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To develop a reliable procedure for the acute expansion of plasma volume (PV), 27 male volunteers were randomly assigned to either a thermoneutral (25°C and 40% RH) or hot/dry (37°C and 25% RH) environment; subsequently, each subject was seated for at least one hour and then infused I.V. with either 100 or 200 ml of a 25% albumin solution or 0.9% saline. On the day before each infusion, PV was estimated by dye dilution using indocyanine green. The net % change in PV (using Hct and Hb values) was calculated at 1, 3, 6, 9, 12 and 24 hours post-infusion. The PV of subjects residing in the heat after a

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100 ml saline infusion increased significantly over 1 hr values at 6, 9 and 12 h, post infusion but not at 24 h. The same trend, although not significant, was apparent at room temperature. The data suggest a slow, isooncotic, circadian pattern of PV expansion and contraction amplified significantly by heat exposure. The infusion of hyperoncotic albumin (25 g) produced a rapid expansion of plasma volume. The expansion due to albumin alone was maximum at 1 hr post-infusion but accounted for only 44% of the expansion at 12 h. The absolute volume increase was greater and more persistent with the larger (50 g) albumin dose. Heat exposure did not enhance the rapid, albumin-induced expansion but did result in a longer half-life of infused protein and a more consistent increase in oncotic pressure. The data suggest a mechanism for the retention of fluid during heat acclimatization and a useful procedure for plasma volume expansion in humans. •

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Effects of Albumin Administration (I.V.) on Plasma Volume
Expansion in the Heat

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Index Terms: albumin infusion; cardiovascular stability; heat acclimation; heat
acclimatization; oncotic pressure; plasma volume; temperature regulation.

Abstract

To develop a reliable procedure for the acute expansion of plasma volume (PV), 27 males volunteers were randomly assigned to either a thermoneutral (25 C and 40% RH) or hot/dry (37 C and 25% RH) environment; subsequently, each subject was seated for at least one hour and then infused I.V. with either 100 or 200 ml of a 25% albumin solution or 0.9% saline. On the day before each infusion, PV was estimated by dye dilution using indocyanine green. The net % change in PV (using Hct and Hb values) was calculated at 1,3,6,9,12 and 24 hours post-infusion. The PV of subjects residing in the heat after a 100 ml saline infusion increased significantly over 1 hr values at 6,9 and 12h, post infusion but not at 24 h. The same trend, although not significant, was apparent at room temperature. The data suggest a slow, isooncotic, circadian pattern of PV expansion and contraction amplified significantly by heat exposure. The infusion of hyperoncotic albumin (25 g) produced a rapid expansion of plasma volume. The expansion due to albumin alone was maximum at 1 hr post-infusion but accounted for only 44% of the expansion at 12 h. The absolute volume increase was greater and more persistent with the larger (50 g) albumin dose. Heat exposure did not enhance the rapid, albumin-induced expansion but did result in a longer half-life of infused protein and a more consistent increase in oncotic pressure. The data suggest a mechanism for the retention of fluid during heat acclimatization and a useful procedure for plasma volume expansion in humans.

Introduction

Many of the benefits of natural heat acclimatization can be achieved artificially by short, daily exposures to exercise in the heat (12). The resultant physiological adaptations or "indices" of heat acclimatization include, with successive exposures, a progressive reduction of core temperature and pulse rate with a concomitant increase in sweat production. Traditionally, the lowered core temperature is considered a consequence of an improved sweat rate (6,15) which allows for a greater rate of evaporative cooling. The transfer of heat from core to skin, however, is primarily accomplished by the circulatory system (14) and reductions in blood volume result in reflex vasoconstriction of many vascular beds, most notably that of the cutaneous vessels (4). Sweating is also dependent on adequate blood flow as reduction in both sweat rate and estimated skin blood flow have been observed to accompany decreases of plasma volume resulting from dehydration and heat exposure (9,10,17). In studies in which euhydration was maintained during acute exposure to heat, hemodilution (18,19) or no change in plasma volume (9,13) has been reported.

During the early stages of heat acclimatization, one consistent observation has been a rapid expansion of the plasma volume (1,20,23). Senay (21,22) attributed this hemodilution to an influx of interstitial protein and fluid delivered to the vascular volume via the lymphatics and retention of this protein within the intravascular space (20). Senay and colleagues (20) further proposed that plasma volume expansion may be the most important physiological adaptation early in the heat acclimatization process. They hypothesized that an expanded plasma volume could provide for improved cardiovascular stability during exercise and this could account for the lower rectal temperature values.

According to Gauer et.al. (5) an increase in blood volume would occur as a two step process: a) an increase in vascular space and b) an increase in vascular

volume. During exercise in the heat, the increased vascular space is created by a combination of exercise hyperemia and cutaneous vasodilation. This space is theoretically available to accept the fluid and protein delivered to the vascular volume via the lymphatics.

Albumin accounts for about 62 percent of the total protein of human plasma and by virtue of its smaller molecular weight and greater net charges, it is more important than globulin in maintaining the colloid osmotic pressure (7). This pressure is the principal force counteracting filtration pressure and thus albumin plays a major role in maintaining the volume of fluid in the blood. A 25 percent solution of albumin is approximately isoviscous with whole blood and its use in the treatment of shock depended on the premise that, due to its high colloid osmotic pressure, it would increase the circulating blood volume by drawing on the tissue fluids (7,11). Experimental evidence indicated that each gram of albumin should hold 18 cc of fluid in the circulation (16) and, consequently, 25 grams of albumin, representing the osmotic equivalent of 500 cc of citrated plasma, was taken as the standard dose (11).

Although the use of this procedure to expand the plasma volume of heat exposed subjects, by drawing interstitial fluid into the vascular space, might be viewed as limiting the pool of water directly available for sweating, it is consistent with the Senay hypothesis (20). Further, by making an improvement in sweat gland function unlikely, it would provide a more rigorous test of the advantages of improved cardiovascular stability. Finally, the expansion of plasma volume at the expense of the interstitial volume is thought to avoid natriuretic effects common to saline or isoncotic plasma - like infusions (3).

These findings and assertions provide the theoretical basis for simulating and evaluating, in a matter of hours, a stage of heat acclimation that usually requires days to achieve. The purpose, in short, was to develop a reliable

procedure for acutely expanding plasma volume with I.V. albumin prior to work studies in the heat. Subjects were exposed to either thermoneutral or hot/dry conditions to evaluate both the importance of cutaneous vasodilation in the expansion process as well as any acute increases in plasma volume due to passive heat exposure.

Two different masses of albumin (25 g and 50 g) were used to assess dosage effects on the extent and duration (retention) of plasma volume expansion.

Methods

Subjects Twenty-seven healthy male volunteers participated in this investigation. Before the initial test session, each subject was informed of the purpose of the study, the extent of their involvement, any known risks, and their right to terminate participation at will. Each expressed understanding by signing a statement of informed consent.

Protocol All testing was begun in late January and completed by mid April to minimize any effects of natural seasonal heat acclimatization. The test subjects were first divided, on a random basis, into thermoneutral (25°C, 40% RH) and hot/dry (37°C, 25% RH) groups. Both of these groups were subdivided into those receiving the high dose of albumin (50 g in 200 ml saline) and those receiving the low dose (25 g in 100 ml). The distribution of subjects into these groups is shown below:

	<u>Low Dose</u>	<u>High Dose</u>
Hot/Dry	n = 9 (Group 1)	n = 10 (Group 2)
Thermoneutral	n = 4 (Group 3)	n = 4 (Group 4)

Sterile human albumin solutions were obtained from the American Red Cross Blood Services.

Each subject repeated the infusion procedure, under identical conditions, with an equivalent volume of 0.9% saline; thereby serving as his own infusion volume control. The sequence of albumin and saline experiments was randomized and separated by a period of at least one week.

Test volunteers reported to the laboratory on the day prior to an experimental test for physical examinations, medical histories, and determination of plasma volumes (PV). All PV measurements were made at an ambient temperature of $25 \pm 2^{\circ}\text{C}$, and all subjects were seated at least 30 minutes prior to and during the PV measurement. A dye dilution method, employing indocyanine green (Cardio-Green, Hynson, Westcott, and Dunning, Inc.) was used. For this, a small volume (0.5 mg/kg) of ICG dye (5 mg/ml) was injected (< 0.6 seconds) into an antecubital vein (19 gauge pediatric catheter) with blood samples (7 ml) withdrawn from a catheter in the contralateral arm vein at precisely 3, 6, 9, and 12 minutes after injection. ICG concentrations were determined spectrophotometrically (Perkin-Elmer Lambda 3). These levels were then retroplotted to time 0, injection time, using standard regression techniques for an exponential dye clearance model. The PV of each subject was measured on two occasions: once, on the day before the albumin infusion and again on the day before the saline infusion. The average difference between the PV measurements was small, $SD_x = 85$ ml, and not significantly different by a paired 't' test for the 27 subjects. The average value of these two PV measurements was taken as the best estimate of the 'normal' PV for that individual and was used to calculate the absolute change in plasma volume following albumin or saline infusion. Following these preliminary procedures, subjects (Ss) were allowed to leave the laboratory for the evening meal, and later returned to spend the night in a chamber maintained at 25°C , 40% RH. They were awakened at 0600 hours, fed breakfast, and then transferred to the hot/dry

test chamber or allowed to remain for the next 26 hours under thermoneutral conditions.

Initial weight and temperature data were obtained. Both rectal and skin temperature were monitored with a 10 channel digital thermometer (Omega 2176 A). Rectal temperature (T_{re} , °C) was obtained from a thermocouple inserted 12 cm past the anal sphincter. Mean weighted skin temperature (T_{sk} , °C) was calculated from thermocouples placed on the chest, arm, and thigh. The Ss were seated no later than 0730 and were required to remain seated a minimum of 30 minutes prior to and during all blood sampling. Pediatric type catheters, 19 gauge, were placed in contralateral arm veins, and after 30 minutes, a 7-10 ml preinfusion blood sample was withdrawn and the infusion of the appropriate dose of albumin or saline then begun. Albumin was administered at a rate of 2-3 ml per minute; thus, infusion required up to 1.5 h in the case of the high dosage. The end of the infusion period, approximately 0900 hours, was designated as time 0, and the infusion catheter removed. All infusions were completed under the close supervision of an attending physician. At exactly 1,3,6,9,12, and 24 hours post infusion, blood samples were withdrawn. Between samples, the catheter was filled with heparinized saline, and during each collection period, the first three ml of blood was discarded before the 6 ml sample was obtained. Quadruplicate determinations were made of hematocrit and duplicate determinations were made of all other blood measurements. Test ss were confined to either test chamber for this 24 h interval; sedentary activities were permitted. All food, recreational and sanitational facilities were provided within the chamber. Ss were encouraged to drink 500 ml of citrus - flavored, non - carbonated beverages during the waking hours, and exact times and volumes consumed were recorded. Meals (T.V. dinners) were provided in the test chamber at 1200, and 1630, and 0600 hours the following morning.

Additional body weight and temperature measurements were made at hourly intervals throughout the day (0 to 12 hours post-infusion) and at 0700 hours the following morning.

Commercial tests were used to determine hemoglobin (Hyclor Cat.#116C), total protein (Worthington Cat.#279347), and albumin (Worthington Cat#27907) on a Gilford 3402 Automatic Enzyme/Endpoint Analyzer Plasma oncotic pressure was determined by a IL Weil Oncometer System 186.

Percent changes in PV following the infusion of saline or albumin were calculated as net % change (from the preinfusion sample) according to the formula of Dill and Costill (2) using measured hematocrit (corrected for trapped plasma) and hemoglobin concentration. Statistical analysis were performed by the student paired and non-paired t test. The null hypothesis was rejected at $p < .05$.

Results

The twenty-seven male volunteers had a mean ($\pm$ SD) age of 25 ± 5 years, weight of 74.6 ± 10.8 kg, height of 177 ± 7 cm and body surface area of 1.91 ± 0.15 m². The importance of maintaining a consistent drinking regimen during waking hours was adhered to by all Ss. The fluid intake for 24 h averaged 2.5 l and 6.5 l for thermoneutral and hot/dry groups, respectively. Not surprisingly, both the thermoneutral and hot/dry groups averaged a net weight gain of 1.4 and 1.7 kg, respectively, during the waking hours (preinfusion to 12 h post-infusion). These results suggest a state of positive fluid balance was achieved.

Another consistent observation was a slow rise in rectal temperature which appeared to peak at approximately 1800 h (9 h post-infusion). The average increase ($p < 0.005$) above pre-infusion values was 0.34°C for the thermoneutral

group and 0.37°C for the hot/dry group. All subjects in the hot/dry environment maintained a T_{re} approximately 1°C higher ($T_{\text{re}} = 37.39 \pm 0.39^{\circ}\text{C}$, $n = 37$, 9 h post-infusion) than that of subjects in the thermoneutral test ($T_{\text{re}} = 36.42 \pm 0.40^{\circ}\text{C}$, $n = 16$, 9 h post infusion). The average mean weighted, pre-infusion, skin temperatures ($T_{\text{sk}} = 35.6 \pm 0.6^{\circ}\text{C}$, $n = 31$) for subjects in the heat remained approximately 2.6°C higher than that of thermoneutral subjects ($T_{\text{sk}} = 33.0 \pm 0.5^{\circ}\text{C}$, $n = 16$) throughout the observation period. Neither group demonstrated any consistent indication of a circadian periodicity of T_{sk} .

In order to compare the measured and theoretical PV, calculations were made for each subject using the hematocrit and the formula of Hidalgo (8). By this formula the average theoretical PV for the group of 27 subjects was 3000 ± 334 ml, while the measured PV, using ICG, was $3,138 \pm 756$ ml. Thus, the two methods appear to give reasonably consistent ($+ 4.6\%$) measures of PV.

Tables 1 and 2 contain the control values and post-infusion changes in plasma protein oncotic pressure. It should be noted that within the 1 to 12 h post-infusion period, all but one (9 hours, 200 ml saline, Table 2) of the oncotic pressures following saline infusion are lower than the pre-infusion measurement. In contrast, Group 1 infused with 25 g albumin in the heat demonstrated a significant ($p < 0.05$) increase in plasma protein oncotic pressure for 6 hours, post-infusion. With higher the dose of albumin (50 g, group 2, 33°C), the elevated oncotic pressure persisted for 12 hours. With either dose of albumin, subjects remaining in the heat had significantly elevated plasma protein oncotic pressures 24 h post-infusion. At room temperature and with the same dose (50 g, group 4), the significant elevation in plasma protein oncotic pressure was maintained for only 3 hours, post-infusion.

Tables 3 and 4 list the effects of saline or albumin infusion on PV. PV increased throughout the day following minimal saline infusion (group 1, 100 ml

saline) in the heat. This increase, relative to the 1 hour post-infusion volume change, was significant ($p < 0.05$) at 6, 9, and 12 hours post-infusion (between 1500 and 2100 hours). The same trend, although not significant, was apparent at room temperature (group 3, 100 ml saline). The change noted at 12 hours post-infusion (± 285 ml) is equivalent to a 9.3 percent increase in PV. The following morning (24 hours, post-infusion), the PV were significantly less than the 1 hour post-infusion volumes (group 1 and 3, 100 ml saline).

The interpretation of the direct effects of albumin on the dynamics of PV expansion is complicated by the slow, spontaneous increase (6-12 hours post-infusion) during the waking hours (noted above). The same effect is evident following albumin infusion (Table 3, group 1) as the PV increased throughout the day and was significantly greater at 9 hours, post infusion (+ 17%). Prior to this (1-3 hours, post infusion), the 25 g dose had increased PV by 13 % which was equivalent to a fluid increase of 15.5 ml per g of albumin. The 50 g dose in the heat (Table 3, group 2) resulted in a significantly larger expansion at 1 hr post-infusion (+ 15%) than did the 25 g dose. Heat exposure did not significantly increase the acute PV expansion (1-3 h, post-infusion) over that found with either dose at room temperature. Although the fluid increase was equivalent to only 10 ml per g of albumin, the expansion obtained with the larger dose in the heat was stable for up to 6 h post-infusion. The duration of the PV expansion (groups 3 and 4, Table 4) was much shorter (1 hour for 25 g, 6 hours for 50 g albumin) for subjects at room temperature. Although the fluid increase per g of albumin administered (7.8 ml per g) was low, the persistence of the expansion with the 50 g dose for up to 6 h, post-infusion, represented an important duplication of results in the heat. The PV changes noted above correspond reasonably well with the changes in plasma protein oncotic pressure noted earlier (Tables 1 and 2).

Net changes in circulating total plasma protein mass (Tables 5 and 6) were calculated as the product of measured changes in plasma protein concentration (mg per ml) and PV (ml) minus the pre-infusion value. These calculations reveal that following saline infusion (100 ml) in the heat (Table 5, group 1) the expanded PV (6-12 hours, post-infusion) contained an additional 9-13 grams of protein presumably derived or translocated from the interstitial compartment. The same trend toward an increasing total plasma protein mass with time at room temperature was evident (Table 6, groups 3 and 4) 9-13 g increment at 12 h post-infusion. The inability to reproduce this effect with 200 ml saline in the heat (Table 5, group 2) was due primarily to two individuals who demonstrated a consistent decline in circulating plasma protein concentration throughout the day (-7.6 and -8.6% at 12 h). The mean reduction in total plasma protein mass of these two subjects was 17.1 g at 12 h. With these two values omitted, the mean increase for the group was 11.0 g.

The effects of the albumin dose on the dynamics of total protein mass and PV are complicated by the concomitant diurnal flux noted above. The albumin effects were isolated by assuming that the changes observed following saline infusion were independent of, but superimposed upon, changes attributable solely to the infusion of albumin. The kinetics of the albumin infusion, therefore, were isolated by subtracting the appropriate saline (control) value from the albumin (experimental) value at 1,3,6,9,12 and 24 h following infusion. This was done using the derived values for the total circulating protein mass (as in Tables 5 and 6). The results for both high and low doses under hot/dry and thermoneutral conditions are shown in Figure 1. These "isolated" curves indicate an initial rapid loss of infused protein from the vascular space which moderated with time in all four experimental situations. In the hot/dry conditions, high and low dose, half of the infused protein had disappeared from the vascular space by 12 hours

and a further substantial decrease was noted at 24 hours post-infusion. In the thermoneutral conditions, both doses, half of the infused protein had disappeared from the vascular space in only 9 hours, but with little or no further decrease at 24 hours post-infusion.

A preliminary attempt was made to characterize the disappearance of infused protein using a least squares curve-fitting procedure. Exponential, logarithmic and linear functions were tested using the 1-12 hour points on all four disappearance curves. The logarithmic function provided the highest coefficients of determination for the four conditions: $R^2 = 0.9380, 0.9823, 0.9255$ and 0.9879 for the hot/dry, low and high doses and thermoneutral low and high doses, respectively.

Discussion

Between 6 and 12 hours following a 100 ml saline infusion, heat-exposed subjects (Table 3, group 1) had a significant expansion of PV (9.3%, 12 h). Although there was a net flux of 9-13 grams of protein into the plasma compartment (Table 5, group 1), the plasma oncotic pressure declined slightly during this interval (Table 1, group 1). The same trend, although not significant, was apparent at room temperature. The larger saline infusion volume (Table 3, group 2) increased the 1 h post-infusion volume change and, thus, masked the effect. By the following morning (24 h post-infusion), the plasma volume had shrunk to less than the 1 hour post-infusion volume. These data suggest a circadian pattern of plasma volume expansion and contraction amplified significantly by some factor or factors related to heat exposure. The reduction in protein oncotic pressure coincident with an apparent influx of protein into the vascular space (Table 5, group 1) suggests that the "driver" for this expansion is not oncotic. This may, in fact, reflect some hormonally or hydrostatically

induced influx of hypooncotic fluid, perhaps via the lymph, from the interstitial space. On the other hand, the ratio of the volume increase to the change in circulating protein mass was very high (19.5 ml per g at 12 h). Since the subjects in the heat had averaged a 1.7 kg weight gain during the waking hours, the high volume to protein mass ratio could reflect a state of hyperhydration. It appears, therefore, that the observed elevations in core and skin temperatures with heat exposure are not the only factors that could explain the expansion of plasma volume between 1500 and 2100 hours. This does not, however, detract from the observation that the circadian pattern of the plasma volume expansion-contraction cycle was significantly enhanced by the 37°C environment.

Given the passive nature of the heat exposure and the slowness of the response, it is possible that exercise, like heat exposure, might amplify this process. For example, Senay and colleagues (20) observed a net transfer of protein into the vascular space following exercise under control and hot, humid conditions. In their study (20), the cumulative gain in total circulating protein during 3.5 h of work on control and heat exposure days averaged 8.6 and 8.8 grams, respectively. Thus, there was no effect of environmental heat on the amount of protein accumulating within the vascular volume (8-9 grams) during the work. By the same token, we found a quantitatively similar net influx of protein (9-13 grams) during the waking hours. This net influx was similar in all control conditions studied (hot or thermoneutral; 100 or 200 ml saline) and, thus, no significant environmental heat effect on the amount of protein accumulating in the vascular volume was measurable. Taken together, these results suggest that exercise, but not heat-exposure, will profoundly alter the time-course of the increase in circulating protein mass during the waking hours. This observation does not address or preclude any heat acclimatization effects on the net retention of protein within the intra-vascular volume.

In contrast to this relatively slow, isooncotic expansion of plasma volume and circulating total plasma protein mass during the waking hours, the increase due to hyperoncotic albumin infusion was rapid. For example, when the increase in Pv following saline infusion was subtracted from the appropriate albumin infusion value, all of the albumin-induced increases were maximum at 1 h post-infusion with no further significant increases. The magnitude and duration of the albumin-induced increases, however, were related to the Mass of protein infused. As noted in the results, the larger dose (50 g) produced a significantly greater and more persistent expansion. With either dose, the albumin-induced expansion (1 h post-infusion) in the heat was no greater than at room temperature. The 50-78 ml increments (1 h post-infusion) in the heat (Table 3 vs Table 4) were not significantly different from the corresponding values at room temperature. Alternately, there was a generally larger fluid increase per gram of protein when administered in the heat. The 25 g dose of albumin in the heat resulted in a 15.5 ml elevation in plasma volume per gram, which was quantitatively similar to that observed by Senay (20) following work in the heat (15.2 ml per g of protein added to the vascular volume). At 25°C the same dose (25 g, 12.0 ml per g) or at 37°C twice the dose (50 g, 9.5 ml per g; $p < 0.0005$) lowered the volume to mass ratio achieved. Thus, both the mass of protein translocated into the vascular space as well as the state of cutaneous vasodilation appear to alter the plasma volume to net protein mass ratio. Likewise, the quantitative significance of the circadian PV expansion is demonstrated by the observation that the 12 h post-saline infusion volume (Table 3) accounts for 56% of the value of the 12 h post-albumin infusion volume.

Senay and colleagues (20) reported that although both non-acclimatized and acclimatizing subjects demonstrated similar net gains of protein and fluid within the vascular space during work, the acclimatizing subjects generally retained a

greater amount of this protein and fluid within the vascular volume over repeated exposures. The small but persistent (Tables 1 & 2, 24 h vs 3 h) elevations in oncotic pressure following albumin infusion in the heat generally supports the observation by Senay (20) that net protein flux into the vascular space is better maintained by acclimatizing subjects. This is further supported by the observation (Figure 1) that the half-life of the infused albumin is greater in the heat (12 h) than in thermoneutral conditions (9 h).

In conclusion, we have described a slow, isooncotic, circadian pattern of plasma volume expansion and contraction over a 24 hour period. The magnitude of the fluid and protein flux is similar to that described by others during 3.5 hours of exercise. A rapid expansion of PV was achieved by the infusion (I.V) of hyperoncotic albumin solutions. The absolute volume was larger and stable longer with the larger (50 g) albumin dose. Residence in the heat did not significantly increase the rapid, albumin-induced plasma volume expansion (1-3 hrs) but it did significantly enhance the slow, isooncotic expansion (9-12 h). Heat exposure following albumin infusion resulted in a longer half life of the infused albumin and a more persistent increase in oncotic pressure. Both observations suggest a mechanism for the persistent increase in plasma volume during heat acclimatization. The data suggest a potentially useful procedure for human studies requiring plasma volume expansion.

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Disclaimers

The views, opinions, and/or findings contained in this report are those of the authors and should not be construed as an official department of the Army position, policy, or decision, unless so designated by other official documentation.

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

Figure Legend

Fig 1. Loss of infused albumin from the vascular space during a 24 hour period under hot/dry and thermoneutral conditions. See text for details.

TABLE 1

Change¹ in Plasma Protein Oncotic Pressure (mmHg) in the Heat

Dose	Mean Pre Infusion Oncotic Pressure	Hours Post Infusion						
		1	3	6	9	12	24	
Group 1 100 ml Saline (n=9)	25.1	- 0.3 ± 1.2	- 0.03 ± 0.8	- 0.7 ± 1.2	- 0.9 ± 1.2	- 1.9 ± 1.4	0.1 ± 0.8	
Group 1 100 ml Albumin (n=9)	25.5	1.3* ± 0.8	1.2* ± 1.7	0.6* ± 1.1	- 0.5 ± 1.9 (8)	- 0.8 ± 1.9	1.4* ± 1.6	
Group 2 200 ml Saline (n=9)	25.5	- 1.2 ± 1.0	- 0.5 ± 0.5	- 1.3 ± 1.4	- 0.5 ± 1.2 (8)	- 1.4 ± 0.9	0.7 ± 0.8	
Group 2 200 ml Albumin (n=10)	24.8	3.3* ± 1.6 (9)	2.3* ± 1.1	1.3* ± 1.2	1.3* ± 1.8	1.0* ± 2.1	2.6* ± 2.0	

¹ Mean ± S.D. of change from individual pre infusion values.* Significant difference ($p < 0.05$) from corresponding saline infusion values.

TABLE 2

Change in Plasma Protein Oncotic Pressure (mm Hg) at Room Temperature

Dose	Mean Pre Infusion Oncotic Pressure	Hours Post Infusion					
		1	3	6	9	12	24
Group 3 100 ml Saline (n=4)	24.1	- 0.8 ± 0.4	- 0.1 ± 1.0	- 0.7 ± 0.7	- 1.0 ± 0.6	- 1.8 ± 1.5	- 0.03 ± 1.2
Group 3 100 ml Albumin (n=4)	24.8	0.5 ± 1.6	- 0.3 ± 1.7 (3)	- 0.6 ± 0.8	- 0.4 ± 1.6 (3)	- 1.1 ± 0.5	- 0.3 ± 1.9
Group 4 200 ml Saline (n=4)	24.0	- 0.9 ± 2.3	- 0.2 ± 0.8	- 0.03 ± 0.8 (3)	0.5 ± 2.9	- 0.1 ± 1.7	1.0 ± 2.6
Group 4 200 ml Albumin (n=4)	24.2	3.2* ± 0.9	3.1* ± 2.8	1.5 ± 1.6	2.0 ± 2.3	1.6 ± 1.2	3.0 ± 2.2

* Significant difference ($p < 0.05$) from corresponding saline infusion values.

TABLE 3

Change in Plasma Volume (ml) in the Heat

Dose	Mean Pre Infusion Plasma Volume	Hours Post Infusion						
		1	3	6	9	12	24	
Group 1 100 ml Saline (n=7)	3073	56 ± 68	71 ± 60	179 ⁺ ± 130	203 ⁺ ± 86	286 ⁺ ± 99	- 63 ⁺ ± 109	
Group 1 100 ml Albumin (n=9)		379* ± 102	394* ± 143	393* ± 220	524* ⁺ ± 215	508* ± 213	61* ⁺ ± 151	
Group 2 200 ml Saline (n=10)	3323	102 ± 100	117 ± 125	164 ± 143	141 ± 159	195 ± 264	- 125 ⁺ ± 153	
Group 2 200 ml Albumin (n=10)		477* [†] ± 80	502* ± 151	463* ± 264	352* ^{††} ± 211	351 ± 222	- 24* ⁺ ± 98	

* Significant difference ($p < .05$) from corresponding saline infusion values.† Significant difference ($p < .05$) from 1 hr post infusion values.†† Significant difference ($p < .05$) from 100 ml dose.

TABLE 4

Change in Plasma Volume (ml) at Room Temperature

Dose	Mean Pre Infusion Plasma Volume	Hours Post Infusion						
		1	3	6	9	12	24	
Group 3 100 ml Saline (n=4)	2727	49 ± 140	16 ± 155	96 ± 154	202 ± 142	179 ± 132	- 93 ± 231	
Group 3 100 ml Albumin (n=4)		301 ± 160	281 ± 270	318 ± 244	295 ± 198	287 ± 206	41 ⁺ ± 182	
Group 4 200 ml Saline (n=4)	3223	161 ± 223	145 ± 148	161 ± 110	109 ± 186	169 ± 155	- 110 ± 182	
Group 4 200 ml Albumin (n=4)		427* ± 147	383* ± 36	353* ± 66	281 ± 50	314 ± 95	- 14 ⁺ ± 112	

* Significant difference ($p < .05$) from corresponding saline infusion values.+ Significant difference ($p < .05$) from 1 hr post infusion values.

TABLE 5

Change in Circulating Total Plasma Protein Mass of Men in the Heat

Hours Post Infusion

Dose	Mean Total Plasma Protein Mass (g)	Hours Post Infusion					
		1	3	6	9	12	24
Group 1 100 ml Saline (n=9)	216	2.5 ± 3.6	6.1 ± 5.3	9.1 ⁺ ± 7.9	13.3 ⁺ ± 7.6	9.7 ⁺ ± 8.4	0.6 ± 7.1
Group 1 100 ml Albumin (n=9)		29.6* ± 7.7	29.8* ± 9.0	26.1* ± 11.5	28.2* ± 12.4	25.1* ± 17.2	9.2* ⁺ ± 12.9
Group 2 200 ml Saline (n=10)	219	2.4 ± 2.8	5.0 ± 6.9	5.0 ± 6.9	3.8 ± 11.0	5.4 ± 15.4	- 2.3 ± 10.5
Group 2 200 ml Albumin (n=10)		46.5* ± 13.3	41.0* ± 13.3	30.4* ⁺ ± 15.8	26.4* ⁺ ± 15.1	24.8* ⁺ ± 17.8	9.0* ⁺ ± 11.0

⁺ Significant difference ($p < 0.05$) from pre to 1 hr. sampling.* Significant difference ($p < 0.05$) from corresponding saline run.

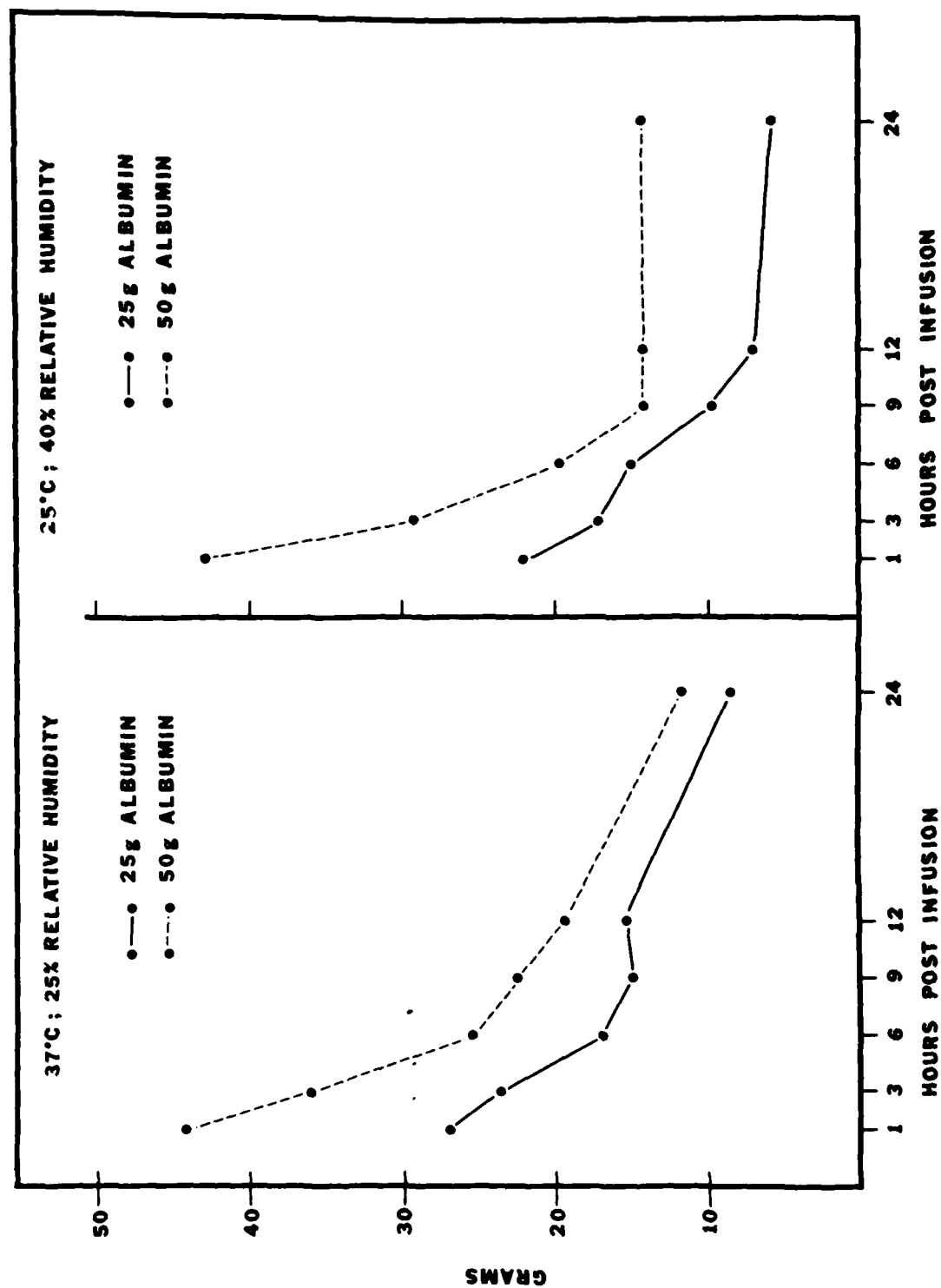
TABLE 6

Change in Circulating Total Plasma Protein Mass of Men at Room Temperature

Dose	Mean Total Protein Mass (g)	Hours Post Infusion						
		1	3	6	9	12	24	
Group 3 100 ml Saline (n=4)	236.4	0.1 ± 8.2	2.7 ± 9.7	1.9 ± 10.4	8.4 ± 6.9	8.6 ± 7.2	- 1.6 ± 7.5	
Group 3 100 ml Albumin (n=4)		22.2* ± 5.0	19.6* ± 4.8	17.1* ± 9.1	18.1* ± 5.1	15.5 ± 6.6	4.2* ± 7.9	
Group 4 200 ml Saline (n=4)	233.8	1.8 ± 4.8	7.2 ± 7.6	9.6 ± 7.8	10.1 ± 11.4	12.9 ± 13.0	0.2 ± 13.1	
Group 4 200 ml Albumin (n=4)		44.6* ± 13.0	36.5* ± 10.7	29.4* ± 7.9	24.3* ± 8.8	27.1* ± 8.6	14.5* ± 8.5	

* Significant difference ($p < 0.05$) from corresponding saline run.+ Significant difference ($p < 0.05$) from pre to 1 hr. sampling.

NET CHANGE IN TOTAL PROTEIN MASS (grams)



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