonged bed rest, with controlled dietary intake, is accompanied by moderate hemoconcentration during the first few days of rest as indicated by statistically significant increases in hematocrit, plasma osmolality (Fig. 3), and plasma glucose (Fig. 4) measured in basal blood samples. The relatively unchanged plasma Na concentration (Fig. 4) could not account for the increased plasma osmolality. Other plasma constituents including total protein, albumin, Cl, Na, uric acid, Ca, K, P, creatinine, and blood urea N — with only a few exceptions — were essentially unchanged during 14 days of bed rest (Figs. 3-5). The two exercise regimens had no consistent effect on basal concentrations of these variables within the first few days of rest. Notable exceptions occurred with plasma K and Ca after 2 weeks of bed rest. Their concentrations were increased significantly during the two exercise regimens (Fig. 5), suggesting that exercise facilitates retention of K and Ca content (PV × concentration) because PV was decreased. Compared with the no-exercise data, there were fewer statistically significant losses of plasma constituent contents with the two exercise regimens (6). In a few instances, a significant decrease of a plasma constituent content early during bed rest was returned to the control level by the end of rest. This restoration occurred for K with isometric exercise, and for K, Cl, and uric acid with isotonic exercise (6). Neither form of exercise eliminated the significant losses of albumin and glucose contents, but isotonic exercise had the greatest inhibitory effect on those losses. By the end of bed rest, plasma albumin content decreased by 29 g with no exercise, by 20 g with isometric exercise, but by only 10 g with isotonic exercise. The attenuating effect on albumin loss by isotonic exercise may be a manifestation of the same mechanism where isotonic exercise facilitates the induction of hypervolemia during exercise training in ambulatory subjects (3). Thus, there were few significant differences between the two exercise regimens in the fluid-electrolyte-protein responses, and both

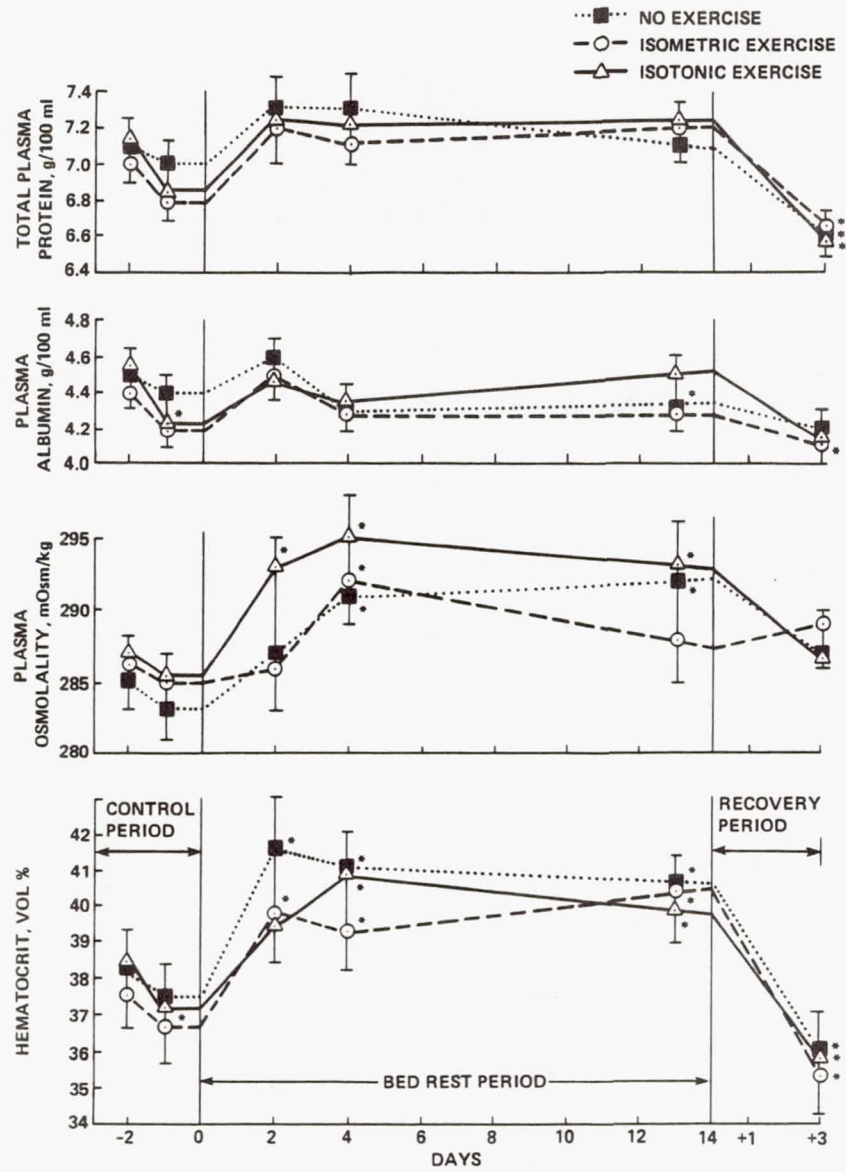


Fig. 3. Mean plasma protein, albumin, osmolality, and hematocrit in seven men during control, horizontal bed-rest, and ambulatory recovery periods. *P < 0.05 from day minus 2 control value. From Ref. 6 with permission.

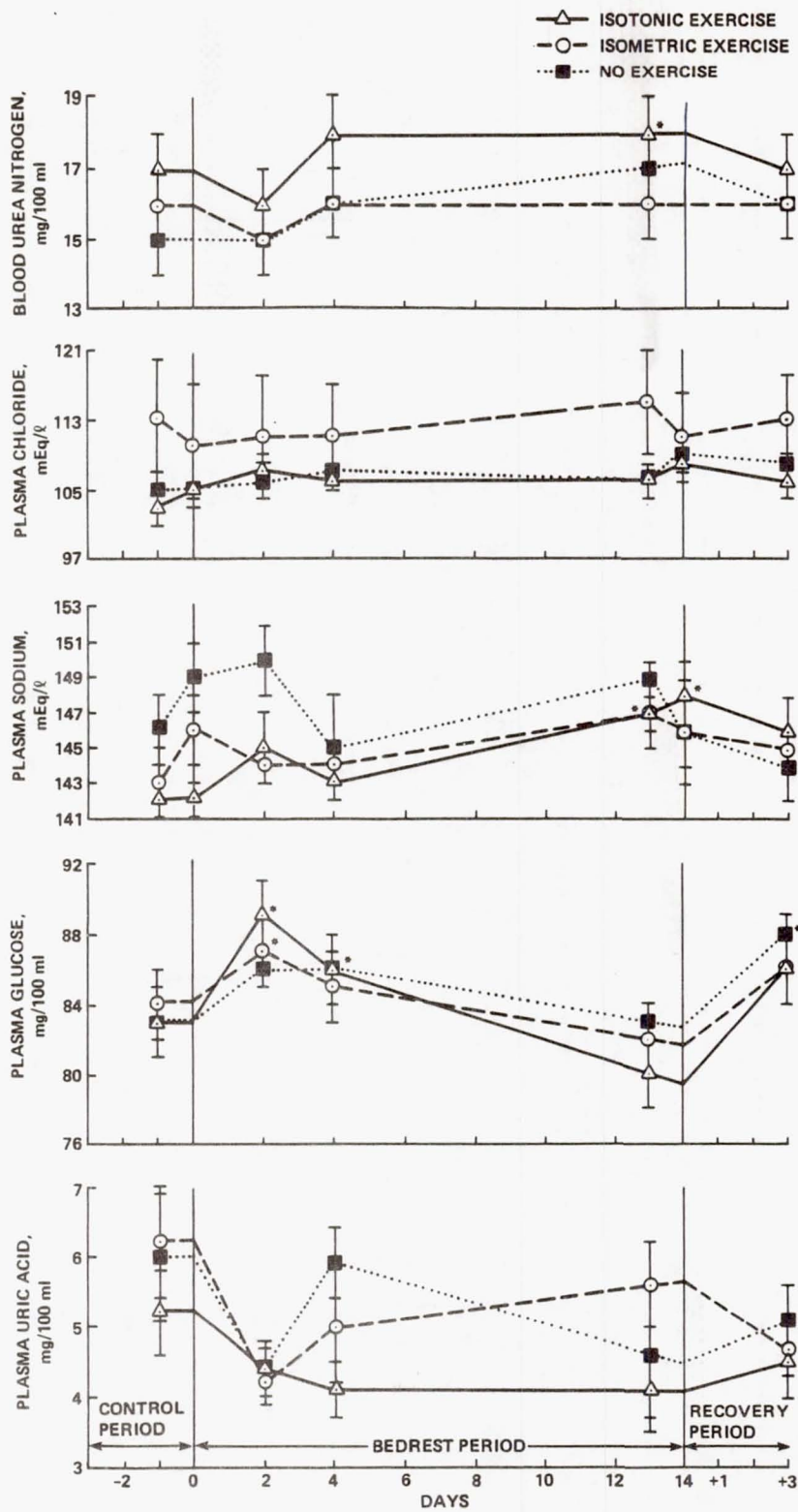


Fig. 4. Mean plasma constituent data from seven men during control, horizontal bed-rest, and ambulatory recovery periods. * $P < 0.05$ from day minus 2 control value. Data from Ref. 6.

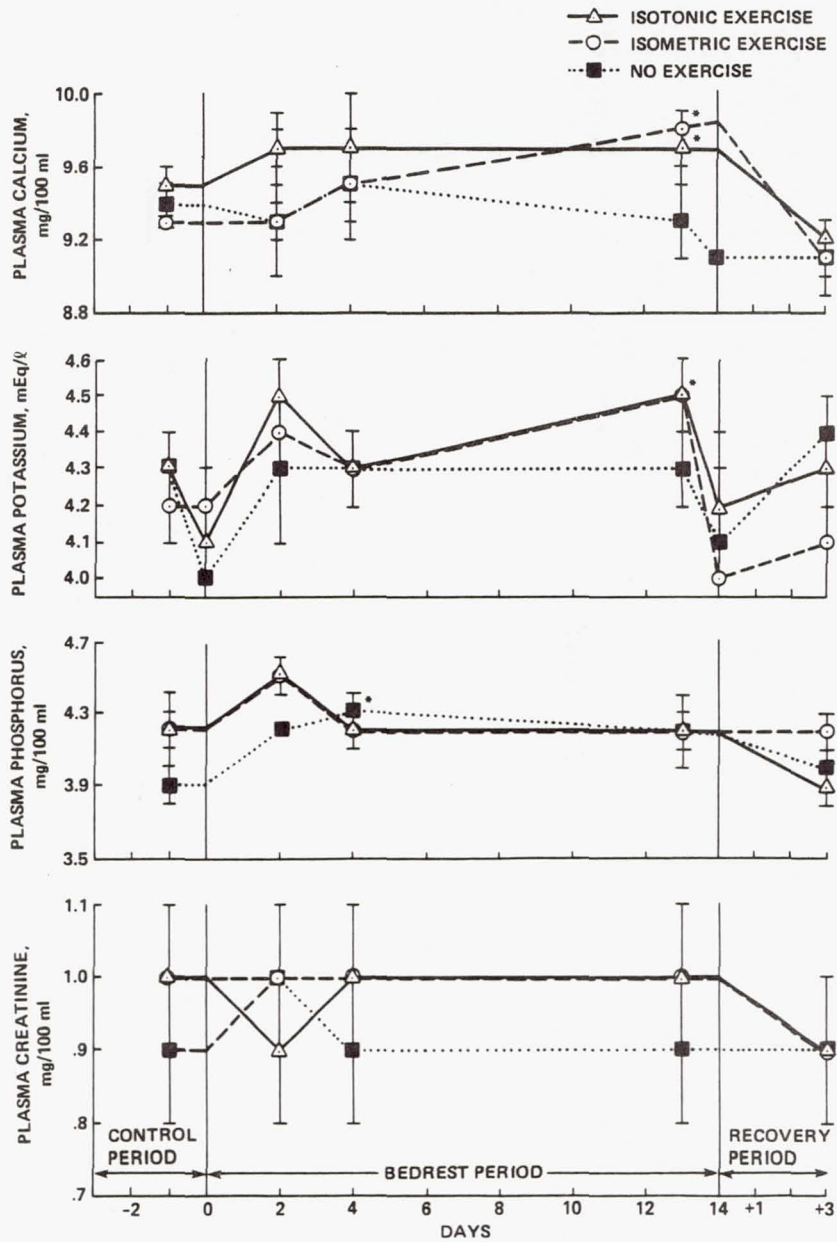


Fig. 5. Mean plasma constituent data from seven men during control, horizontal bed-rest, and ambulatory recovery periods. *P < 0.05 from day minus 2 values. Data from Ref. 6.

regimens facilitated stabilization and attenuation of shifts in plasma constituent contents.

URINE ELECTROLYTE AND NITROGEN RESPONSES

Urine creatinine and urea N excretion were essentially unchanged from ambulatory control levels during rest (Fig. 6). Urine Ca excretion was significantly increased on the first day of rest for the two exercise regimens, and was significantly elevated in all three regimens by day 6 of rest (Fig. 6).

There was a marked, significant diuresis during the first 24 hr of bed rest with the no-exercise and isometric exercise regimens from a control level of 1.5 ℓ /24 hr (1.0 ml/min) to 2.5 ℓ /24 hr (1.7 ml/min) (Fig. 7). Performance of isotonic exercise resulted in a smaller but significant diuresis of 1.8 ℓ /24 hr (1.2 ml/min). During the 14 days of bed rest the cumulative urine volumes were 26.9 ℓ with no exercise, 26.6 ℓ with isometric exercise, but only 22.2 ℓ with isotonic exercise. This reduction in urine volume with isotonic exercise was not due to differences in diet, total fluid intake, voluntary fluid intake (Fig. 7), or to nonurine output such as diarrhea or vomiting. In fact, total fluid intake was decreasing during the first few days of rest. Sweating was negligible during isometric exercise, but was about 600-700 ml/hr during isotonic exercise at a load equivalent to 68% of the subjects' peak oxygen uptake. At this exercise intensity the PV would have been reduced by 10%, and plasma vasopressin and renin activity both would have been elevated about twofold above resting levels to 2.8 pg/ml and 4.9 ng Ang 1/(ml \times hr), respectively (4). These combined responses would tend to promote renal Na and water reabsorption to assist in restoration of the hypovolemia, with a resulting reduction in urine volume for perhaps 1-2 hr/day during the isotonic exercise and for some undefined period thereafter.

Urine Na, Cl, and osmotic losses increased significantly along with the 24-hr diuresis with the two exercise regimens and the no-exercise regimen (Fig. 7). But there were no excessive losses or retention of these ions and osmols during rest with isotonic exercise (Fig. 7). There were statistically significant increases in urine K (Fig. 6) and Na (Fig. 7) with all three regimens during rest, especially with isometric and no exercise, and significant reductions in output to below control levels during the ambulatory recovery periods. Chobanian et al. (2) have observed negative Na and K balances throughout 2-3 weeks of bed rest in conjunction with unchanged plasma renin activity and aldosterone secretory rates. On the other hand, Keil and Ellis (16) reported that plasma renin activity increased by 91% above ambulatory control values on days 10-15 of bed rest, whereas plasma vasopressin decreased by 33% on days 2-17 of rest. A decrease in vasopressin could explain the continued moderate increase in urine volume during the second week of bed rest. The combined effects of a natriuretic hormone, which would inhibit the Na-retention effect of aldosterone, acting in concert with the K-dumping action of aldosterone, could explain these paradoxical urine ion losses after the first 24 hr of rest. The increased loss of Na within the first 48 hr of bed rest is the appropriate response to hypovolemia to maintain plasma Na concentration within normal homeostatic limits. The reason for the continued increased loss of Na in urine during the second week of rest is not clear in view of the fact that plasma volume with the exercise regimens had stabilized and the extracellular fluid volume had returned to control levels. Apparently, fluid-electrolyte homeostasis had not reached equilibrium by 14 days of bed rest.

It is fitting that we end with an Asher (1) aphorism: "Teach us to live that we may dread, unnecessary time in bed. Get people up and we may save, our patients from an early grave."

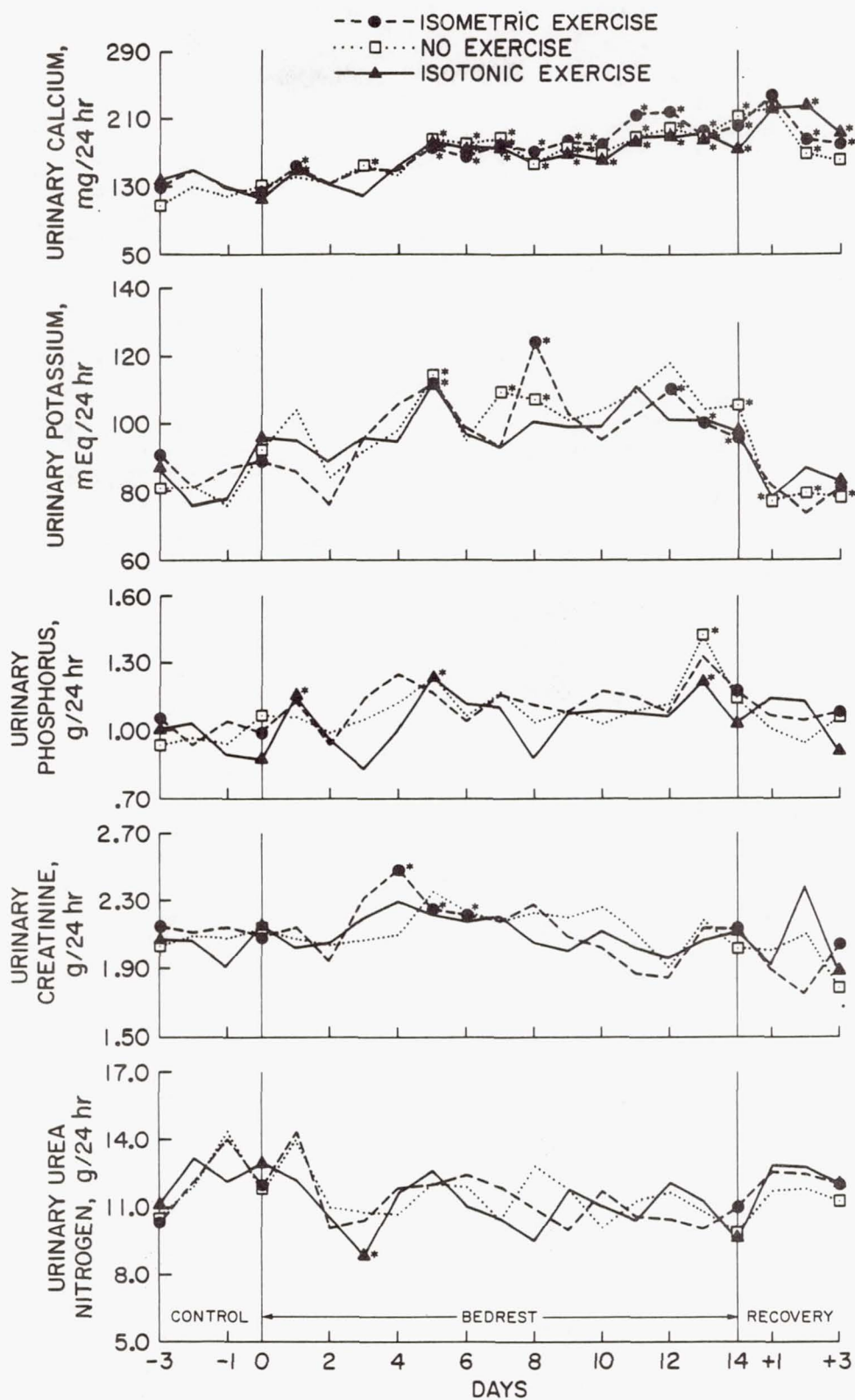


Fig. 6. Mean urine constituent losses from seven men during control, horizontal bed-rest, and ambulatory recovery periods. *P < 0.05, from day minus 1 control value. From Ref. 5 with permission.

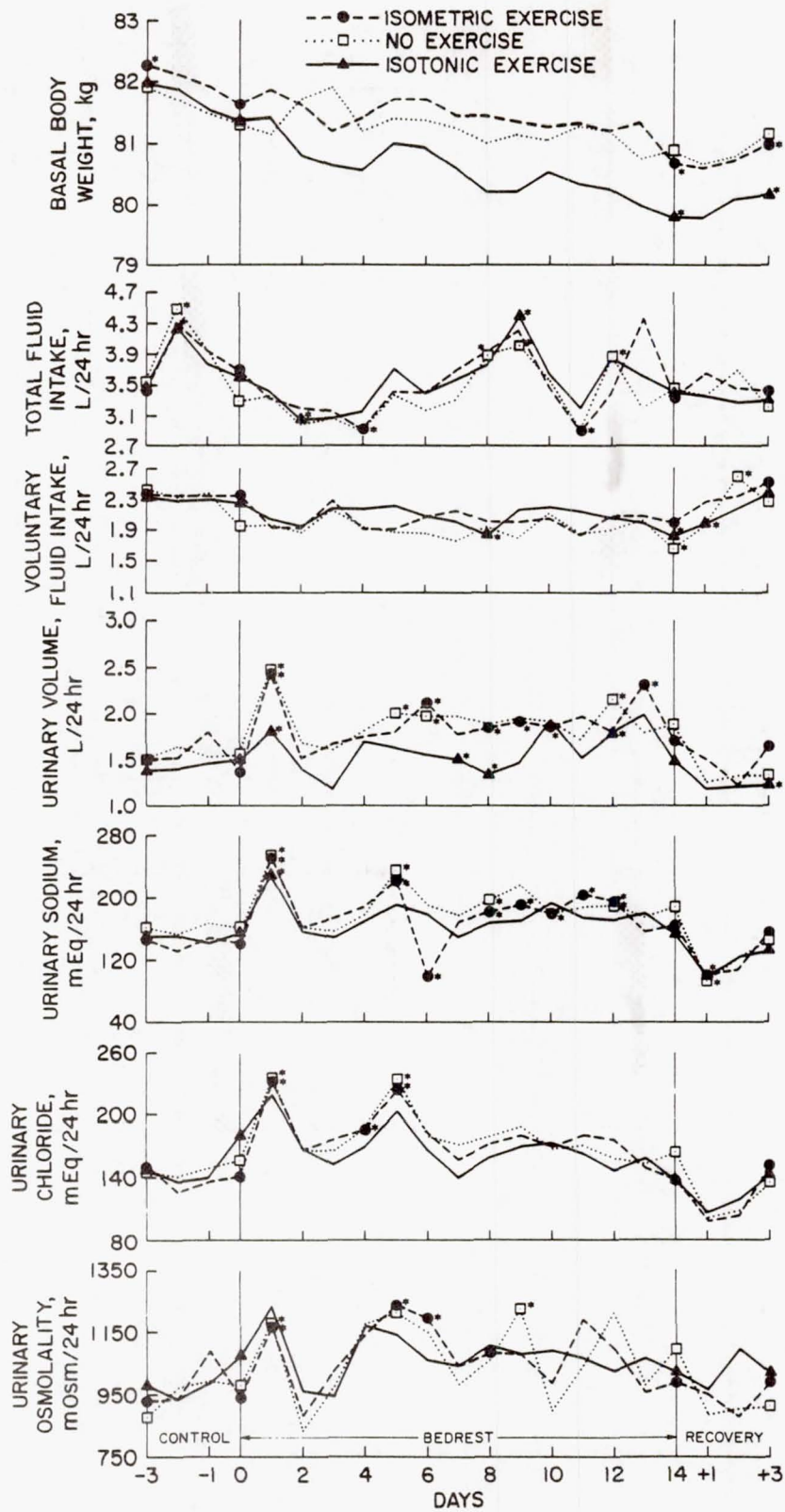


Fig. 7. Mean body weight, fluid intake, and urine volume and electrolyte excretion during control, horizontal bed-rest, and ambulatory recovery periods. * $P < 0.05$ from day minus 1 control value. From Ref. 5 with permission.

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16. Abstract Acute and chronic changes in hydrostatic and osmotic pressures have a major influence on body fluid-electrolyte composition and distribution in humans. Acute changes in body position (e.g., standing) result in a decrease in plasma volume (PV), and subsequent assumption of the horizontal position restores the depleted PV. Long-term confinement in the horizontal position for 2-3 weeks results in a chronic decrease in PV, increased interstitial fluid volume, and unchanged or slightly increased extracellular fluid volume. Concentrations of blood electrolytes, glucose, and nitrogenous constituents remain within normal limits of variability when maintenance levels of isometric or isotonic exercise are performed for 1 hr/day. Hematocrit and plasma osmolality can be elevated significantly throughout bed rest (BR). Significant diuresis occurs on the first day, and increases in urine Na and Ca continue throughout BR, although voluntary fluid intake is unchanged. Urine Na and K are elevated during the second week of BR in spite of stabilization of PV and extracellular volume. The initial diuresis probably arises from the extracellular fluid while subsequent urine loss above control levels must come from the intracellular fluid. Preservation of the extracellular volume takes precedence over maintenance of the intracellular fluid volume. These findings suggest the functioning of a natriuretic factor (hormone) to account for the continued increased loss of Na in the urine.					
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