FLUID BALANCE IN ARTIFICIAL ENVIRONMENTS: II. INFLUENCE OF PHYSIOLOGICAL CHANGES UPON RATES OF SKIN INSENSIBLE WATER LOSS

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PREFACE

A prior report submitted in fulfillment of this contract (Fluid Balance in Artificial Environments: I. Role of Environmental Variables) reported on the influence of the environment on skin insensible water loss and the resultant development of physical signs and symptoms. The research reported in this paper now summarizes the effect of state of hydration on skin insensible water loss. Use of both of these documents now provides a detailed analysis of the interaction of man and the environment as it relates to loss of water through the skin.

The authors wish to express their appreciation to the many individuals in the USAF School of Aerospace Medicine that contributed to the conduct of this study. In particular, we would like to express our thanks to Colonel Frank R. Lecocq, USAF (MC) for his helpful comments in the design of the experiment and the review of the results, to Major William J. Sears, USAF (BSC) for his assistance in data reduction, and to Captain Philip G. Brown, USAF (BSC) for his assistance in establishing and controlling the environmental variables in the chamber.

B. E. WELCH, Ph.D.

I. INTRODUCTION

In a previous series of experiments conducted in this laboratory the relationship of skin insensible water loss (IWL_S) to environmental variables has been thoroughly explored (1). The significant and reproducible effects of ambient temperature (T_a), water vapor pressure (P_{H_2O}), total barometric pressure (P_B), wind speed (V), and atmospheric gas composition (G.C.) upon the rate of water loss from human skin under non-sweating conditions were documented. During these studies, all experimental subjects were kept in a state of normal hydration with a fixed fluid and salt intake and a rigid daily program. It was felt that physiological extremes were adequately controlled during these studies and that the true effect of physical changes in the environment could be clearly documented.

The present series of studies were designed to vary the physiologic status under constant environmental conditions. With careful control of the physical parameters of the environment, i.e., T_a, P_{H_2O}, P_B, V, and G.C., it would be possible to vary the physiological state of the experimental subjects and document any significant changes in rates of skin insensible water loss that might be related to these physiological changes.

II. SUMMARY

1. Changes in the state of hydration of the human body can alter rates of skin insensible water loss by as much as 30% under conditions of this study.
2. Skin insensible water loss rates are altered significantly in conditions of both overhydration and underhydration.
3. Antidiuretic hormone (or Pitressin) does not appear to play a direct role in these alterations of skin insensible water loss rates.
4. Mechanical and physical forces working in the dehydrated or overhydrated skin may be directly responsible for changes in insensible water loss rates.
5. Peripheral vasodilatation, even though accompanied by small changes in skin temperature, does not alter rates of skin insensible water loss.
6. There is no evidence that rates of skin insensible water loss can be adapted or acclimatized by environmental challenges.
7. Overall, within the limits of this study, there is little or no evidence that skin insensible water loss rates can be actively and directly altered by physiological changes other than state of hydration. If physiological changes are also associated with physical or mechanical alterations in the dermis-epidermis and in the skin-air interface, then modification of rates of IWL_S may occur, passively and indirectly.

III. BACKGROUND INFORMATION

The marked influence of environmental variables upon rates of skin insensible water loss has been well documented in the literature and has led many investigators to conclude that IWL_S is controlled exclusively by environmental factors (2, 3, 4, 5, 6, 7, 8). However, numerous studies have also been undertaken to quantitate any physiological effects on IWL_S related to changes in body hydration, salt content, antidiuretic hormone levels, peripheral circulation, and previous adaptation to unusual environments. Many of these studies have produced inconclusive or conflicting data although the great majority have tended to show negative results.

Investigations of the relationship of the state of hydration to rates of skin insensible water loss date back to 1929 when Zak (9) proposed that edematous patients in congestive heart failure actually absorbed water through their skin from the air around them. One of his students, Neurath (10), followed up this line of investigation and later published data claiming a "negative insensible perspiration" in several of his patients. Studies by many other investigators failed to substantiate the claims of Zak and Neurath (11, 12, 13).

In 1931, however, Manchester, Husted, and McQuarrie performed several studies in which they believed that they had demonstrated a reduced rate of skin water loss when body water content was also diminished (14). The following year Levine and Wyatt (15) determined that skin water loss in infants diminished greatly (11%) after dehydration,

although a significant fall in respiratory quotient could have accounted for some of this apparent reduction. Other studies by Newburgh and Johnson (16) and by Hall and McClure (17) contradicted this data and indicated that reduction in body water by as much as 6% did not alter rates of skin insensible water loss. Reduction in body water by more than 6%, however, did result in a fall in IWL_S.

Studies in overhydrated subjects were also conducted. Hall and McClure (17) forced subjects to ingest as much as 3700 cc of water over a three-hour period without noting significant changes in IWL_S. A similar study performed on children (18) also demonstrated no change in IWL_S rates. All of these subjects were given water loads without significant salt, however, and the effect of these loads on plasma volume and body water expansion is not known. Hypotonic and isotonic volume expansion were not examined.

A possible role for circulating hormones in the regulation of IWL_S was suggested by the work of Barker-Jorgensen (19) and Ussing (20) who showed that posterior pituitary extract (Pitressin) increased the rate of water passage through frog skin. Follow-up studies by Peiss (7) indicated that posterior pituitary extract might also act to increase diffusive water loss through isolated dog skin, but quantitative data has not been made available, and no human work has been forthcoming.

The effect of alterations in the peripheral vasculature with variations in peripheral blood flow has also been extensively investigated.

The role of blood flow is closely tied to skin temperature since the latter is largely dependent upon the former. The rate of skin insensible water loss has been observed to increase with rising skin temperature by numerous investigators (3, 4, 7, 21), so one might naturally conclude that peripheral blood flow changes would have a similar effect on IWL_S. This significant effect of peripheral blood flow upon IWL_S rates has, however, not been confirmed. Hardy and Soderstrom (22) found that vascular changes did not alter rates of skin insensible water loss when skin temperatures were below 28° C., and Pinson (2) concluded that vascular changes had no effect upon IWL_S rates when skin temperature did not vary more than a few degrees. Grice and Bettley (23) applied agents locally to cause vasoconstriction and vasodilatation under skin capsules. They found no significant changes in skin water loss rates although skin temperature changed as much as 1.5° C. when the agents were applied. When skin temperature was diminished drastically through the use of a hypothermia apparatus, then IWL_S rates fell as much as 38%. Another study by Baker and Kligman (24), also using the capsule technique, supported the conclusion that mild to moderate changes in peripheral blood flow had no significant effect upon rates of skin insensible water loss.

A final role for physiological alterations of skin water loss rates concerns the processes of adaptation or acclimatization. Thermal sweating, being an active physiological process, exhibits remarkable adaptability with significant adjustments to changing environmental situations.

When a subject is placed in a very warm environment, over a period of time he acclimatizes to that environment by altering his sweat gland response. He is gradually able to supply more sweat to his skin for a given environmental stimulus. Is there such an acclimatization with skin insensible water loss? Does exposure to one environment alter the basic response of the subject to that environment or to another environment? There is very little data in the literature to answer this question one way or the other, but the finding of adaptability or acclimatization in the rate of skin water loss would have important implications as to its physiological control.

The questions of physiological responsiveness of the IWL_S mechanisms in terms of state of body hydration, level of antidiuretic hormone, changes in peripheral circulation, and possible acclimatization will be explored in this paper.

IV. METHODS

All experimental techniques were identical to those described in the previous study (1). Skin insensible water loss was measured utilizing the whole-body gravimetric technique on a sensitive metabolic scale. Metabolic weight loss and respiratory insensible water loss were also measured so that skin insensible water loss rates could be isolated.

Six volunteer subjects were selected from basic trainees at Lackland AFB, Texas. The subjects, all male Caucasians between the

ages of 18 and 21, were thoroughly screened for metabolic, renal, thyroid, pulmonary, hematologic, or dermatologic abnormalities (see table I). During the studies subjects wore Beta-cloth briefs and rubber sandals, allowing a maximum body surface to be free for evaporation. Throughout the study, subjects were on a fixed diet of rehydrated freeze-dried foods and measured amounts of liquid. Careful records of all intake and output were kept. For this study, subjects were housed in a large environmental complex located at the USAF School of Aerospace Medicine, Brooks AFB, Texas. The complex had an interior volume of 5450 cubic feet and was controlled with respect to ambient temperature, water vapor pressure, and wind speed. Total barometric pressure and gas composition reflected the outside ambient conditions and varied over a very narrow range. The studies were conducted from February through April 1970, with control periods and several experimental periods as outlined in table II.

During the initial control period lasting 12 days, subjects were exposed to standard environments of 24° C. with water vapor pressures of 6.5 and 14 mm. Hg. During the control studies at 24° C. and 6.5 mm. Hg P_{H_2O}, the subjects averaged 2300 cc of fluid intake and 200 meq of Na/24 hrs (this included ad lib water as well as the free water in food together with that calculated to be formed by combustion of food). These fluid and salt provisions represented the average load that subjects ingested voluntarily during preliminary studies under identical environmental conditions.

The first experimental period, lasting 6 days, was designed to study the effects of body overhydration. In the initial phase of

overhydration, subjects were forced to consume 2100 cc of hypotonic electrolyte-glucose solution (Gatorade) during each 24-hour period. Total fluid intake amounted to 4200 cc and sodium intake to 250 meq/24 hours. The subjects eliminated virtually all ad lib water ingestion when faced with the forced fluid load. The hypotonic solution was administered in 150 cc doses at 14 fixed intervals during each 24-hour period.

During the final phase of overhydration, subjects were given two separate 1000 cc infusions of saline (0.45 gm. NaCl/100 cc fluid); each infusion lasting 3 hours and spaced 12 hours apart. The continuation of the hypotonic-fluid feedings in the amount of 2100 cc/24 hrs. along with these I.V. infusions brought total 24-hour fluid intake to a mean of 6100 cc and total 24-hour Na intake to 410 meq.

The second experimental period, lasting 8 days, was designed to study the effects of body dehydration upon rates of skin insensible water loss. In the first phase, subjects were subjected to hypertonic dehydration for 24 hours by being placed in a very hot, dry environment where diaphoretic salt and water losses were high. During exposure to the hot environment, fluid intake was restricted to about 1550 cc/24 hrs. In the second phase of this experimental period, subjects were dehydrated through administration of an oral diuretic agent (hydrochlorthiazide) but were allowed to drink when thirsty.

In the studies following diaphoretic dehydration, subjects were restricted to their basic dietary fluids and salt with no ad lib drinking allowed. Total fluid intake averaged 1550 cc/24 hrs. and sodium intake

160 meq/24 hrs. When undergoing diuretic dehydration, subjects were allowed to drink water ad lib to satisfy any thirst and consumed an average of 2600 cc/24 hrs.; sodium intake was fixed at 200 meq/24 hrs. During the 4 days that subjects were being diuresed, they were given a total dose of 450 mg of hydrocholothiazide (Hydrodiuril). Dosage schedules consisted of an initial loading dose of 100 mg one hour before the start of the study followed by 50 mg every 12 hours thereafter, until the termination of the study.

The third experimental period concerned the effects of peripheral vasodilatation upon rates of skin insensible water loss. During the vasodilatation studies, control conditions were reinstituted with a fluid intake of 2450 cc and sodium intake of 200 meq/24 hrs. Vasodilatation was accomplished with the oral administration of tolazoline HCl (Priscoline). Each subject was given 50 mg of the drug two hours before a measurement of skin insensible water loss was to take place. A total of 200 mg of tolazoline was administered to each subject over a single 24-hour period. Activity of the drug was denoted by the onset of mild flushing, a subjective feeling of warmth, and a clear rise in the average skin temperature.

The fourth experimental period was designed to study the effects of antidiuretic hormone upon rates of IWL_S (table II). Subjects received an oral fluid load (hypotonic solution) in the control phase, and in the second phase subcutaneous injections of Pitressin (10 units of posterior pituitary extract) were given along with the fluid load. The effect of

the posterior pituitary extract in a situation where it is normally physiologically absent was then observed.

The fifth and final experimental period was designed to study the possible development of adaptation or acclimatization in the response of skin insensible water loss to environmental changes. Subjects were placed in a hot dry environment (30.5° C., 6.5 mm. Hg P_{H_2O}) for 6 days during which time both sensible and insensible skin water loss rates were very high. Subjects were again allowed free access to water so that significant dehydration would not take place. The subjects consumed an average of 3100 cc/day during the exposure to the hot, dry environment with a standard 200 meq of Na/24 hrs. They were then transferred to a normal or control environment (24° C., 14 mm. Hg P_{H_2O}) and the rate of skin insensible water loss studied. When placed back in a normal environment they received 2600 cc fluid and 200 meq Na/day.

Throughout the various studies, careful monitoring of urinary volumes as well as urinary electrolytes, creatinine, specific gravity, and osmolarity were carried out. Monitoring of serum electrolytes, osmolarity, creatinine, and BUN as well as hematocrit, hemoglobin and white counts were also accomplished. The subjects were weighed on a daily basis to substantiate any major fluid shifts. Other physiological data recorded included deep body temperature, average skin temperature (a weighted average of seven skin sensors), heart rate, and respiratory rate.

In order to determine the component of weight loss due to metabolic gas exchange, multiple measurements of subject O_2 consumption and CO_2

productions under the experimental conditions were carried out (table III). These data were utilized to determine IWL_G or that portion of insensible loss due to the excess weight of CO_2 expired over the weight of O_2 utilized.

The effects of each experimental condition upon rates of IWL_S were initially analyzed by a comparison of differences in paired-sample means between control and experimental condition. Mean values of IWL_S for each of the subjects were tabulated for a series of experiments in which all environmental parameters except the one being examined were identical. P values were derived by looking at the t-scores of the average paired-sample difference. These values are shown in figure 1. All other procedures and techniques were identical to those of the previous studies (1).

V. RESULTS

The rates of skin insensible water loss for each of the 6 volunteer subjects as well as the group mean are shown in figures 1 and 2. Corresponding changes in the subject physiological measurements are shown in figure 3. Additional physiological data are tabulated in table IV.

In the initial control period at 24° C., 6.5 mm. Hg P_{H_2O} (fig. 1) the mean skin insensible water loss rate for the 6 subjects was 8.7 gm. $m.^{-2}$ $hr.^{-1}$ with a range from 7.6 up to 9.4 gm. $m.^{-2}$ $hr.^{-1}$. As reported in the previous studies, the experimental subjects who tended to show rates of skin water loss lower than the mean were consistently lower throughout the experimental profile, while those who lost water more rapidly than the mean value were consistently on the high side.

Subjects A and C generally maintained the lowest values throughout the series of experiments while subjects D, E, and F generally maintained the highest values.

During this control period, physiological measurements were stable with a urine S.G. averaging 1.018 and an osmolarity averaging 701 mOsm/l (fig. 3). Total fluid intake from all sources approximated, 2300 cc, while total sensible output averaged approximately 1900 cc. Serum osmolarity was 293 mOsm/l. Other mean serum values were Na of 140 meq/l, K of 4.3 meq/l, and BUN of 18.0 mg%.

The oral-overhydration study resulted in significant changes in the rate of skin insensible water loss as well as in the subject physiological measurements. The average IWL_S rate increased to 10.25 gm. $m.^{-2}$ $hr.^{-1}$, an 18% increase over control values, and the values for each subject increased by a similar amount. This change in water loss rate was significant to the 0.001 level. Accompanying this change in skin water loss rate, subject urine S.G. dropped to 1.009 while urine osmolarity decreased to 432 mOsm/l. Total mean fluid intake had been increased to about 4200 cc and urine output rose to 3280 cc/24 hrs. Serum osmolarity dropped to 292 mOsm/l. Other serum values included Na of 141 meq/l, K of 4.6 meq/l and BUN of 14.2 mg%. The average weight of the subject also increased during this period of oral overhydration.

During the period of oral and intravenous overhydration, significant changes in IWL_S rates also occurred. The average rate of skin insensible water loss rose further to a value of 10.4 gm. $m.^{-2}$ $hr.^{-1}$, representing an

increase of 20% over the control values of 8.7 gm. $m.^{-2}$ $hr.^{-1}$. This change was also significant to the 0.001 level. The range of values for the 6 individual subjects also tended to increase, with subject C showing the lowest water loss rate of 8.7 gm. $m.^{-2}$ $hr.^{-1}$ compared with his control value of 7.6 gm. $m.^{-2}$ $hr.^{-1}$ and subject E showing the highest rate of 12.1 gm. $m.^{-2}$ $hr.^{-1}$ compared with his control value of 9.3 gm. $m.^{-2}$ $hr.^{-1}$.

Urine S.G. was 1.008 and urine osmolarity diminished to 334 mOsm/1. Serum osmolarity averaged 295 mOsm/1. Total fluid intake had increased to 6100 cc and total sensible output rose to 4370 cc/24 hrs. Other serum changes included Na of 141 meq/1, K of 4.4 meq/1, and BUN of 14.8 mg%.

The effects of dehydration through fluid restriction and forced diaphoresis are shown in figures 1 and 3 and table IV. Again a very significant change in the rate of skin insensible water loss took place, with a decrease in the rate of 10% below the control value. This change was significant to the 0.005 level. While the average value of IWL_S fell to 7.8 gm. $m.^{-2}$ $hr.^{-1}$ when compared to the control value of 8.7 gm. $m.^{-2}$ $hr.^{-1}$, the IWL_S value of subject C fell to 6.3 gm. $m.^{-2}$ $hr.^{-1}$ (control, 7.6) and the value of subject E fell to 8.7 gm. $m.^{-2}$ $hr.^{-1}$ (control, 9.3).

Physiological measurements also shifted dramatically, with urine S.G. rising to 1.031 and urine osmolarity increasing to 1240 mOsm/1. Serum osmolarity rose sharply to 310 mOsm/1. Total fluid intake averaged about 1550 cc, while total sensible output fell to 923 cc/24 hrs. Serum BUN rose to 22.4 mg% while serum Na rose to 145 meq/1 and K to 4.6 meq/1, during the fluid deprivation.

Following the recovery period during which baseline values were reproduced, subjects were given a pharmacological diuresis with the administration of hydrochlorthiazide. During this procedure the rate of skin insensible water loss showed no significant deviation from control values with a mean of 8.7 gm. $m.^{-2}$ $hr.^{-1}$ for the 6 subjects. Urine S.G. averaged 1.015 with an osmolarity of 657 mOsm/1. Serum osmolarity averaged 294 mOsm/1. Total sensible output rose to 3540 cc/24 hrs. during the first day of diuresis. Fluid intake averaged approximately 2600 cc/24 hrs. Subjects lost an average of 1600 gm. of total body weight during the first day of diuresis, remaining essentially at the new weight for the remainder of this phase of the study. BUN was 18 mg%, Na 145 meq/1 and K 4.7 meq/1. Urinary Na rose initially to 587 meq/24 hrs. with a concentration of 166 meq/1.

In the subsequent study of the effects of oral overhydration, with and without the administration of aqueous Pitressin, significant increases in the rate of skin insensible water loss were again seen. With an oral fluid load of 3700 cc/24 hrs., IWL_S rates increased to 9.5 gm. $m.^{-2}$ $hr.^{-1}$ without exogenous Pitressin and 9.2 gm. $m.^{-2}$ $hr.^{-1}$ with exogenous Pitressin. Both these values were significant to the 0.01 level when compared with control values but were not significantly different from each other. Urine S.G. averaged 1.009 without Pitressin and 1.014 with Pitressin administration. Urine osmolarities were 403 and 595 mOsm/1 respectively. Serum osmolarity was stable at 289 without Pitressin and 286 mOsm/1 with Pitressin. With an oral intake of 3700 cc subjects without exogenous

Pitressin had a 24 hour urine output of 3300 cc while after Pitressin administration this decreased to 2400 cc.

During the vasodilatation studies, no significant change in the rate of skin insensible water loss was observed. An average value of 8.6 gm. $m.^{-2}$ $hr.^{-1}$ was document for the 6 subjects (fig. 1) despite significant changes in average skin temperature (table V). A mean increase in average skin temperature of 1.0° C., significant to the 0.005 level, was observed after administration of oral tolazoline. At 24° C., 6.5 mm. Hg P_{H_2O} subjects had a skin temperature of 31.5° C. before tolazoline and 32.5° C. after administration of tolazoline. This rise in temperature occurred in all 6 experimental subjects.

Urine and serum chemistries during vasodilation were comparable to the control values (fig. 3 and table IV). No significant weight change was observed, and average total fluid intake was maintained at 2450 cc/24 hrs.

In the final study where subjects were "acclimatized" to a hot, dry environment, changes in the rate of skin insensible water loss took place as ambient conditions were varied. Initial control values (fig. 2) at 24° C. T_a, 14 mm. Hg P_{H_2O} resulted in an average IWL_S of 7.4 gm. $m.^{-2}$ $hr.^{-1}$. When subjects were exposed to 30.5° C., 6.5 mm. Hg P_{H_2O}, the rate of skin water loss rose immediately, so that during the first day of exposure a mean rate of 17.1 gm. $m.^{-2}$ $hr.^{-1}$ was recorded. This high rate represents not only skin water loss by diffusion and mental sweating, but also a component of active thermal sweating. Thermal sweating could be observed in these subjects when the ambient temperature rose above 29° C.

The mean value of 17.1 gm. $m.^{-2}$ $hr.^{-1}$ does not include data where thermal sweating was obvious.

During the 6 days of subject exposure to this high temperature, low humidity environment, the mean rate of skin water loss varied from a high of 17.1 gm. $m.^{-2}$ $hr.^{-1}$ to a low of 14.7 gm. $m.^{-2}$ $hr.^{-1}$ and on the last day was 15.9 gm. $m.^{-2}$ $hr.^{-1}$. When subjects were returned to the control environment of 24° C. T_a and 14 mm. Hg P_{H_2O} the rate of skin water loss immediately began to drop. At the first measurements taken after return to control environment the rate of IWL_S was slightly higher than the control values (8.1 gm. $m.^{-2}$ $hr.^{-1}$.). Within 24 hours of returning to the control environment, however, the IWL_S rate had returned to 7.2 gm. $m.^{-2}$ $hr.^{-1}$ and remained at this level, again showing no significant difference from pre-exposure control values.

As can be seen in table IV, the physiological alterations during the acclimatization exposure were small. Urine S.G. rose during exposure reaching 1.019 on the sixth day of exposure when urine osmolarity reached an average of 751 mOsm/l. Serum osmolarity averaged 288 mOsm/l on the sixth day. Since subjects were allowed free access to water during the exposure to the hot, dry environment, the total fluid intake rose to over 3100 cc, but fell rapidly to 2600 when subjects were returned to the control environment. By the end of the recovery period, urine and serum parameters were very close to the control levels.

VI. DISCUSSION

The role of physiological changes within a human subject in the determination of rates of skin insensible water loss is still unsettled in the literature. Despite the fact that several studies have attempted to define the role of fluid balance and of the peripheral vasculature in this problem, conflicting findings have prevented arguments from being resolved. In the fluid balance studies, a major difficulty has rested with the type of hydration or dehydration to which experimental subjects are exposed. Hall and McClure (17) as well as Ginandes and Topper (18) administered water only to force overhydration on their subjects, and they found no change in rates of IWL_S. In order to effect a rapid and significant volume expansion, one should give an osmotically active fluid rather than pure water. Indeed, when some subjects were given a heavy salt load (18) without supplemental fluids, an actual decrease in the rate of skin water loss was observed. High values of serum osmolarity were observed with a significant increase in serum osmotic pressure.

In the current study, we have attempted to increase subject hydration by administration of large amounts of hypotonic solution. Thus, in the oral overhydration program more than 250 meq of sodium as well as 4200 cc of fluid were administered over a 24 hour period. With I.V. as well as oral feeding, more than 410 meq of sodium with 6100 cc of fluid were administered in a 24 hour period. During this fluid load, the rate of skin insensible water loss clearly increased significantly so that maximum values were

20% higher than control values. This increase occurred in all 6 subjects and was quantitatively similar in all subjects. When exposed to a very large hypotonic fluid load, the human body is definitely able to increase the rate of skin insensible water loss.

In previous studies on the effect of dehydration or diminished body fluid reserves on IWL_S rates, the type of dehydration has also varied. The subjects of Newburg and Johnston (16) were dehydrated approximately 6% of total body weight by the withholding of water and the feeding of 10 gms. NaCl/day. It is not clear from this approach whether the subjects were isotonically or hypertonically dehydrated. With the administration of significant quantities of NaCl without water, one would suspect that significant hypertonic dehydration would occur. In the current study dehydration was undertaken in two ways.

Subjects were forced to lose water and salt through significant diaphoresis, and in this procedure an excess of fluid over salt was wasted. After dehydration, the subjects, therefore, tended towards hypertonicity. The restriction of dietary fluids further compounded this type of dehydration. The values of 310.5 mOsm/l serum osmolarity is consistent with the state of hypertonic dehydration in these subjects. In addition, the BUN rise to 22.4 and the change in serum creatinine to 1.27 (up from 1.05 mg% in control) all reflect a reduced intravascular volume and hemoconcentration. The average subject weight loss of 1900 gms. during the forced dehydration was largely water and represented an approximate 4% loss of body fluids. With urine output falling to 923 cc/24-hrs and urine osmolarity rising above

1240 mOsm/l, a maximum effort to conserve fluid was being made by the renal system.

During this forced hypertonic dehydration the rate of skin insensible water loss fell significantly by more than 10% in all subjects. It returned to normal levels as soon as subjects were rehydrated and blood chemistries approached normal.

In the second dehydration attempt, subjects were forced to diurese with the administration of hydrochlorthiazide over a four-day period. Subjects would be expected to lose significant amounts of fluid and salt, with the ultimate state of dehydration being dependent upon subsequent intake of fluid and salt. In this study subjects were allowed free access to fluids and given a liberal sodium intake of 200 meq/24 hrs. It was anticipated that an initial rapid diuresis would lead to a shrinking of the body fluid volume, stimulate thirst centers, and prompt the subjects to rehydrate themselves. In this way the subjects would limit the shrinkage of their vascular and total fluid volumes and prevent significant dehydration from continuing. Subjects did lose an average of 1600 gms. during the first day of diuretic administration, but they increased their fluid intake significantly to compensate partially for the urinary losses in the following days. During the last 2 days of diuresis, serum osmolarity stabilized at 291 mOsm/l and serum electrolytes remained within the normal range. The urine S.G. of 1.016 with an osmolarity of 695 were close to control values, demonstrating that urinary concentration was not excessive.

During this time, the rate of skin insensible water loss did not vary from control levels. Despite the fact that subjects lost some weight and showed a mild degree of isotonic dehydration, skin water loss rates did not change.

In considering the profound effects of both hypotonic overhydration and hypertonic dehydration on the rates of skin insensible water loss, the question immediately arises as to the mechanism of this apparently physiological control over water loss. If one were to implicate a hormonal substance, the most likely suspect would be antidiuretic hormone or ADH, an agent which plays a major role in water transport through the kidneys. As mentioned above, this substance has also been shown to alter rates of water diffusion through isolated amphibian and dog skin.

On the other hand, one could hypothesize that the affect of fluid load or dehydration on IWL_S is purely a mechanical or physical one. In the overhydrated state, two things might occur: First, there might be more free water available around the cells of the upper dermis and deep epidermis so that skin "wettedness" would be greater and diffusional forces higher; and secondly, an increased skin turgor might open up microscopic skin folds and surface features enlarging the total surface area of the skin that is available for diffusion.

Conversely, when the subject is significantly dehydrated, the supply of free water in the dermis and lower epidermis may diminish, reducing the "wettedness" of the skin and reducing the amount of water available for diffusion. Secondly, with dehydration and diminished skin turgor,

microscopic skin folds will increase and the total skin surface area exposed to the environment will diminish, further limiting water diffusion.

During the administration of oral fluids and of oral plus I.V. fluids, one would expect the circulating levels of ADH in the experimental subjects to be minimal. ADH release is shut off by expansion of the vascular volume (table VI). The observed increase in IWL_S under these conditions should, therefore, be accompanied by a reduced level of ADH. During the phase of diaphoretic dehydration with a marked contraction of fluid volume, one would expect ADH levels to be high or maximal. The decreased rate of IWL_S observed in this state should then be accompanied by very high levels of circulating ADH.

Urine and serum chemistries observed in these studies lend support to the hypotheses that ADH levels are low in the first case and high in the second. When a diuresis is forced by the use of diuretics, one would expect an initial rise in ADH levels as fluid volume contracts. As one drinks and consumes salt to attempt to compensate for the increased renal losses, ADH production may then fall. As long as the subject maintains a deficit in his oral intake, however, there should be a continued, but small, stimulus to ADH production. In this study, rates of skin water loss were normal despite the fact that one would expect some elevation in ADH production.

As a further test of the relationship of ADH levels to the rates of skin insensible water loss, it was then decided to overhydrate the subjects and administer exogenous ADH (i.e., Pitressin) simultaneously. One would

then have the condition where endogenous ADH production would normally be shut off by the large fluid load while Pitressin would be supplied exogenously (table VI). If, indeed, increases in IWL_S are directly related to very low levels of ADH then the administration of Pitressin here should abolish or at least diminish the response of IWL_S rates to a fluid load. Correspondingly, since diminished rates of IWL_S had been associated with physiological states in which ADH levels were very high, one might even expect a lower-than-normal rate of IWL_S with the administration of Pitressin even though the subjects were overhydrated.

When Pitressin was administered to the overhydrated subjects, a significantly increased rate of skin insensible water loss still occurred (fig. 1). This rate did not differ statistically from the rate obtained in the same subjects when overhydrated without exogenous Pitressin. This result would appear to lend support to the idea that physiological ADH levels do not play a prominent role in determining rates of skin water loss. Whether other circulating substances are involved, or the effects of hydration are purely physical and mechanical will require further investigation.

The role of the peripheral vasculature in the determination of IWL_S rates has long been interwoven with the effects of skin temperature. Significant vasoconstriction and vasodilatation in the dermis will alter skin temperature and may or may not alter the rate of skin water loss. Most of the studies reported in the literature have been based on the skin capsule technique and the local application of pharmacologically active

substances to the skin. In their most recent study Grice and Bettley (23) confirmed the observations of Pinson (2) that vasoconstriction and vasodilatation had no significant effect upon skin insensible water loss even though changes in skin temperature did take place.

The findings of this study agree with those results. Following administration of tolazoline, evidence of peripheral vasodilatation appeared in the form of mild subject flushing and a 1^{o} C. rise in average skin temperature. Despite the skin temperature changes, no significant change in the rate of skin water loss in any of the 6 test subjects was observed (fig. 1). These results lend support to the hypothesis of Peiss (7) and others that small rises in skin temperature increase the vapor pressure of water in the skin but also decreases the relative hydration of the skin or its "relative humidity." The opposing effects of these two actions result in little or no change in the actual rate of skin water loss. When changes in the peripheral circulation are such that extreme alterations of skin temperature result, then the situation becomes more complicated. Autonomic activity may increase and lead to the activation of eccrine glands; at the same time skin temperature changes may be so great that changes in skin water vapor pressure overwhelm smaller changes in skin hydration or vice versa. With these major vascular changes, then, significant alterations in IWL_S rates will certainly occur.

The question of adaptation or acclimatization in the control mechanism of skin insensible water loss is an intriguing one. Such phenomena certainly occur in other bodily responses which are under

physiological control, i.e., sweating and cold tolerance. IWL_S, being responsive to thermal and other environmental stimuli, might behave in a parallel manner.

No evidence of acclimatization or adaptation was observed, however, in these studies. During the subjects' exposure to the high temperature, low humidity environment, there was little change in total skin water loss over the 6 days (fig. 2). When subjects were reintroduced to a normal or non-sweat environment, the rate of skin water loss fell rapidly to control levels. An initial high reading shortly after the beginning of the recovery period was probably related to residual water left on the skin from sweating in the just-evacuated uncomfortable environment. After 24 hours, the subjects' response to the control environment was in no way altered by his exposure to the high temperature, low humidity environment, and rates of IWL_S were similar to earlier control values.

Thus, neither peripheral vascular changes nor acclimatization procedures exerted any significant effect upon rates of skin insensible water loss. In both cases, an attempt to induce physiological changes in the skin or in the skin-air interface that would alter rates of skin water loss was not successful.

In the case of major shifts in body fluid, a definite alteration in rate of skin insensible water loss was demonstrated; with both overhydration and dehydration, IWL_S rates could be changed as much as 30%. Whether this phenomenon represents a truly physiological adjustment, however, remains quite doubtful. There is some evidence that ADH levels

are not important to the changes in IWL_S, and it is possible to explain the changes in water loss rate on a purely physical or mechanical basis. Increases or decreases in dermal and epidermal fluid can change tissue turgor and passively influence the diffusion of water from the skin.

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TABLE I

SUBJECT PROFILES

Subject	Ht. (cm)	Wt. (kg.)	BSA (m^2)	$\dot{V}e$ (l/min)	T_3 (%)	T_4 (ugms%)	Hct (%)	Hb (g.)	BUN (mg%)	Serum Creat. (mg%)	Serum Osm (mOsm/l)
A	182.9	66.5	1.86	6.99	33.1	8.6	43.5	14.3	15	1.05	291.3
B	175.3	69.2	1.84	7.21	35.8	5.3	45.0	15.1	17	1.05	288.3
C	188.0	87.8	2.14	7.83	38.5	8.2	43.0	14.1	19	1.10	291.0
D	177.8	87.5	2.05	7.81	35.0	7.5	45.0	14.6	19	0.95	293.4
E	182.9	72.1	1.93	7.68	30.8	7.9	42.1	13.3	17	1.05	291.9
F	173.9	73.9	1.88	8.29	32.3	6.1	46.0	14.8	13	1.10	291.8
Mean	180.1	76.2	1.95	7.64	34.3	7.3	44.1	14.4	16.7	1.05	291.3

TABLE II

LIST OF EXPERIMENTS

PERIOD	CONTROL 1	OVERHYDRATION Oral 2	OVERHYDRATION Oral + I.V. 3	DEHYDRATION Diaphoretic 4	DEHYDRATION Diuretic 5	Vasodilatation 6	ORAL OVERHYDRATION Without ADH 7	ORAL OVERHYDRATION With ADH 8	ADAPTATION Hot, Dry 9	ADAPTATION Recovery 10
Duration (days)	12	4	2	4	4	1	1	1	6	2
Temperature (^{o}C)	24	24	24	33/24	24	24	24	24	30.5	24
P_{H_2O} (mm. Hg)	6.5/14	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	14
Pressure (mm. Hg)	740-750	740-750	740-750	740-750	740-750	740-750	740-750	740-750	740-750	740-750
Velocity (ft/min)	~40	~40	~40	~40	~40	~40	~40	~40	~40	~40
Gas Composition	Ambient	Ambient	Ambient	Ambient	Ambient	Ambient	Ambient	Ambient	Ambient	Ambient
Total Fluid (ml/24 hrs)	2300	4200	6100	1550/1550	2600	2450	3700	3700	3100	2600
Total Na (meq/24 hrs)	200	250	410	160	200	200	230	230	200	200

TABLE III

RESPIRATORY AND METABOLIC GAS EXCHANGES

Subject	$\dot{V}_e$ (L/min)	Volume (L/hr)	R.Q.	O_2 Cons. (L/min)	O_2 Cons. (L/hr)	O_2 Cons. (gm/hr)	CO_2 Prod. (L/hr)	CO_2 Prod. (gm/hr)	$O_2 - CO_2$ (gm/hr)
A	7.0	420.	0.80	0.29	17.4	24.9	13.9	27.3	2.4
B	7.2	432.	0.80	0.26	16.6	23.7	13.3	26.1	2.4
C	7.8	468.	0.75	0.35	21.0	30.0	15.8	31.0	- 1.0
D	7.8	468.	0.80	0.38	22.8	32.6	18.2	35.6	- 3.0
E	7.7	462.	0.81	0.33	19.8	28.3	16.0	31.4	- 3.1
F	8.3	498.	0.78	0.31	18.8	26.8	14.7	28.9	- 2.1
Mean	7.6	458.	0.79	0.32	19.4	27.7	15.3	30.1	- 2.3

TABLE IV

SUMMARY BLOOD URINE ANALYSIS

Period	SERUM					URINE					
	Creatinine mg %	BUN mg %	Na meq/liter	K meq/liter	Osmolarity mOsm/liter	Specific Gravity	Creatinine mg %	Na meq/liter	K meq/liter	Osmolarity mOsm/liter	Urine Vol ml/24 hrs
Control	1.05±0.05*	18.0±6.7	140±1.6	4.3±0.3	293±3.2	1.018±0.004	88±31	168±44.9	44±15.4	701±210	1900
Oral Overhydration	1.25±0.13	14.2±2.9	141.1±2.8	4.6±0.5	292.3±3.0	1.009±0.002	49±11	110±31.8	26.8±10.3	432±93	3280
Oral + IV Overhydration	1.23±0.08	14.8±3.0	141.3±4.1	4.44±0.46	295.4±5.5	1.008±0.0002	32±9	79.2±13	17.4±5.8	334±48	4370
Dehydration Post Diaphoresis	1.27±0.08	22.4±3.3	145±1.5	4.62±0.32	310.5±6.4	1.031±0.004	188±34	213±22	90.6±14.8	1240±126	923
Pharmacologic Diuresis	1.11±0.12	17.5±2.9	145±3.7	4.7±0.15	294±6.1	1.015±0.002	52±27	166±43.7	22±7.3	657±157	3540
Vasodilatation	1.24±0.06	23.5±2.2	145±2.8	4.3±0.45	289±3.7	1.019±0.006	124±69	115±36	21.8±6.2	633±220	1872
Oral Overhydration Without Pitressin	1.16±0.08	15.5±1.8	142.4±1.6	4.48±0.22	289±2.8	1.009±0.003	75±18	83.3±17	21.0±6.9	403±186	3300
Oral Overhydration With Pitressin	1.24±0.09	17.4±1.2	141.1±1.3	4.31±0.34	286±3.1	1.014±0.003	104±33	95.3±24.5	24.4±4.3	595±121	2400
Adaptation (Hot, Dry)	1.16±0.09	15.0±2.6	140.7±2.3	4.4±0.25	288±5.8	1.019±0.005	68±27	154.3±58.6	35.1±15	751±231	1874
Adaptation (Recovery)	1.19±0.11	17.0±1.7	143±1.5	4.4±0.4	287.2±5.7	1.016±0.004	63±14	146±34.8	31.3±9.5	675±148	1808

*Mean ± S.D.

TABLE V

Average Skin Temperatures
(24°C T_a, 6.5 mm. Hg P_{H_2O})

	SUBJECTS							
	A.	B.	C.	D.	E.	F.	Mean ± S.D.	
Control	31.4	31.4	31.7	31.9	31.4	31.3	31.5±0.23	P
Peripheral Vasodilatation	32.1	32.2	32.6	33.5	32.5	32.2	32.5±0.51	<0.005

TABLE VI

RELATIONSHIP OF STATE OF HYDRATION TO PRESUMED ADH LEVELS AND CHANGES IN THE RATE OF SKIN INSENSIBLE WATER LOSS

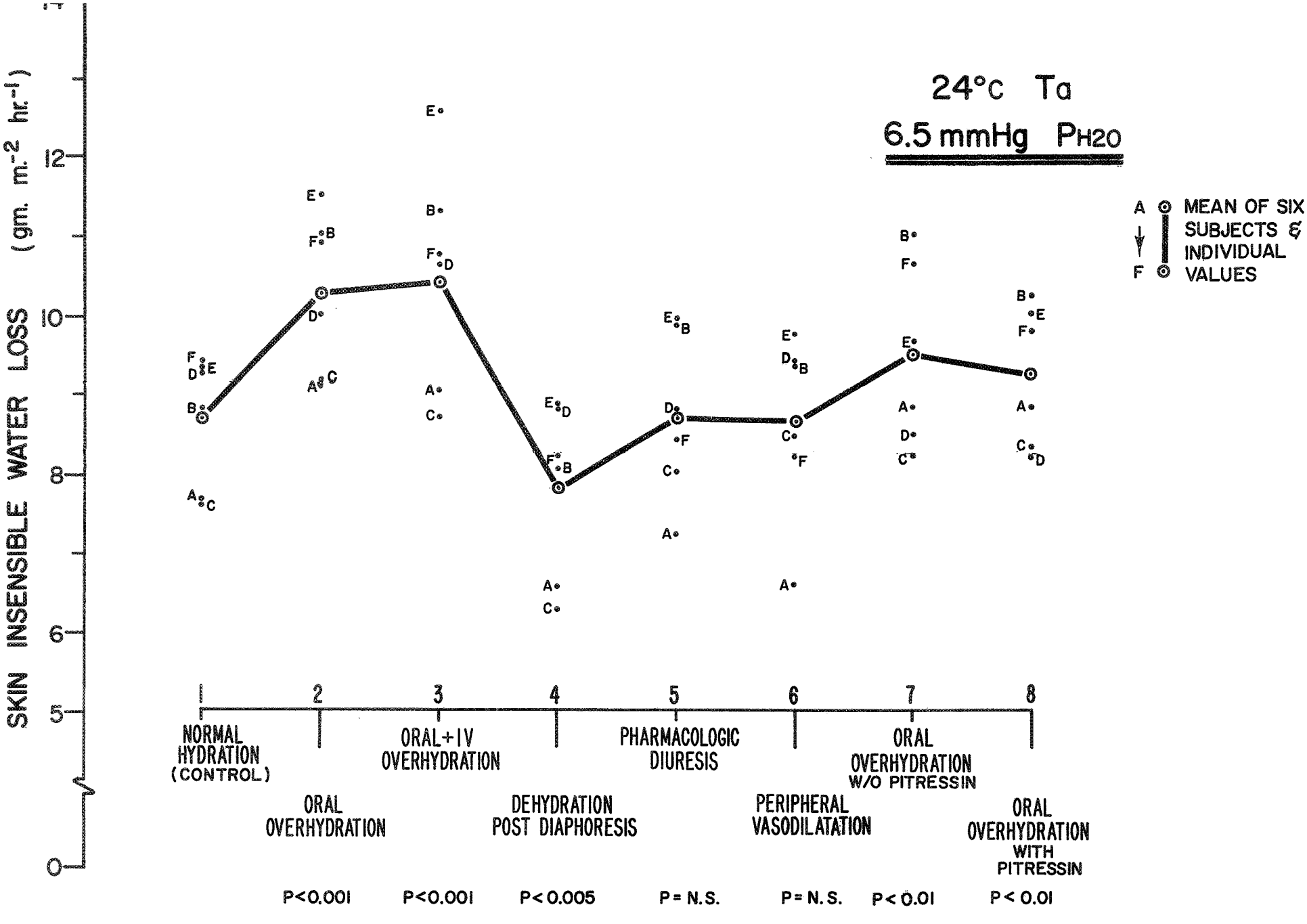
Period	Body Fluid Load	Serum Osmolarity	Presumed ADH Levels	Observed Skin Insensible Water Loss Rate
2. Oral Overhydration	↑	→	↓	↑
3. Oral + I.V. Overhydration	↑↑	→	↓↓	↑↑
4. Diaphoretic Dehydration	↓↓	↑↑	↑↑	↓
5. Diuretic (pharmacologic dehydration)	↓	→	↑	→
8. Oral Overhydration Exogenous Pitressin	↑	↓	↑	↑

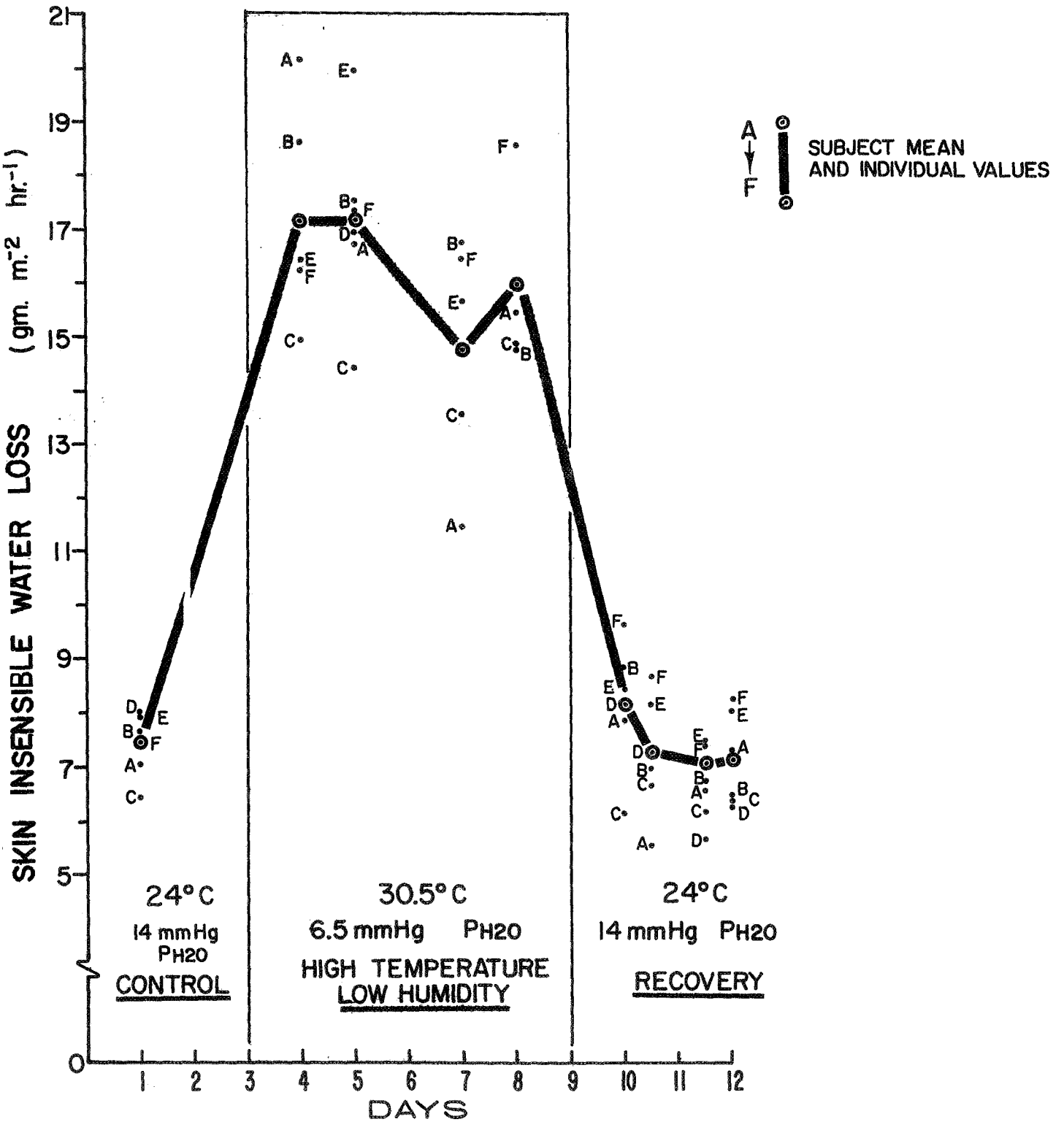
LEGENDS

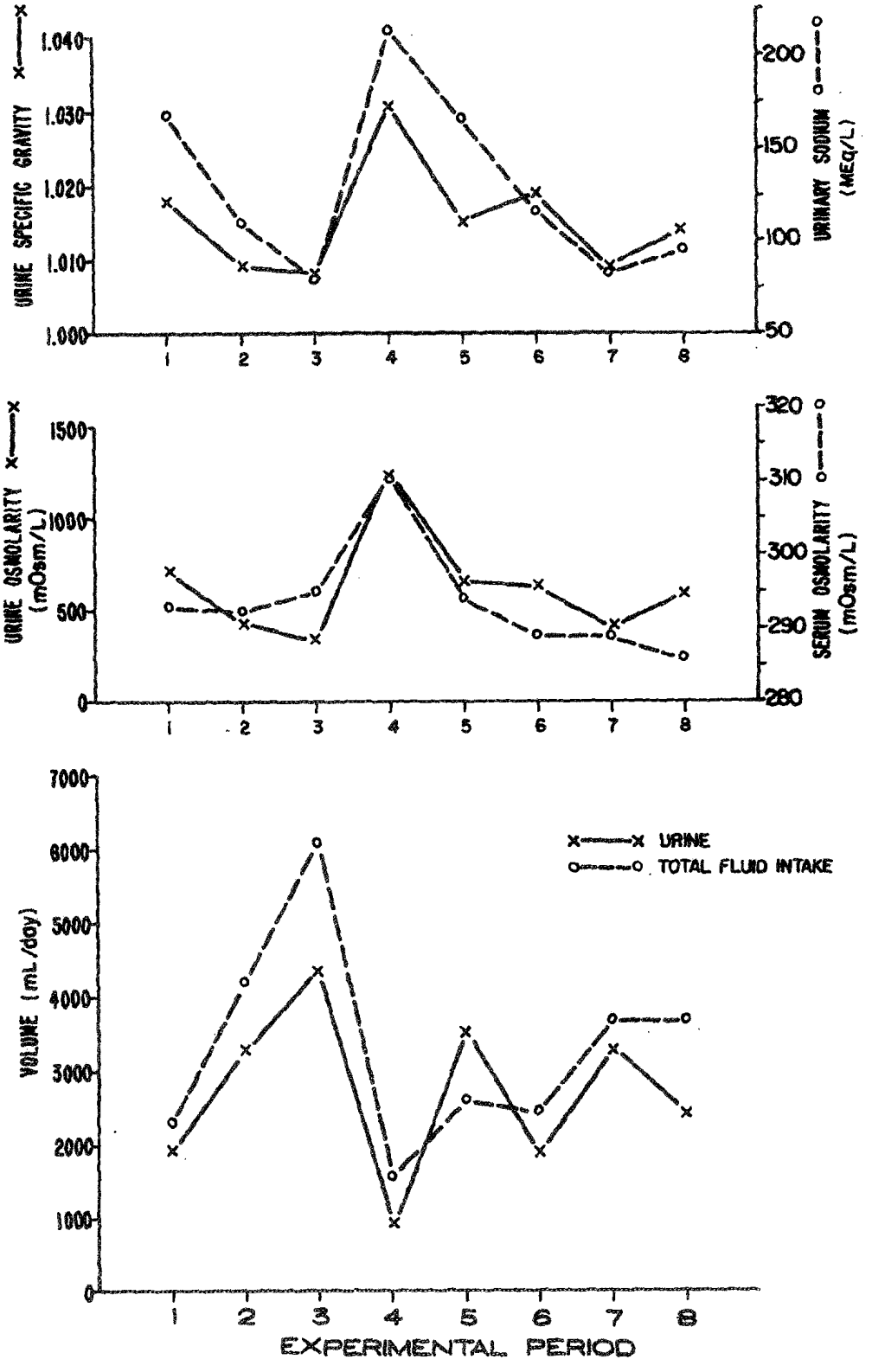
Fig. 1 Influence of physiological changes upon rates of skin insensible water loss. Means and individual insensible water loss values are given for 6 subjects.

Fig. 2 Influence of prior exposure to elevated temperature upon rates of skin insensible water loss. Mean and individual insensible water loss values are given at two different temperatures and water vapor pressures. Individuals showing sensible water loss at 30.5° C were not included.

Fig. 3 Relationship of sensible intake/output and urine and serum chemistries collected on 6 subjects exposed to eight different experimental conditions at 24° C and 6.5 mm. Hg P_{H_2O}. (1) Normal hydration (control), (2) oral overhydration, (3) oral + IV overhydration, (4) dehydration (post-diaphoresis), (5) pharamacologic diuresis, (6) peripheral vasodilation, (7) oral overhydration without Pitressin, and (8) oral overhydration with Pitressin.


SKIN INSENSIBLE WATER LOSS (gm. m.-2 hr.-1)
24°C Ta
6.5 mmHg PH2O
A MEAN OF SIX SUBJECTS &
F INDIVIDUAL VALUES
0
5
6
8
10
12
1 NORMAL HYDRATION (CONTROL)
2 ORAL OVERHYDRATION
3 ORAL+IV OVERHYDRATION
4 DEHYDRATION POST DIAPHORESIS
5 PHARMACOLOGIC DIURESIS
6 PERIPHERAL VASODILATATION
7 ORAL OVERHYDRATION W/O PITRESSIN
8 ORAL OVERHYDRATION WITH PITRESSIN
P<0.001
P<0.001
P< 0.005
P= N.S.
P= N.S.
P< 0.01
P< 0.01


SKIN INSENSIBLE WATER LOSS (gm. m.-2 hr.-1)
21
19
17
15
13
11
9
7
5
0
1 2 3 4 5 6 7 8 9 10 11 12
DAYS
A
F
SUBJECT MEAN
AND INDIVIDUAL VALUES
24° C
14 mm Hg
PH2O
CONTROL
30.5° C
6.5 mm Hg PH2O
HIGH TEMPERATURE
LOW HUMIDITY
24° C
14 mm Hg PH2O
RECOVERY


URINE SPECIFIC GRAVITY
1.040
1.030
1.020
1.010
1.000
URINARY SODIUM (MEq/L)
200
150
100
50
1 2 3 4 5 6 7 8
URINE OSMOLARITY (mOsm/L)
1500
1000
500
0
SERUM OSMOLARITY (mOsm/L)
320
310
300
290
280
1 2 3 4 5 6 7 8
VOLUME (mL/day)
7000
6000
5000
4000
3000
2000
1000
0
URINE
TOTAL FLUID INTAKE
1 2 3 4 5 6 7 8
EXPERIMENTAL PERIOD

APPENDIX

SUMMARY OF EFFECT OF STATE OF HYDRATION ON SIGN/SYMPTOM DEVELOPMENT

I. INTRODUCTION

An exhaustive and detailed account of subject sign and symptom development during exposure to varying environmental parameters was presented in an earlier series of experiments (1). It was shown that the rate of development and the ultimate severity of signs and symptoms related to the environment were closely dependent upon T_a, P_{H_2O} and P_B, with some dependence upon the composition of the gas being used. At ground level pressures, signs and symptoms increased rapidly only after exposure to a P_{H_2O} lower than 6.5 mm. Hg, with little change occurring in the temperature range of 24° to 28° C.

Since the present series of studies were designed to vary the physiologic status under constant environmental conditions, P_B, P_{H_2O} and T_a were maintained at a level that would not be expected to cause progressive or severe sign and symptom development in the experimental subjects. It was considered necessary, however, to follow sign and symptom development during this study to insure the health, comfort, and performance of the subjects.

II. METHODS

All of the experimental subjects were trained to evaluate their own symptoms and to detect and evaluate signs in other subjects. They were familiarized with the signs and symptoms which might develop throughout the course of the study and were given practice in evaluating and grading them by use of subjective and objective evaluation sheets which

were provided (table AI). Before each experiment, a subject would evaluate himself by the Subjective Evaluation Sheet and would then evaluate a specific partner with the Objective Evaluation Sheet. Upon entering the chamber, and at specific intervals throughout the study, these subjective and objective evaluations would be carried out. The subjects made final evaluations immediately upon leaving the chamber.

During the first 8 hours of an experiment, subjective evaluations were conducted hourly and objective evaluations every 2 hours. After 8 hours, subjective evaluations were conducted at 2 hour intervals and objective evaluations at 4 hour intervals (except when subjects were sleeping). Evaluations were usually programmed to occur both immediately before and immediately after a sleep period.

During the study all subjects were allowed only mild activity and were provided with television, radio, games, reading and writing material.

III. RESULTS

The mean objective and subjective evaluation, along with the maximum range within any one individual, are shown in tables AII and AIII for eleven different experimental conditions. As expected, the environmental conditions selected for the study caused little change in sign and symptom development. However, exposure to the 33° C. temperature prior to experiment #4 (table AII) did produce a significant increase in the severity of signs and symptoms with a residual effect remaining throughout the 24 hour post diaphoretic period. An increas-

ing trend in signs and symptom development can also be noted during exposure to 30.5° C. (table AIII).

In a summary of all experiments, there was no significant trend in the frequency and severity of symptom development in each of the anatomical areas or categories. The "Lips," were most frequently involved followed closely, and in decreasing order, by the "Skin," "Nose," "Eyes," "Scalp," "Pharynx," "Tongue," "Mouth," and "General." There was a striking difference in the frequency and severity of sign development. The "Eyes" were most frequently involved followed in order by "Scalp," "Lips," "Nose," "Skin," "Tongue," "Pharynx," "Mouth," and "General." The subjective (symptom) evaluation was considered to be the more sensitive index of the response to the varying experimental conditions.

IV. SUMMARY

In summary, little change was noted in the frequency or severity of sign and symptom development throughout this series of studies. At the higher temperatures there was, as might be expected, an increasing trend toward discomfort and performance decrement, with temperatures in the area of 30° C. being borderline. Sign and symptom development, with their possible effects on subject comfort and performance, should always be critically followed in any study involved with the effects of varying environmental and physiologic stresses on man.

TABLE A-I

OBJECTIVE EVALUATION

Area	1.	2.	3.	4.	5.
EYES	NORMAL	Mild tearing	Moderate tearing	Mild Redness	Mod-severe redness
NOSE	NORMAL	Mild edema/redness	Mod-severe edema/red	Crusting/cracking	Bleeding
LIPS	NORMAL	Slightly dry	Moderately dry	Cracking/peeling	Bleeding
TONGUE	NORMAL	Sl. -Mod. dry	Coated	Redness	Crusting/cracking
MOUTH	NORMAL	Slightly dry	Moderately dry	Redness	Crusting/cracking
PHARYNX	NORMAL	Slightly red	Mod.-severe redness	Cracking/edema	Exudate, bleeding
SCALP	NORMAL	Mild scaling	Mod.-scaling	Severe scaling	Crusting/bristling
SKIN	NORMAL	Sl. dry/scaling	Mod. dry/scaling	Severe dry/scaling	Cracking/peeling
GENERAL	NORMAL	Slightly ill	Moderately ill	Very ill	Request termination
OTHER		List signs from 1. to 5. and describe			

SUBJECTIVE EVALUATION

	1.	2.	3.	4.	5.	6.
EYES	NORMAL	Slight burning	Mild burning	Mod-burning/pain	Severe burning/pain	Blurring vision/other
NOSE	NORMAL	Slightly stuffy	Mod. dry/stuffy	Coryza	Post-nasal drip	Obstruction/other
LIPS	NORMAL	Slightly dry	Mod. dry/chapped	Severely dry/chapped	Cracking	Painful/burning/other
TONGUE	NORMAL	Slightly dry	Moderately dry, burning	Very dry/burning	Painful/sev. burning	Loss of taste/other
MOUTH	NORMAL	Slightly dry	Moderately dry/burning	Very dry/burning	Painful/sev. burning	Swelling/other
PHARYNX	NORMAL	Slightly dry	Moderately dry/burning	Very dry/diff. swall.	Painful/burning	Difficulty swallowing/other
SCALP	NORMAL	Mild itch	Moderate itch	Severe itch/burning	Severe burning	Tingling/other
SKIN	NORMAL	Slightly dry/itch	Moderate itch	Severely dry/itching	Cracking/painful	Burning/other
GENERAL	NORMAL	Slightly ill	Moderately ill	Very ill, uncomfortable	Request termination	- - - - - - - - - - - - - -
OTHER		List symptoms from 1. to 6. and describe				

TABLE A-II
OBJECTIVE AND SUBJECTIVE EVALUATION OF THE
EFFECTS OF EIGHT EXPERIMENTAL CONDITIONS

	Eyes	Nose	Lips	Tongue	Mouth	Pharynx	Scalp (Hair)	Skin	General
Exp #1 Normal Hydration (Control)									
Objective	2.0(1-5)*	1.2(1-2)	1.2(1-2)	1.2(1-3)	1.1(1-2)	1.1(1-2)	1.2(1-2)	1.3(1-2)	1.0(0)
Subjective	1.3(1-3)	1.4(1-3)	1.4(1-2)	1.1(1-3)	1.2(1-3)	1.2(1-3)	1.1(1-2)	1.3(1-2)	1.0(0)
Exp #2 Oral Overhydration									
Objective	2.7(1-4)	1.2(0)	1.2(1-2)	1.1(1-3)	1.0(0)	1.2(1-2)	1.8(1-2)	1.3(1-2)	1.0(0)
Subjective	1.2(1-3)	1.2(1-3)	1.1(1-2)	1.0(0)	1.0(0)	1.0(0)	1.1(1-2)	1.4(1-2)	1.0(0)
Exp #3 Oral + IV Overhydration									
Objective	2.9(1-4)	1.4(1-4)	1.3(1-2)	1.0(0)	1.0(0)	1.0(0)	1.7(0)	1.2(1-2)	1.0(0)
Subjective	1.4(1-3)	1.1(1-4)	1.3(1-3)	1.0(1-2)	1.0(1-2)	1.0(1-2)	1.1(1-2)	1.4(1-2)	1.0(0)
Exp #4 Dehydration (Post Diaphoresis)									
Objective	4.2(2-5)	1.6(1-3)	2.8(2-4)	2.8(1-2)	2.5(1-3)	2.6(1-3)	2.6(2-3)	1.4(1-2)	1.0(1-2)
Subjective	1.5(1-2)	1.5(1-2)	2.8(2-6)	3.5(2-6)	3.1(2-4)	2.9(2-4)	1.7(1-3)	1.7(0)	1.6(1-3)
Exp #5 Pharmacologic Diuresis									
Objective	3.5(1-5)	1.0(0)	1.4(1-2)	1.0(0)	1.0(0)	1.1(1-2)	1.8(1-2)	1.2(1-2)	1.0(0)
Subjective	1.2(1-3)	1.1(1-2)	1.5(1-3)	1.0(1-3)	1.0(1-3)	1.1(1-3)	1.2(1-2)	1.1(0)	1.0(0)
Exp #6 Peripheral Vasodilatation									
Objective	3.6(1-5)	1.2(0)	2.1(1-3)	1.1(1-3)	1.0(0)	1.2(0)	1.8(0)	1.4(1-2)	1.0(0)
Subjective	1.2(1-3)	1.4(1-4)	2.4(1-5)	1.0(0)	1.0(0)	1.1(1-3)	1.5(1-3)	1.8(0)	1.0(0)
Exp #7** Oral Overhydration w/o Pitressin									
Objective	1.0(0)	1.3(0)	1.0(0)	1.0(0)	1.0(0)	1.0(0)	1.6(0)	1.0(0)	1.0(0)
Subjective	1.1(1-2)	1.0(0)	1.0(0)	1.0(0)	1.0(0)	1.0(0)	1.0(0)	1.3(0)	1.0(0)
Exp #8*** Oral Overhydration with Pitressin									
Objective	2.9(1-5)	1.0(0)	1.6(1-3)	1.0(0)	1.0(1-2)	1.0(0)	2.3(2-3)	2.1(1-3)	1.0(0)
Subjective	1.4(1-2)	1.1(1-3)	1.7(1-3)	1.0(0)	1.0(1-2)	1.0(0)	1.0(0)	2.1(2-3)	1.0(0)

* - Subject mean and maximum range within one individual at 24^0 C and 6.5 mm Hg P_{H_2O}.

** - Subjects A, B, C only.

*** - Subjects D, E, F only.

TABLE A-III
OBJECTIVE AND SUBJECTIVE EVALUATION OF THE
EFFECTS OF ADAPTATION TO ELEVATED TEMPERATURES

	Eyes	Nose	Lips	Tongue	Mouth	Pharynx	Scalp (Hair)	Skin	General
Exp #9 Normal Hydration (Control) T_a - 24° C P_{H_2O} - 14 mm Hg									
Objective	1.9(1-4)*	1.2(1-3)	1.1(1-2)	1.1(1-3)	1.1(1-4)	1.1(1-3)	1.1(1-2)	1.1(1-2)	1.0(1-2)
Subjective	1.1(1-3)	1.6(1-4)	1.2(1-2)	1.1(1-2)	1.1(1-3)	1.2(1-4)	1.0(1-2)	1.1(1-2)	1.1(1-3)
Exp #10 Adaptation to Elevated Temperature T_a - 30.5° C P_{H_2O} - 6.5 mm Hg									
Objective	3.6(1-5)	1.3(2-3)	2.1(1-3)	1.2(1-3)	1.1(1-2)	1.1(1-2)	2.2(1-3)	1.3(1-2)	1.1(1-2)
Subjective	1.5(1-3)	1.7(1-3)	2.0(1-3)	1.1(1-2)	1.2(1-2)	1.2(1-3)	1.4(1-2)	1.4(1-2)	1.0(1-2)
Exp #11 Recovery T_a - 24° C P_{H_2O} - 14 mm Hg									
Objective	3.8(1-5)	1.8(2-3)	1.3(1-2)	1.2(1-3)	1.0(0)	1.2(0)	2.5(0)	1.0(1-2)	1.0(0)
Subjective	1.3(1-3)	1.2(1-2)	1.3(1-2)	1.0(1-2)	1.0(0)	1.1(1-3)	2.1(2-3)	1.0(1-2)	1.0(0)

* - Subject mean and maximum range within one individual.