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NONINVASIVE ESTIMATION OF FLUID SHIFTS BETWEEN BODY COMPARTMENTS BY MEASUREMENT OF BIOELECTRIC CHARACTERISTICS

Final Report

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ABSTRACT

Previous research has established that bioelectrical characteristics of the human body reflect fluid status to some extent. It has been previously assumed that changes in electrical resistance (R) and reactance (X) are associated with changes in total body water (TBW). The purpose of the present pilot investigation was to assess the correspondence between body R and X and changes in estimated TBW and plasma volume during a period of bedrest (simulated weightlessness). R and X were measured pre-, during, and post- a 13 day bedrest interspersed with treatments designed to alter body fluid status. Although a clear relationship was not elucidated, evidence was found suggesting that R and X reflect plasma volume rather than TBW. Indirect evidence provided by previous studies which investigated other aspects of the electrical/fluid relationship, also suggests the independence of TBW and electrical properties. With further research, a bioelectrical technique for noninvasively tracking fluid changes consequent to space flight may be developed.

INTRODUCTION

That body fluid volumes are altered as a consequence of simulated or actual space flight is well established (7). It is generally believed that the loss of intravascular fluid (blood plasma) contributes significantly to the observed decline in orthostatic tolerance subsequent to microgravity exposure. Body fluid compartments have been studied in simulated weightlessness studies (bedrest, and water immersion) by invasive means, but the time requirements and the necessity of blood withdrawal and isotope injection required by these measurements, have generally precluded their use during space flight. The development of an accurate noninvasive technique for estimating the shift in body fluids throughout the course of an extended duration space flight would provide considerable information useful in understanding and protecting against the adverse effects of prolonged microgravity exposure.

The work of Nyboer (18) and others has shown that bioelectrical characteristics respond to changes in body fluids. This technique involves introduction of 0.8-4 milliamps of high frequency (50-100 kHz) current into the body via surface electrodes. These current levels at these frequencies are safe and painless. Tetrapolar electrodes are employed with two electrodes used for current injection and two used for voltage pickup, which obviates skin-electrode impedance complications (14,18). Knowledge of the injected current and frequency and the voltage drop and phase shift across a body part can be used to calculate resistance and reactance which can be combined to yield impedance. Basic electrical theory can be used to derive an equation for volume:

$$\text{volume}=\text{resistivity}*\text{length}^2/\text{resistance}. \qquad \text{(Eq.1)}$$

Since within a given subject, under certain conditions, short term resistivity and length (distance between electrodes) remain constant, resistance and volume are inversely related.

Previous cross-sectional research (4,5,10,13,14,23,24,27) has demonstrated strong relationships between impedance and TBW or fat free mass (which is correlated to TBW). Numerous investigators have observed high test-retest reliability and also good correspondence between separate laboratories (12).

Studies by Nyboer, (18), Spence et al. (25) and Patterson (19) have demonstrated strong correlations between impedance and acute weight changes (i.e. fluid volume changes) in hemodialysis patients, and studies by Carlson et al. (2), and Mayfield and Uauy (15), have demonstrated strong correlations between impedance and hydration status of burn victims, and infantile diarrhea patients, respectively. It has been demonstrated that bioelectrical properties can be used to estimate cardiac output (9), total body water (23), and limb blood flow (11).

Recently, Patterson (19) has argued that measures of impedance of individual limbs and the trunk (segmental measures) should be better predictors of TBW or fat free mass than the right side whole body measurements. Right side whole body measurement is the most common technique used currently. He bases his argument on the observation that the small bony cross-sections of the wrist and ankle contribute to produce limb impedances which are much higher than trunk impedance. Consequently, when these impedances are summed, the trunk, where most of the resting blood volume is located, has a disproportionately small contribution to the overall measured impedance value. Conversely, the wrist and ankle, which are not much influenced by fluid shifts, strongly influence the total impedance. Patterson presented data from duplicate measurements on patients before and after hemodialysis and found that combined segmental measures yielded a higher correlation coefficient, ($r=.87$) than whole body measures ($r=.64$), in predicting weight changes subsequent to dialysis. However, Patterson's report did not include a rigorous statistical analysis of all the data.

All the bioelectrical/hydration relationship studies, have been cross-sectional or acute treatments without consideration of fluid shifts or of specific resistivity changes. A comprehensive longitudinal (i.e. pre-post systematic fluid manipulation) study of the relationship between hydration status and segmental and whole body resistance and reactance in healthy humans has not been reported. The purpose of the present pilot investigation was to determine the correspondence between changes in segmental limb R and X and estimated changes in body fluid compartments.

Because fluid shifts and losses have been implicated in orthostatic intolerance, decreased cardiovascular function, and space adaptation syndrome, the ability to continuously monitor fluid levels would contribute greatly to our understanding of the physiological responses to acute and chronic exposures to microgravity. The use of reactance measurements as well as resistance measurements may permit discrimination between extra- and intra- cellular water compartments (15,16,17).

METHODS

Subjects

Subjects were two volunteers for a previously approved 13 day bedrest study at Johnson Space Center. Subjects had given prior informed consent for measurement of bioelectrical properties. Subjects were fully advised of the nature of this specific aspect of the bedrest study, and gave permission prior to each measurement.

Conditions

These measurements were made during the course of a 13 day six degree head down tilt bedrest (-6HDT) which was intended to determine the effectiveness of lower body negative pressure (LBNP) and fluid loading in ameliorating loss of orthostatic tolerance consequent to fluid shifts associated with -6HDT and similar to those observed in microgravity. After a two day ambulatory hospitalization, subjects underwent a 13 day bedrest interrupted by LBNP response tests and LBNP and fluid treatments. Subjects were kept on a 2476 Kcal diet with 2500 ml of additional daily fluid intake. This food and fluid level replicates the average intake of the astronauts during Shuttle flights. Body weights were determined with a portable bed scale (Techtronix) just after the noon meal each day. Blood samples were collected prior to breakfast each day. Blood volumes were determined from red blood cells labeled with ^{51}Cr. Plasma volumes were determined from blood volumes corrected for blood removal and hematocrits.

Bioelectrical Measurements

Resistance and reactance were measured at three sites with a RJL analyzer at 50 Khz with 0.8 mA induced current. Prejelled double electrodes (BOMED) were located at the antecubital fossa, just anterior and centered on the acromium process, just distal to the inguinal fold on the anterior surface, and on the anterior surface superior to the patella. In each case, except the inguinal, the electrode was located with the distal border located at the landmark. Injection and current pick-up electrodes were 5cm apart. Inter-electrode distances and limb circumferences at the midpoint between electrodes were measured with a cloth tape. This electrode arrangement permitted determination of three separate electrical measurements designated arm, trunk, and leg. Segmental measurements were used rather than whole-body measurements in keeping with Patterson's (19) observations regarding joint-induced alterations in electrical resistivity. For simplicity, segmental R's were summed to represent an estimator of total body R and designated "combined R". For ease of comparison, resistances and reactances values were also converted to their inverse, conductance.

RESULTS

Figures 1a and 1b, and 2a and 2b, are illustrations of alterations in segmental resistance and reactance throughout the time course of bed rest for subjects A and B, respectively. Subject B underwent two LBNP treatments with saline ingestion and a presyncopal LBNP (labeled PSL) which are shown in the figures.

Figures 3a and 3b portray combined conductance (inverse resistance) and body weight changes (which approximate TBW changes) by day for each subject. Figures 4a and 4b portray combined conductance and plasma volume for each test day of the experiment. Figures 5a and 5b portray combined reactive conductance and plasma volume by day for each subject.

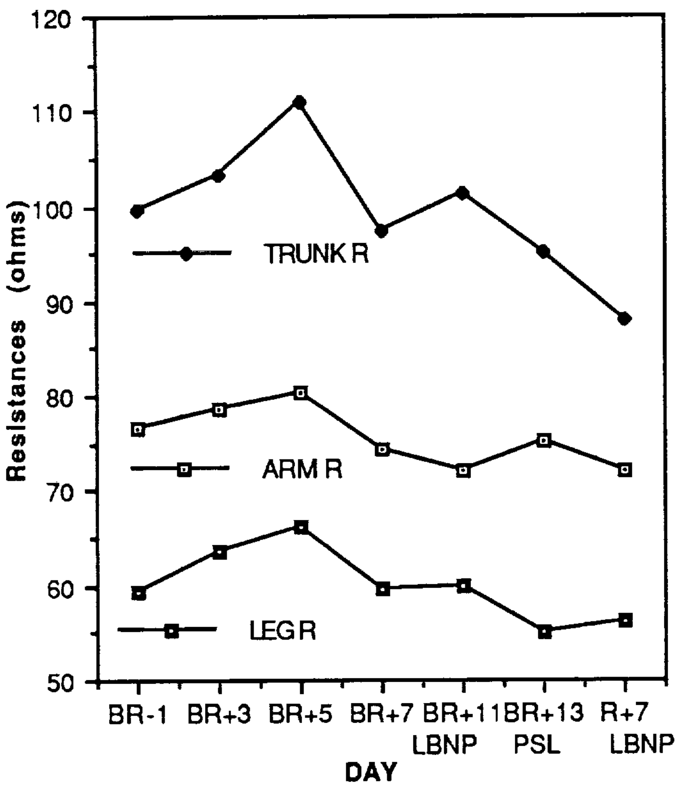

FIG.1a. Segmental resistances by day. Subj A.

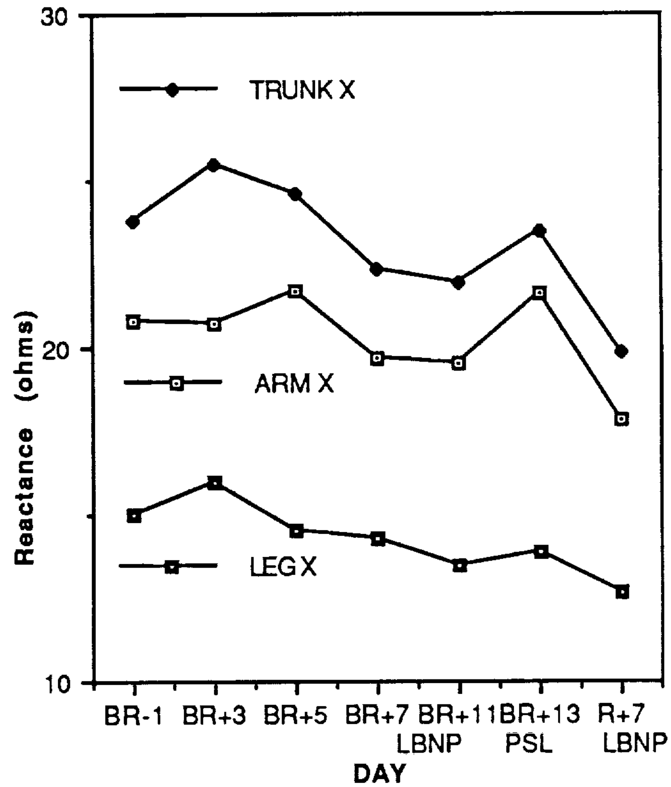

Fig 1b. Segmental Reactances by day. Subj. A.

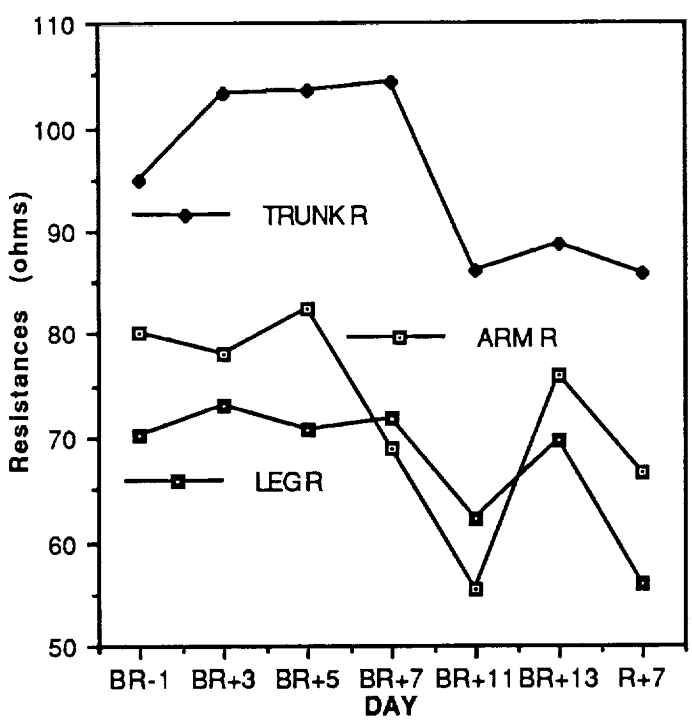

Fig 2a. Segmental resistances by day. Subj. B.

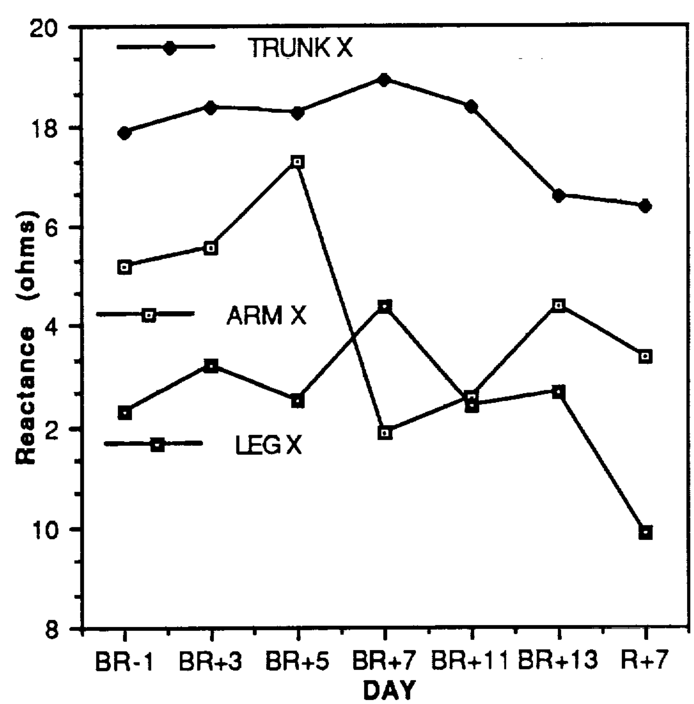

Fig. 2b. Segmental reactances by day. Subj B.

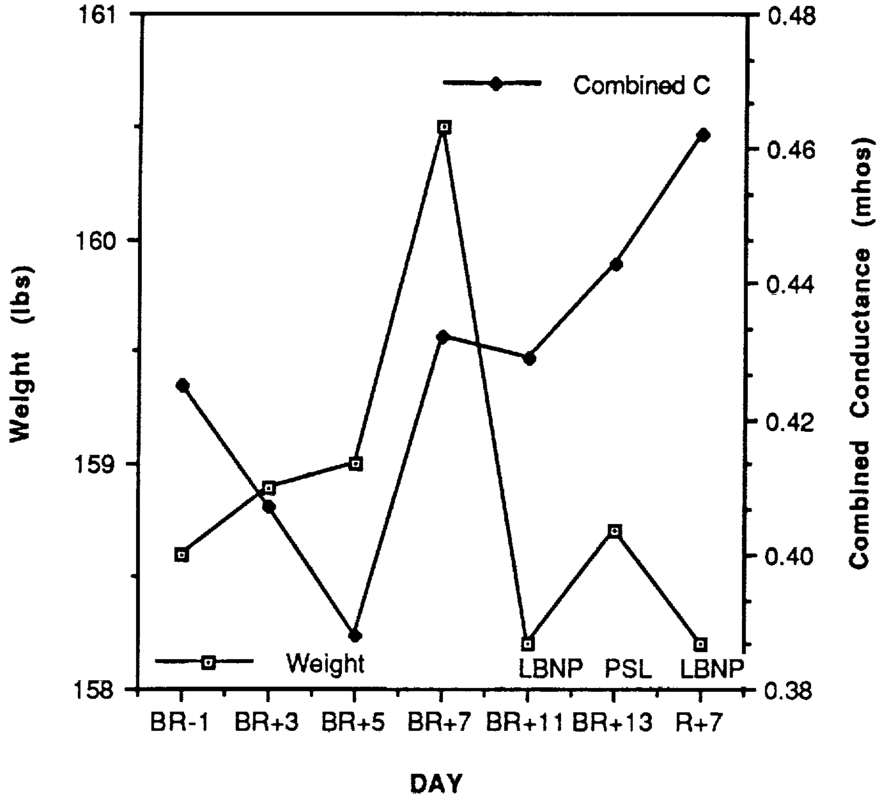

Fig 3a. Combined conductance and body weight by day. Subj A.

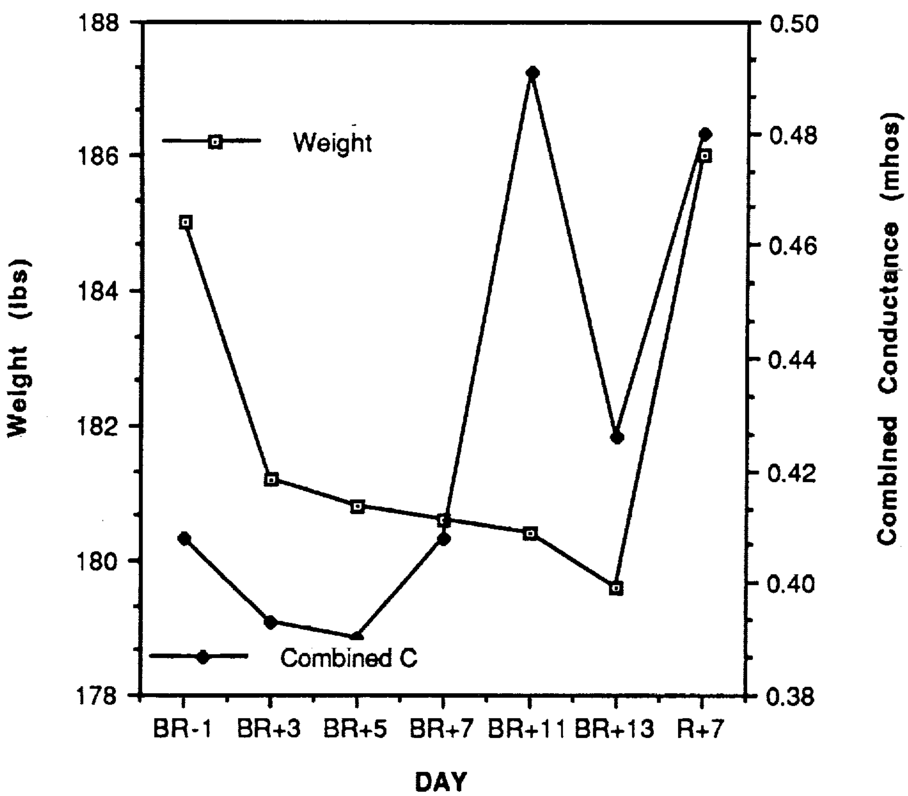

Fig 3b. Combined conductance and body weight by day. Subj B.

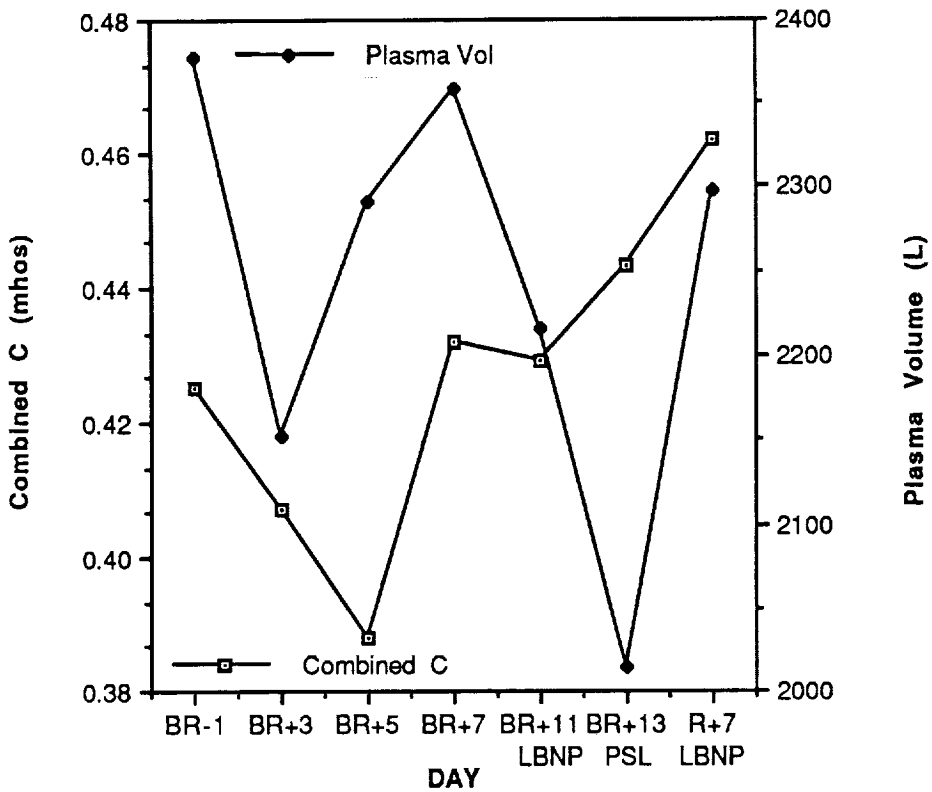

Fig 4a. Combined Conductance and plasma volume by day. Subj. A.

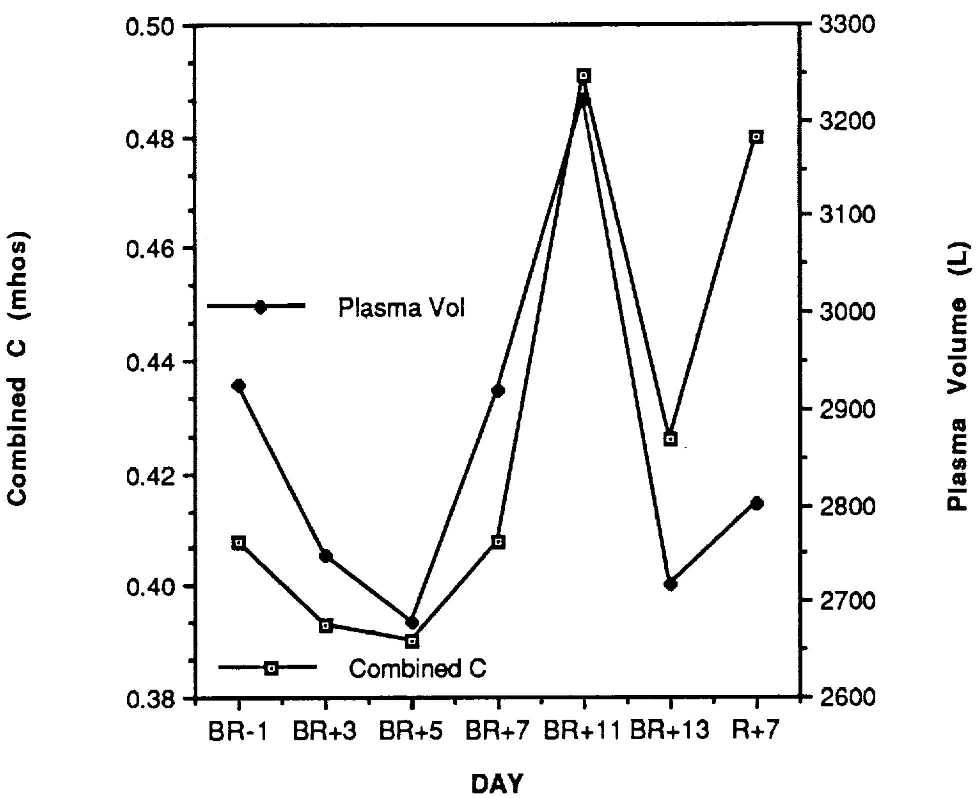

Fig. 4b. Combined conductance and plasma volume by day. Subj. B.

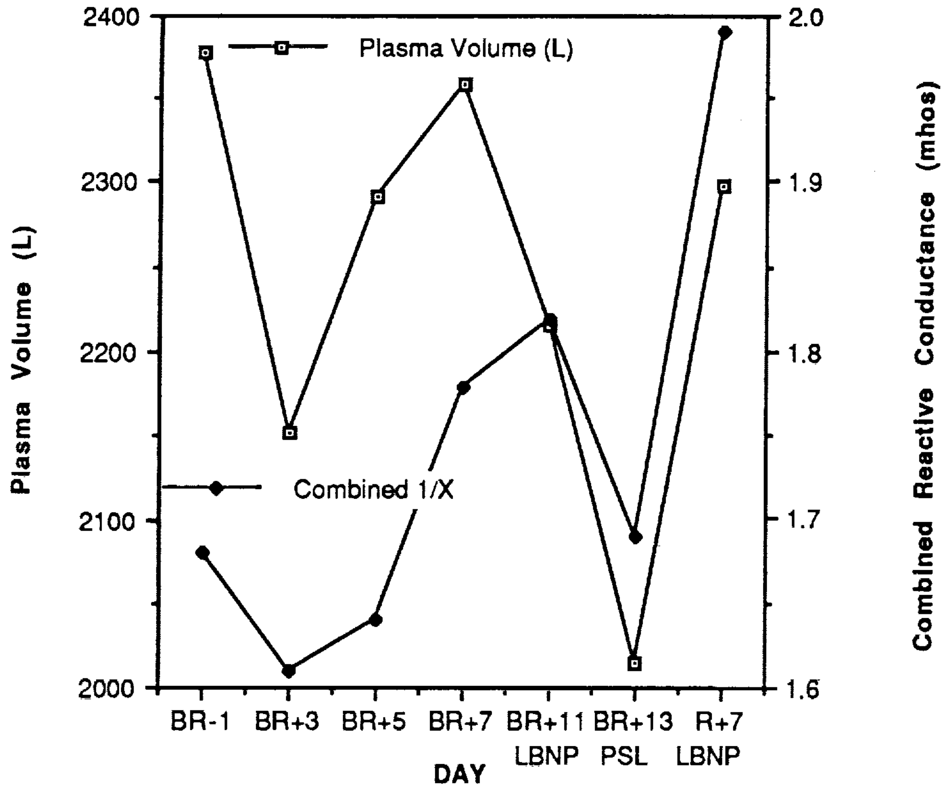

Fig. 5a. Combined reactive conductance and plasma volume by day. Subj. A.

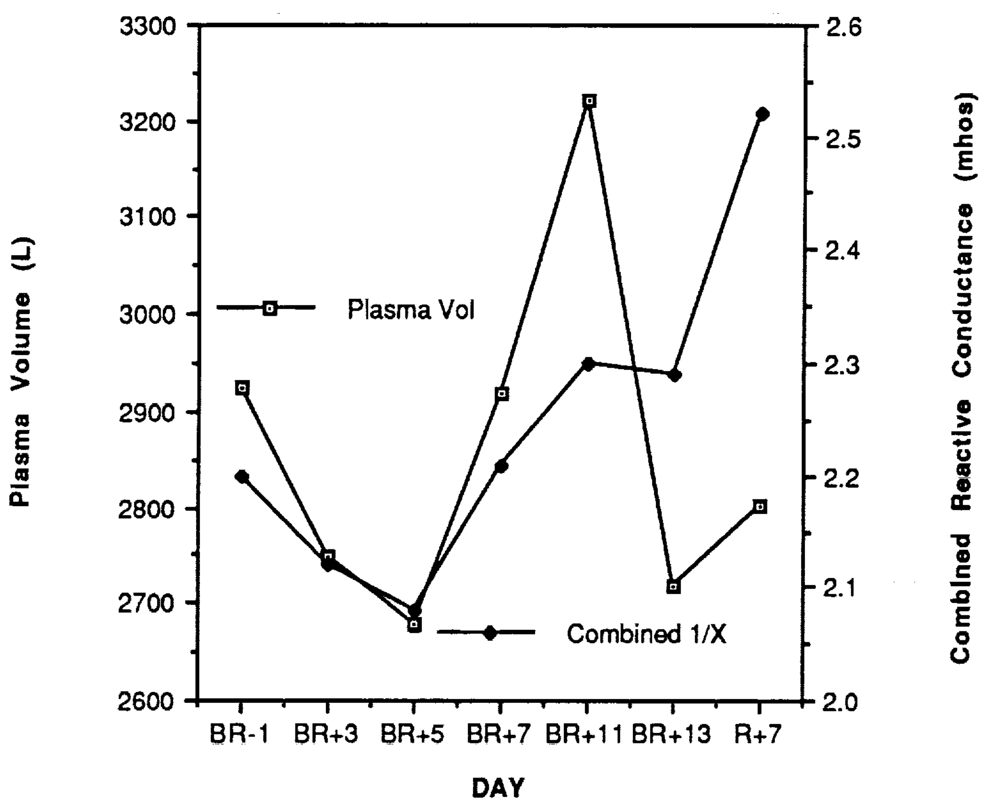

FIG. 5b. Combined reactive conductance and plasma volume by day. Subj. B.

DISCUSSION

Previously cited works suggest that total body water is strongly related to electrical resistance. The findings in the present investigation suggests that human bioelectrical properties may be related to fluid levels in various compartments rather than total body water. For both subjects, individual segmental R's and X's roughly paralleled each other, except arm R and X in Subject B showed an exaggerated drop on bedrest day 5 (BR+5). The segmental approach resulted in arm, trunk, and leg R's which were similar in magnitude. This approach appeared to alleviate previously discussed joint interference problems. In both subjects, body weight loss, which should reflect TBW, appears to be disassociated from conductance (inverse resistance). If TBW and resistance were inversely related, as has been generally believed, good correspondence should have been observed. Since TBW is not altered during LBNP, if R and TBW were related, this relationship should remain robust. In Subject B, rapid weight loss, which should reflect TBW loss, was not closely paralleled by any bioelectrical measurement (Fig.3b). In subject A, combined R roughly tracked plasma volume, but LBNP apparently changed somewhat the relationship between plasma volume and resistance. But, for subject B, combined resistance was closely linked to plasma volume changes (Fig.4b). Combined X appeared to track changes in plasma volume better than R in subject A, but less well than R in subject B (Figs. 5a and 5b).

Interpretation of these data is complicated by the observation that changes in resistance measurements do not consistently relate to changes in fluid levels in a simple way. In the case of dehydration by heating, Hutcheson et al. (6) report a decrease in body weight accompanied by a decrease in impedance (which would be interpreted as an increase in TBW by equation 1). Likewise, Caton et al.'s (3) observations that resistance decreases as skin temperature increases, suggests that the distribution of blood (i.e. into the skin in the case of heating) influences electrical properties. The authors speculate that the shift of fluid between plasma and interstitium may also be involved. This is further substantiated by the observation that impedance changes with changes in posture (20). Obviously, temperature changes and postural changes reflect fluid redistribution rather than changes in total body fluid volume. Changes in specific resistivity are too small and in some cases in the wrong direction to account for these observations.

Many previous investigators have assumed that specific resistivity was unchanged throughout the course of their measurements of bioelectrical properties. Bonnardeaux (1) and Salansky and Utrata (21) reported data from animal studies which suggest that blood osmolality and impedance are inversely related. Likewise Kobayashi et al. (8) reports on a paper written in Japanese by Tanaka et al. (26) which observed that specific resistivity of blood in humans was related to hematocrit. Kobayashi et al. (8) found that adjustment of specific resistivity for hematocrit resulted in much improved impedance cardiography. Postural changes, changes resulting from dehydration due to unreplaced sweat loss, and metabolic activity can all influence the electrical characteristics of blood which would likely result in alterations of electrical properties independent of changes in fluid volumes. In the present study, plasma osmolality was frequently measured and changed only slightly during the measurement period. For Subject A, however, a lower body negative pressure treatment preceded three of the bioelectrical measurements and caused among other things, hemoconcentration. Despite the lack of fluid loss consequent to LBNP, the resistance measurements were influenced (Fig 4a.).

In view of this somewhat cloudy picture, a number of questions remain unanswered. Among these are:

1) How does specific resistivity vary among individuals?

2) Within individuals, how does specific resistivity vary as intravascular, interstitial, and intracellular fluid levels change?

3) Why do segmental resistances and reactances vary in response to the same general body fluid alteration? (i.e. Why did the resistance and reactance values for the segments fail to unanimously track each other in a parallel fashion?)

4) Which fluid compartment(s) exert the greatest influence on electrical resistance and reactance?

CONCLUSIONS

A large body of literature exists which suggests that alterations in body electrical properties are related to alterations in fluid levels. Among these are studies which demonstrate good correspondence between impedance and cardiac output (8,9), impedance and limb volume (11), and impedance and weight changes consequent to dialysis (19). The present data, although limited to two subjects, suggests that electrical changes may be more closely linked to blood volume rather than TBW. This does not directly contradict previous studies, in that TBW and blood volume are probably closely related. Undoubtedly some of the relationships between electrical characteristics and fluid volumes and distributions are causal. The exact nature of these relationships awaits further research.

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