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HORMONAL AND HEMODYNAMIC EFFECTS OF HEAT AND COLD TOLERANCE TESTS BEFORE AND AFTER MULTIPLE COLD AIR EXPOSURES

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NOTICES

TECHNICAL REVIEW AND APPROVAL

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The experiments reported herein were conducted according to the principles set forth in the current edition of the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council.

This technical report has been reviewed by the NMRI scientific and public affairs staff and is approved for publication. It is releasable to the National Technical Information Service where it will be available to the general public, including foreign nations.

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Ten male volunteers were repeatedly exposed, semi-nude, to cold (4° C) air for 30 minutes. Prior to and following the repeated cold air exposures, each subject was given a heat tolerance test (HTT) and a cold tolerance test (CTT), consisting of a 30 minute exposure to 48° C or 5° C air, respectively. Skin and core (rectal) temperatures, hear rates, blood pressures, and blood and urine samples were taken prior to during, and following the thermal exposures.

Acute effects of the thermal tolerance tests had the following endocrinological effects:

a) Plasma norepinephrine (NE) levels rose 175%, associated with vasoconstriction and a rise in mean arterial pressure (MAP), during this relatively mild CTT.

b) Plasma epinephrine (E) levels rose significantly during the HTT but not during the CTT.

c) Plasma Renin Activity (PRA) was elevated in the heat but not in the cold, suggesting

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19) that Angiotensin II does not contribute to the general pressor effect associated with cold exposure.

When compared before and after the repeated cold exposures, the physiological and biochemical changes that occurred during the thermal tolerance tests showed the following differences:

a) Though the repeated cold air exposures did not significantly change E and NE responses to a CTT, finger skin temperatures were significantly lower during the final CTT. This drop in peripheral skin temperatures may be indicative of "insulative" cold adaptation.

b.) The NE response to a HTT increased significantly following the repeated cold exposures. During or following the second HTT, MAP and plasma levels of E, prolactin, cortisol, and aldosterone also differed from the levels found during the first HTT. These findings tend to confirm the hypothesis that repeated cold exposures can alter responses to a standardized heat exposure and that adaptation to cold may decrease man's ability to tolerate heat. (AW)

SECURITY CLASSIFICATION OF THIS PAGE

TABLE OF CONTENTS

LIST OF TABLES, FIGURES, AND APPENDIX

INTRODUCTION

BACKGROUND:

Thermal stress is a major source of decreased performance, increased morbidity and mortality for military personnel during operational conditions. The ability to increase man's tolerance for heat by repeated exposures to a hot environment is well known (1, 2, 3, 4, 5, 6, 7). Improved performance in the cold after repeated cold exposures has not been shown and considerable controversy exists concerning man's ability to adapt to the cold. Cross-sectional studies on the effects of geographical and racial differences, or longitudinal studies of seasonal differences, have demonstrated "insulative" types of changes (8, 9, 10, 11, 12). Two laboratory studies that did address the effects of repeated cold exposures used cold water immersion and reported the same type of "insulative" changes (13, 14). These changes are characterized by a decreased shivering threshold, a decreased rectal temperature, and a decreased discomfort, and by an increased peripheral vasoconstriction, during cold exposures. The intensity or duration of cold stress necessary to induce this type of "insulative adaptation" are not known. At present there have been no studies to indicate that an actual decrease in core temperature is a prerequisite for cold adaptation. The fact that seasonal changes can occur without the subject population experiencing hypothermia, rather than a cold stress of such magnitude to decrease core temperature, would suggest that cold exposure may be a sufficient stimulus to induce some of these changes. Therefore, the possible physiological effects of repeated cold exposures on future heat tolerance, when deploying military or civilian personnel from one thermal extreme to an opposing thermal extreme, are unknown and should be examined.

OBJECTIVES:

The first objective of this study was to examine the acute effects of a cold tolerance test (CTT) and a heat tolerance test (HTT) on the same subject population. The thermal exposures were administered for each subject at the same time of day and season to provide a baseline for further study on cold adaptive changes.

A second objective was to determine if repeated, mild cold air exposures, without associated drops in rectal temperature, can produce cold adaptive changes. The term "adaptation" as used here is "the summation of modifications in the original responses to stress that results in a more economical and broader homeostasis and reduces the strain on body and mind, resulting from a prolonged or repeated exposure to a stress condition" (15).

The final objective of this study was to test the hypothesis that repeated mild cold air exposures can change an individual's response to a subsequent exposure to heat.

MATERIALS & METHODS

Subjects: Ten healthy males volunteered to be subjects in this study after being familiarized with the experimental procedure and signing an informed consent (Table I).

Protocol: The subjects completed a medical, exercise, and geographical history questionnaire. After a resting 12-lead EKG, each subject was given a maximum oxygen uptake (VO_2 max) test on a motor driven treadmill (Quinton 18LDE). Using a modified Bruce protocol (16), the speed and grade were increased at three minute intervals until voluntary exhaustion. Heart rate (HR) was monitored with a Burdick M200 EKG and exhaled oxygen (O_2) and carbon dioxide (CO_2) levels were monitored continually with a SensorMedics 4400 metabolic cart. The subject's body composition was measured hydrostatically

Table I - Descriptive Characteristics of Subjects. Mean (SE)

	Age	Surf. Area	Max VO2	% Fat
	21	1.92	42.0	23.2
	24	2.02	35.9	22.5
	25	2.00	43.9	21.5
	27	1.83	40.1	13.1
	27	1.87	48.3	12.8
	27	1.94	41.7	18.6
	28	2.10	39.8	27.8
	30	2.13	37.2	18.3
	31	1.72	47.2	15.6
	33	2.04	37.2	29.7
Mean	27.3	1.63	20.3	41.3
(SE)	(1.1)	(.24)	(1.8)	(1.3)

Age = years; Surf. Area = cubic centimeters;

Max.VO2 = ml/kg/min

and the pulmonary residual volume was determined by nitrogen dilution on the SensorMedics 4400 metabolic cart.

A one day recall dietary record was completed and discussed with a registered dietitian at the beginning and at the end of the study. Standardized cold tolerance tests (CTT) and heat tolerance tests (HTT) were given to each subject prior to and following the cold air acclimation exposures. Prior to these tests the subjects fasted for 12 hours. Upon arrival at the lab each subject voided and changed into shorts, socks, and a T-shirt. The subject then sat in a wheel chair, drank 500 ml of deionized water, and the subject's brachial vein was then cannulated with a 20-gauge catheter. After resting for 20 minutes at ambient temperature (24°C) the subject was wheeled into the environmental chamber where the temperature was 48.4°C (+/- 0.31) for the HTT or 5.2°C (+/- 0.19) for the CTT with a wind velocity of 750 cubic feet per minute and relative humidity of 30% (+/- 5%). After 30 minutes, the subject was wheeled out of the chamber and returned to ambient temperature where he rested for another 20 minutes (Table II). Exposures were always in the same sequence (HTT prior to CTT) and at the same time of day for each subject. The cold acclimation protocol consisted of daily 30 minute exposures to cold air (4°C) in the environmental chamber described above, for a total 16 (+/- 3) exposures.

<u>Physiological Variables:</u> EKGs were monitored continuously (Hewlett--Packard model 78268) for pulse; blood pressures were recorded on a digital blood pressure monitor (Somatronix Research Corporation model 751) at 15 minute intervals. Mean Arterial Pressure (MAP) was determined by the formula: MAP (mmHg) = diastolic + (1/3 systolic-diastolic). Fingertip skin temperatures and rectal temperatures (probe inserted 10 cm distal to the anal sphincter) were monitored continuously using series 400 thermistors (Yellow-Springs Instrument Corps.) with a digital display (Cole-Palmer model 8502-14).

Table II. Summary of Thermal Tolerance Test Protocol.

Resting 24°C		Thermal Exposure (4 or 48°C)		Recovery 24°C
*	x	x	x	x
-20	0	15	30	+20

Time (minutes)

Legend:

* = Brachial Vein Cannulation

x = Blood Sample, Heart Rate (HR), Blood Pressure (BP), and Temperatures (rectal & skin) collected.

Blood and Urine Data: Blood samples were drawn into 10ml tubes containing 143 units of heparin (USP). Hematocrits were measured after centrifuging a capillary tube filled with heparinized venous blood. The test tubes were centrifuged immediately in a refrigerated centrifuge and 2 mls of plasma transferred to tubes containing a solution of 8 mM EGTA and 6.5 mM glutathione for catecholamine analysis. The remaining plasma was divided into aliquotes for future hormone assays and all samples were frozen at -80°C, so that, each individual's pre and post cold exposure samples could be assayed together. The catecholamine samples were extracted by alumina adsorption with 3,4-dihydroxybenzylamine (DHBA) included as an internal standard. The extracted samples were assayed for catecholamines using high performance liquid chromatography (HPLC) and electrochemical detection (Waters Division of Millipore Corp.) after extraction with alumina (efficiency = 52%). Interassay variations for norepinephrine (NE) and epinephrine (E) were 5% and 9% respectively. Each subject's samples were run in a single assay. Plasma Renin Activity (PRA) was measured with a specific RIA (17), and plasma aldosterone (aldo) levels were determined with a commercially available RIA kit (Diagnostic Products, Los Angeles, California) at the University of Virginia Medical Center. Serum cortisol levels were measured using a commercially available RIA kit (Diagnostics Products, Los Angeles, California). Serum prolactin was measured by commercially available RIA kit (Organon Teknika, Irving, Texas). Blood sodium (Na) and potassium (K) values were determined with a Kodak Ektachem System. Urinary creatinine, chloride, potassium, and sodium levels were determined by Ektochem (model 400) Autoanalyzer Spectrophotometry.

Statistical Analysis: Statistical significance ($p < .05$) was determined by using analysis of variance for repeated measures (SPSSx, Inc.), two-tailed

T-tests with repeated measures, and Duncans' Multiple Range Test for differences between means. Data are reported as mean (+/- SE).

RESULTS

<u>Physiological Changes:</u> The raw data have been included in Appendix A for the convenience of the reader. As can be seen in Table III and Figure 1, the finger temperatures fell during the CTTs and rose during the HTTs. Following repeated cold air exposures, finger temperatures at the end of the 30 minute CTT were slightly cooler compared with pre-acclimation temperatures.

Rectal temperatures (Tre) did not decrease significantly during the CTTs, however, rectal temperatures did increase by 15 minutes and remained elevated at 30 minutes of exposure during the HTT. Tre did not return to baseline values after 20 minutes of recovery (Fig. 2).

As can be seen in Figure 3, the heart rate (HR) did not change significantly during the CTTs and rose significantly during the HTTs. MAPs decreased significantly during both HTTs and remained depressed for 20 minutes following the second HTT. MAP rose during the CTTs, although this elevation was only statistically significant during the second CTT, as seen in Figure 4.

Percentage change in plasma volume (%PV) was calculated using the following equation: %PV = ((Hb1/Hb2) X ((100-Hct2)/(100- Hct1))-1) X 100 (1 = control values; and 2 = subsequent test values) (18). The initial CTT and HTT produced a 1.41% (5.1) and 7.56% (2.9) hemoconcentration respectively, while the second CTT and HTT induced a 9.45% (1.2) and 7.35% (1.5) hemoconcentration.

<u>Endocrinological Changes:</u> Table IV summarizes the plasma levels of epinephrine (E), norepinephrine (NE), cortisol, and prolactin prior to, during, and 20 minutes after both cold and heat tolerance tests. The NE levels rose 3% during the first HTT; however, they increased by 73% during the second HTT (Fig. 5), and increased a similar amount (165% to 175%) during both

Table III. Finger and rectal temperatures, heart rate (HR), and mean arterial pressure (MAP) prior to (0), during (15 & 30 mins) and following (+20 mins) a cold or heat tolerance test before and after repeated cold air exposures. Data = means (+/- SE) ; * = sig. diff. btw. pre & post tolerance test values; # sig. diff. btw. CTT & HTT values; + = sig. diff. btw. before & after cold exposure values.

Variable	Test	Time	0	15	30	+20
Finger Temp (^oC)	Cold	before	29.20 (1.54)	15.61* (1.24)	12.24* (1.05)	21.31 (1.71)
		after	30.48 (1.27)	13.39* (1.43)	10.93*+ (0.87)	23.20 (1.65)
	Heat	before	29.75 (1.42)	38.67*# (0.89)	39.12*# (0.45)	30.61# (0.83)
		after	31.72 (0.70)	40.28*# (0.37)	38.27*# (0.86)	34.54# (1.25)
Rectal Temp (^oC)	Cold	before	37.52 (0.12)	37.42 (0.08)	37.53 (0.10)	37.53 (0.14)
		after	37.38 (0.11)	37.29 (0.09)	37.41 (0.12)	37.45 (0.12)
	Heat	before	37.47 (0.11)	37.67*# (0.12)	37.79*# (0.11)	37.59* (0.08)
		after	37.43 (0.09)	37.47 (0.09)	37.76* (0.13)	37.80* (0.12)
H.R.	Cold	before	68.80 (3.36)	74.30 (4.56)	72.70 (4.28)	65.10 (3.83)
		after	68.00 (3.96)	67.10 (2.47)	71.80 (4.92)	62.90 (2.76)
	Heat	before	70.50 (3.14)	84.10* (4.00)	98.50*# (3.26)	74.50 (1.90)
		after	71.80 (4.60)	93.56*# (6.53)	107.70*# (8.47)	82.10 (8.35)
MAP (mmHg)	Cold	before	88.10 (3.49)	94.50 (3.48)	94.40 (4.16)	87.80 (2.94)
		after	85.10 (2.22)	92.30* (3.20)	93.50 (4.00)	88.20 (2.82)
	Heat	before	87.00 (3.61)	79.70*# (2.45)	76.80*# (2.87)	85.80 (3.86)
		after	87.70 (1.51)	76.00*# (1.73)	74.40*# (1.79)	81.10* (1.3)

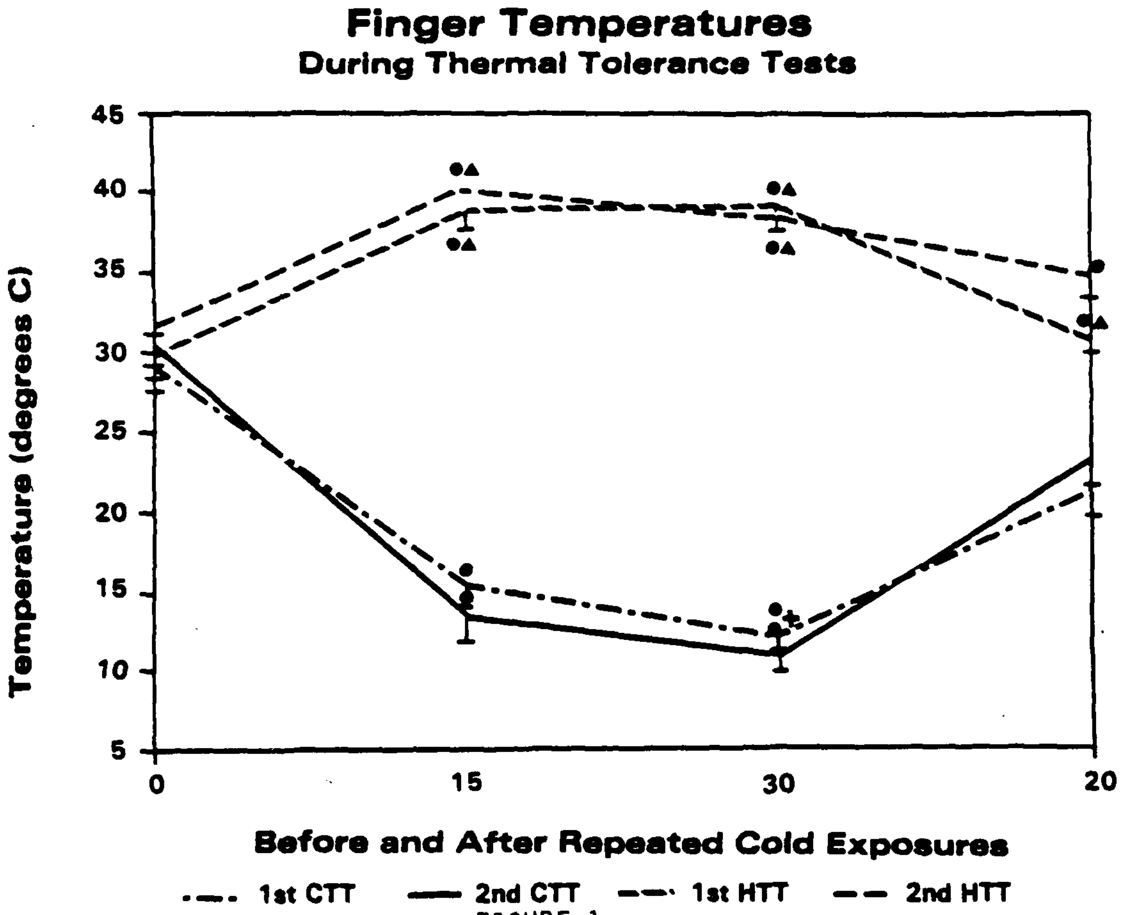

FIGURE 1

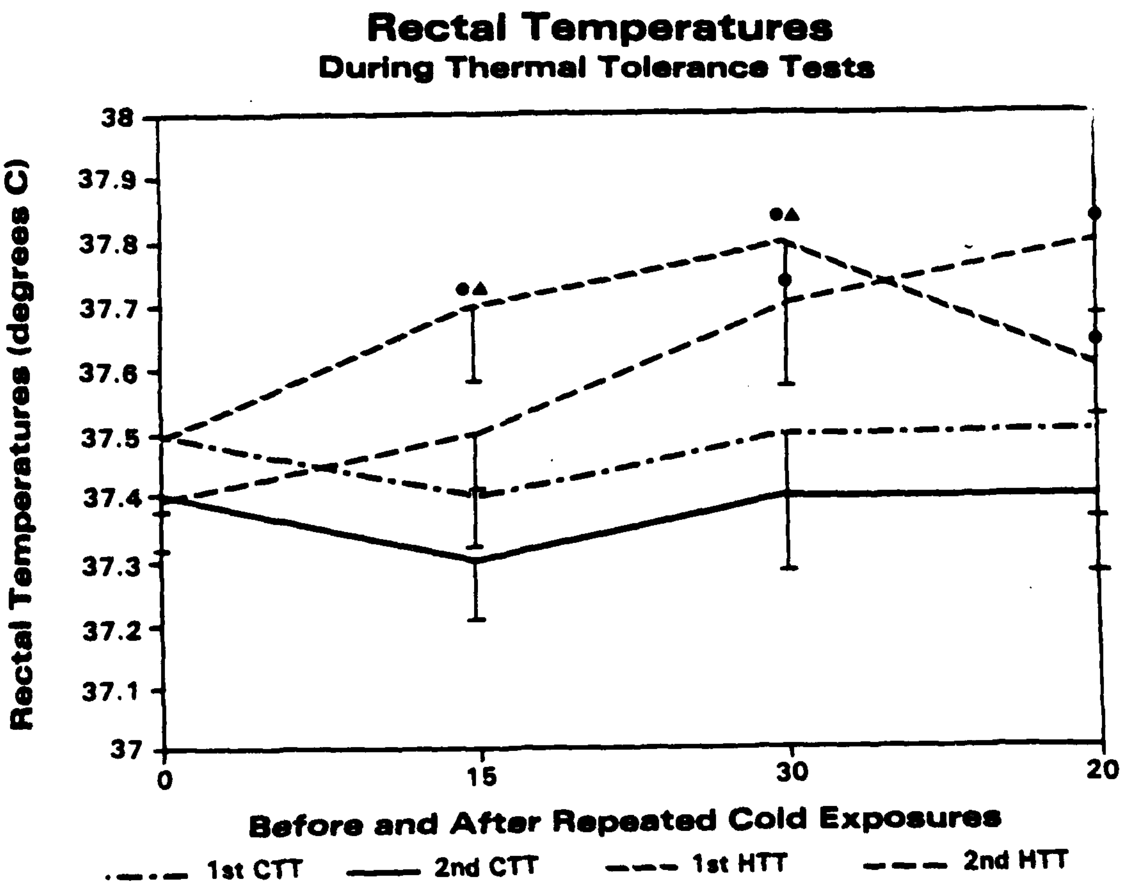

FIGURE 2

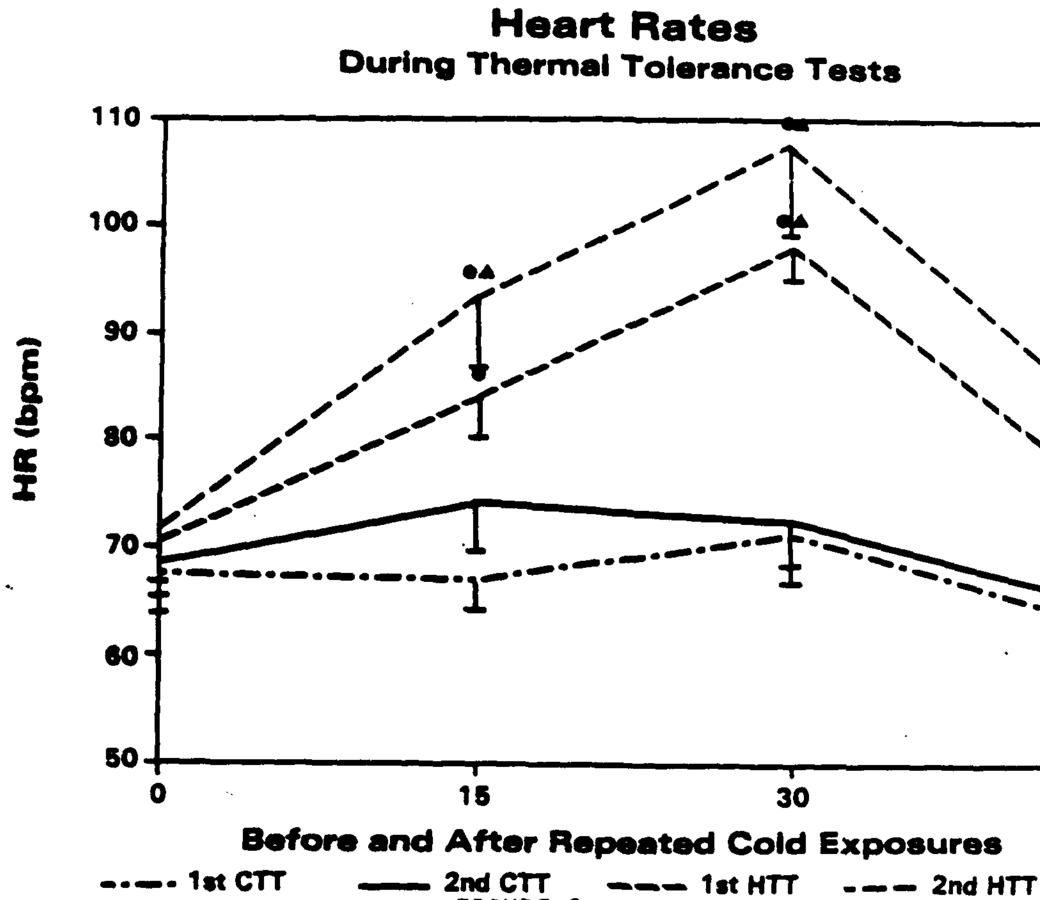

FIGURE 3

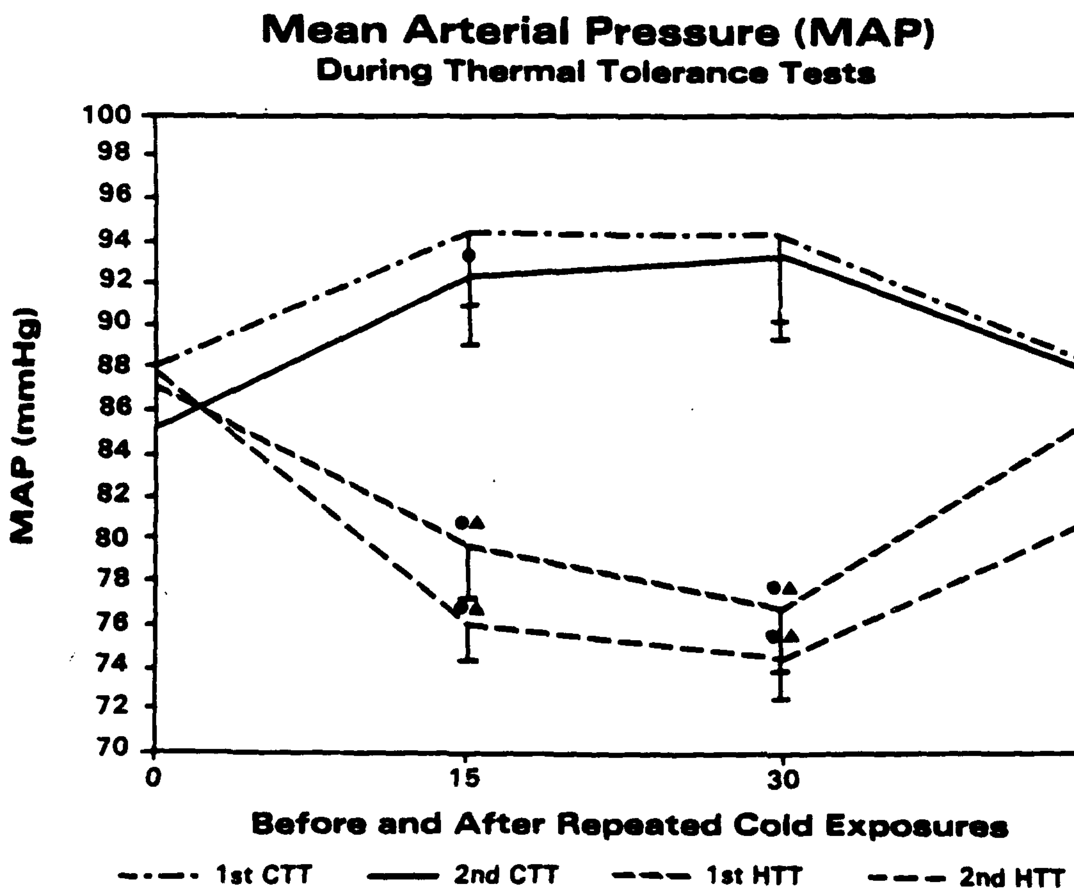

FIGURE 4

Table IV. Epinephrine (EP), Norepinephrine (NE), Cortisol, and Prolactin levels prior to (0), during (15 & 30 mins) and following (+20 mins) a cold or heat tolerance test before and after repeated cold air exposures. Data = means (+/- SE); * = significant difference between pre & post tolerance test values; # = significant difference between CTT & HTT values; + = significant difference between before & after cold exposure values.

Variable	Test	Time	0	15	30	+20
EP (pg/ml)	Cold	before	31.00 (10.01)	28.30 (7.41)	53.00 (16.51)	41.11 (12.23)
		after	42.67 (13.03)	43.11 (13.71)	56.11 (17.18)	52.67 (15.89)
	Heat	before	30.13 (11.85)	59.78*# (14.09)	83.22* (15.66)	30.67 (11.96)
		after	41.44 (10.01)	72.50*# (19.97)	133.33* (46.61)	78.22* (21.33)
NE (pg/ml)	Cold	before	363.90 (40.96)	897.90*# (101.36)	1004.80*# (112.59)	857.56*# (115.95)
		after	367.80 (61.38)	885.60*# (107.33)	975.00*# (115.16)	655.20*# (81.85)
	Heat	before	341.10 (36.87)	323.60 (47.40)	428.60* (49.54)	409.44 (51.81)
		after	419.10 (49.27)	499.60+ (59.70)	724.00*+ (81.69)	537.00*+ (50.12)
Prolactin (ng/ml)	Cold	before	7.30 (0.53)	5.99*# (0.43)	5.18*# (0.56)	5.56*# (0.59)
		after	7.15 (1.18)	9.48 (1.30)	6.06 (0.82)	6.03 (0.76)
	Heat	before	8.71 (1.26)	9.92 (0.92)	10.32 (0.83)	9.80 (1.57)
		after	7.49 (0.89)	8.59 (0.99)	13.93*# (1.71)	9.92 (1.27)
Cortisol (ug/dl)	Cold	before	12.66 (1.44)	12.79 (1.53)	12.07 (1.38)	10.21* (1.08)
		after	12.64 (1.95)	11.92 (2.04)	10.93 (1.47)	9.78 (1.20)
	Heat	before	13.89 (1.69)	12.60 (1.52)	12.84 (2.13)	12.04 (2.12)
		after	12.26 (1.28)	9.60* (1.02)	10.35* (1.33)	11.86 (2.10)

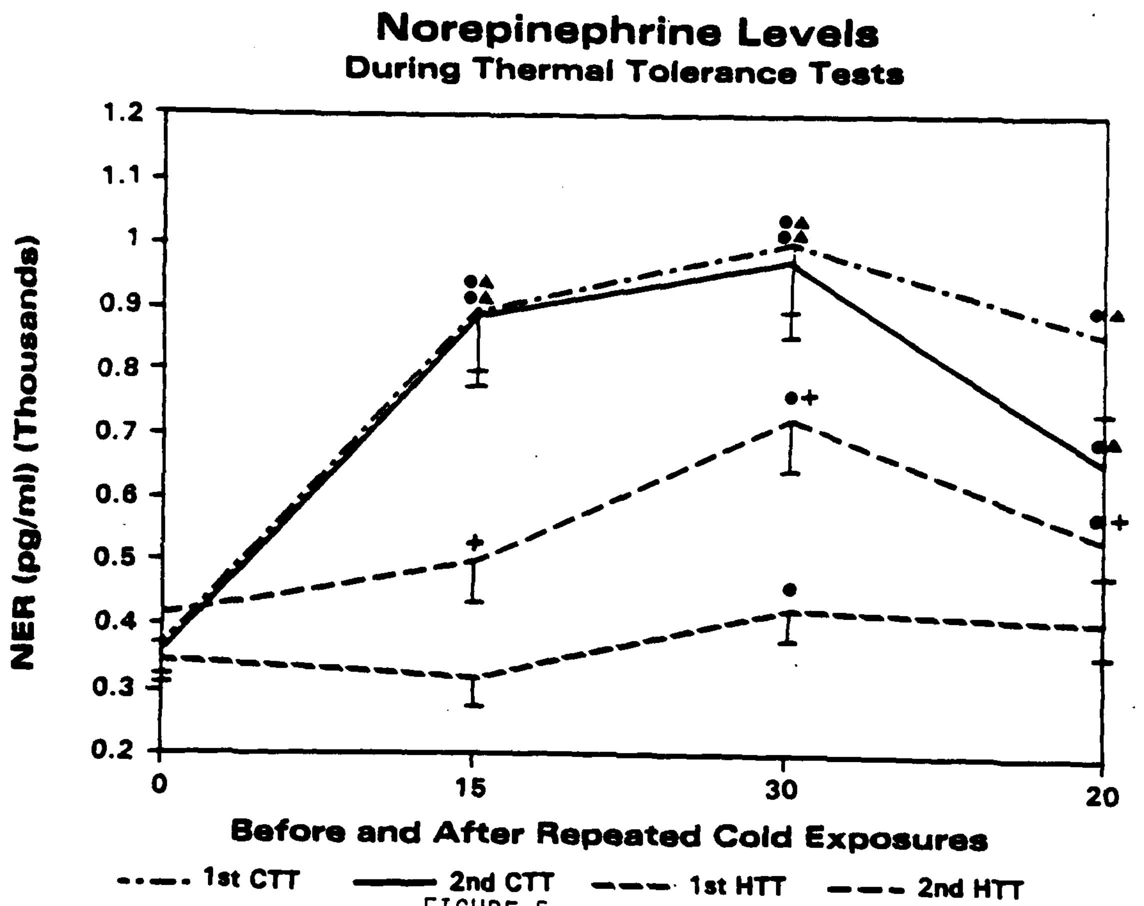

FIGURE 5

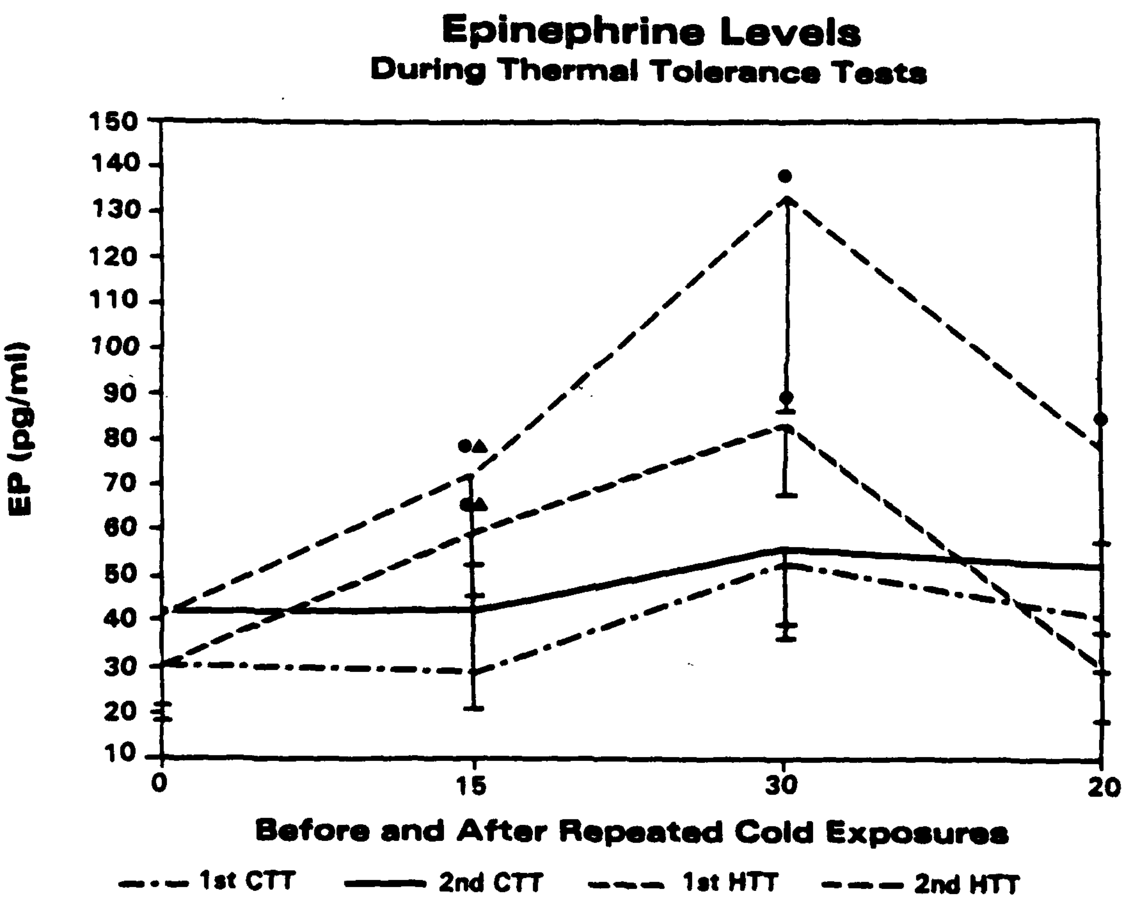

FIGURE 6

CTTs. Epinephrine levels did not change significantly during the CTT and rose 176% and 222% during the first and second HTTs respectively with the plasma levels consistently higher during the second CTT (Fig. 6).

Figures 7 and 8 depict plasma prolactin and cortisol levels during both CTTs and HTTs. Prolactin levels fell significantly during the first CTT; however, there were no significant changes following the second CTT. Conversely, prolactin levels did not change during the first HTT and rose significantly during the second HTT. Plasma cortisol levels fell slightly following the CTTs, although the second CTT did not reach significant levels. Cortisol levels did not change during the first HTT, but dropped significantly during the second HTT.

Table V summarizes Plasma Renin Activity (PRA) and aldosterone levels during the first and second CTT and HTTs. The PRA was depressed slightly during the CTTs, but this drop was only significant for the second CTT. The PRA was elevated by 133% and 148% during the first and second HTTs respectively. The aldosterone levels remain unchanged following the CTTs and were significantly higher at the end of the first HTT but not for the second HTT (Fig. 9 and 10).

Electrolyte Changes: Table VI lists plasma sodium (Na) and potassium (K) levels during the CTT and HTT before and after the repeated cold air exposures. Sodium levels did not change significantly during either thermal tolerance test; however, potassium levels were significantly elevated during both CTTs (Fig. 11). Potassium levels did not change significantly during the TTs. The possible effects of hemolysis on potassium levels during the CTT cannot be negated; however, it is believed to be a rare, confounding variable.

Appendix B summarizes urine solutes changes in response to both CTTs and HTTs. The ratio of urine sodium, potassium, or chloride to creatinine levels did not change significantly following any of the thermal tolerance tests.

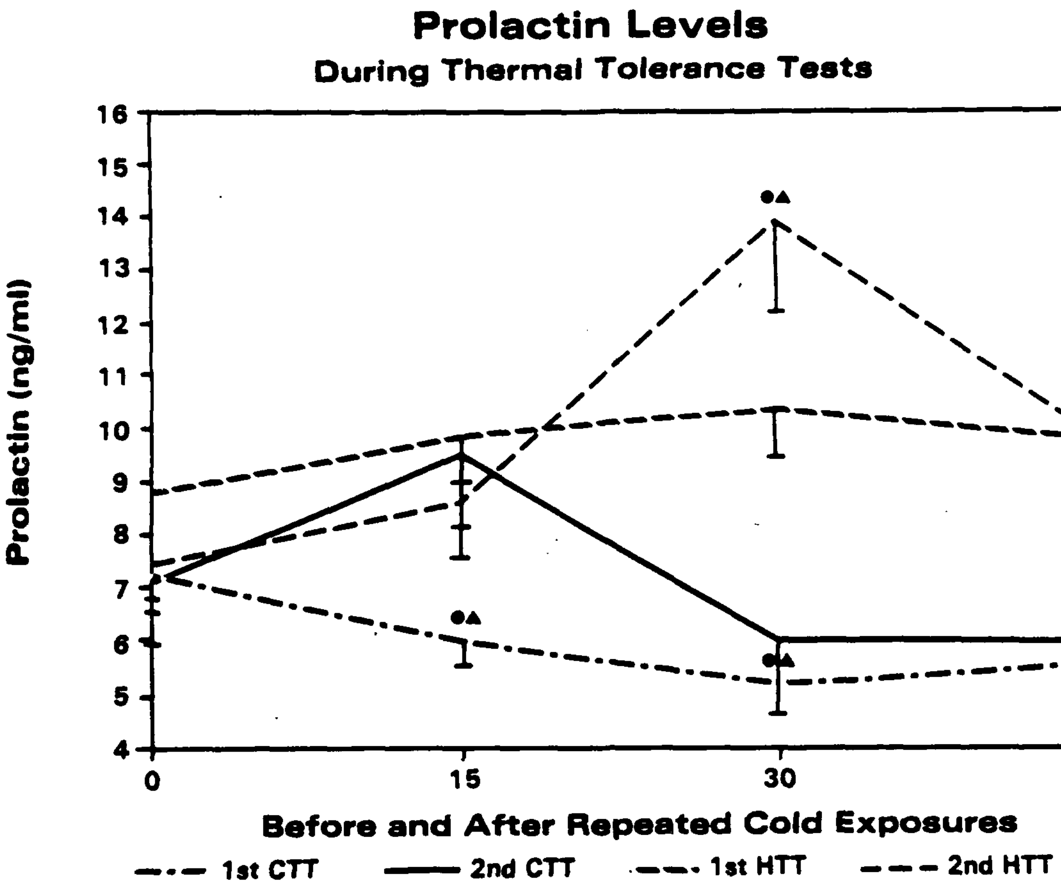

FIGURE 7

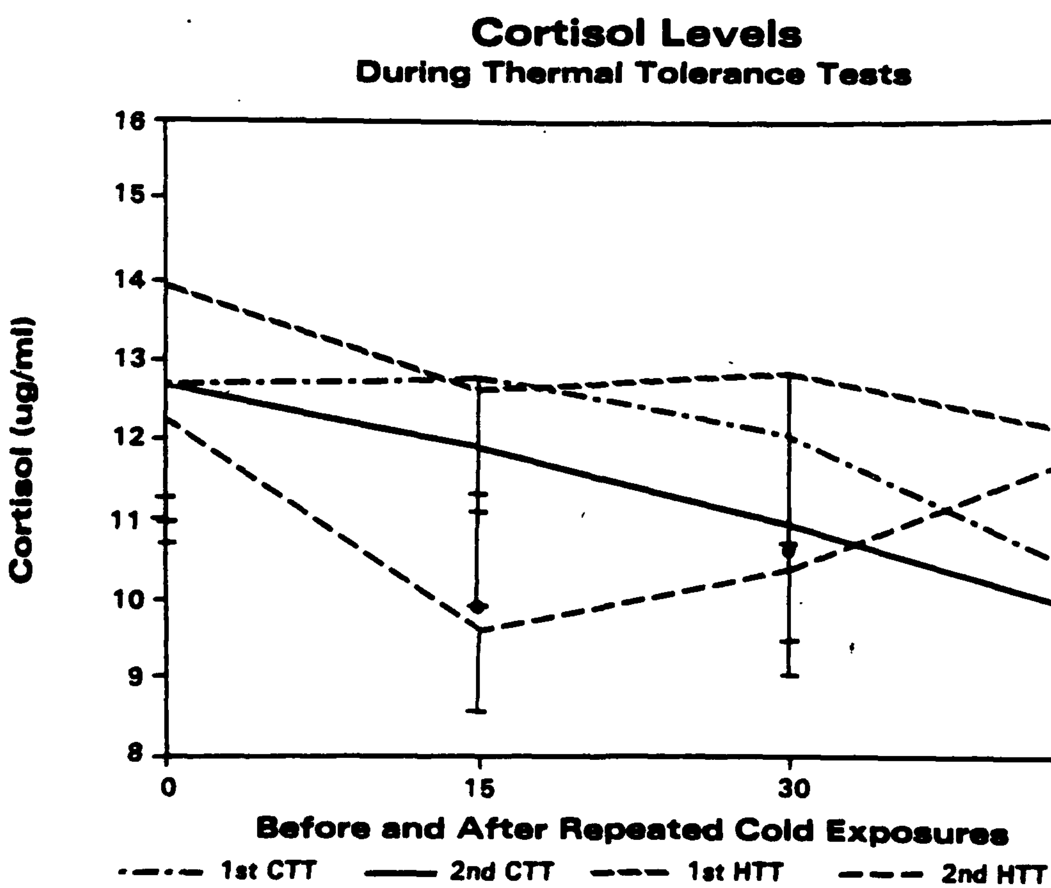

FIGURE 8

Table V. Plasma Renin Activity (PRA) and aldosterone (aldo) prior to (0), and during (15 & 30 mins) cold and heat tolerance tests before and after repeated whole body cold exposures. Plasma volume (PV) data are listed for percent change during each thermal tolerance test. Data = means (+/- SE); * = significant difference between pre and post tolerance test values; # = significant difference between CTT & HTT values.

Variable	Test	Time	0	15	30
P.R.A.	Cold	before	1.78	1.38	1.43
(ng/ml/hr)			(.34)	(.17)	(.20)
		after	2.17	1.70*	1.76
			(.43)	(.28)	(.32)
	Heat	before	1.82	2.54*#	4.20*#
			(.35)	(.44)	(.87)
		after	2.00	3.44*#	4.95*#
			(.33)	(.78)	(1.06)
aldo	Cold	before	10.91	13.78	12.22
(pg/ml)			(1.81)	(2.23)	(2.04)
		after	12.01	12.84	12.86
			(3.08)	(3.40)	(2.37)
	Heat	before	13.96	13.94	20.16#
			(1.24)	(2.80)	(3.43)
		after	13.82	13.49	13.82
			(2.68)	(1.94)	(2.73)
PV	Cold	before			-1.41
(% change)					(5.05)
		after			-9.45
					(1.24)
	Heat	before			-7.56
					(2.85)
		after			-7.35
					(1.53)

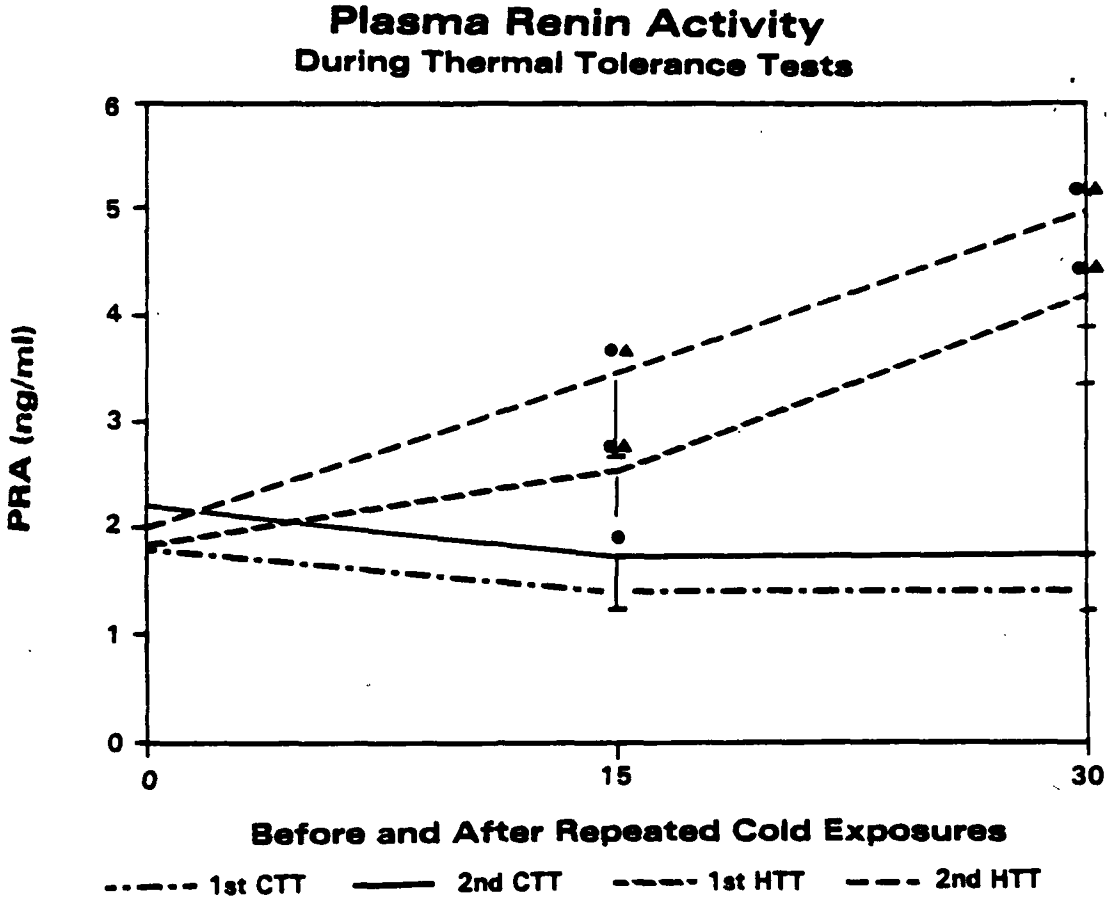

FIGURE 9

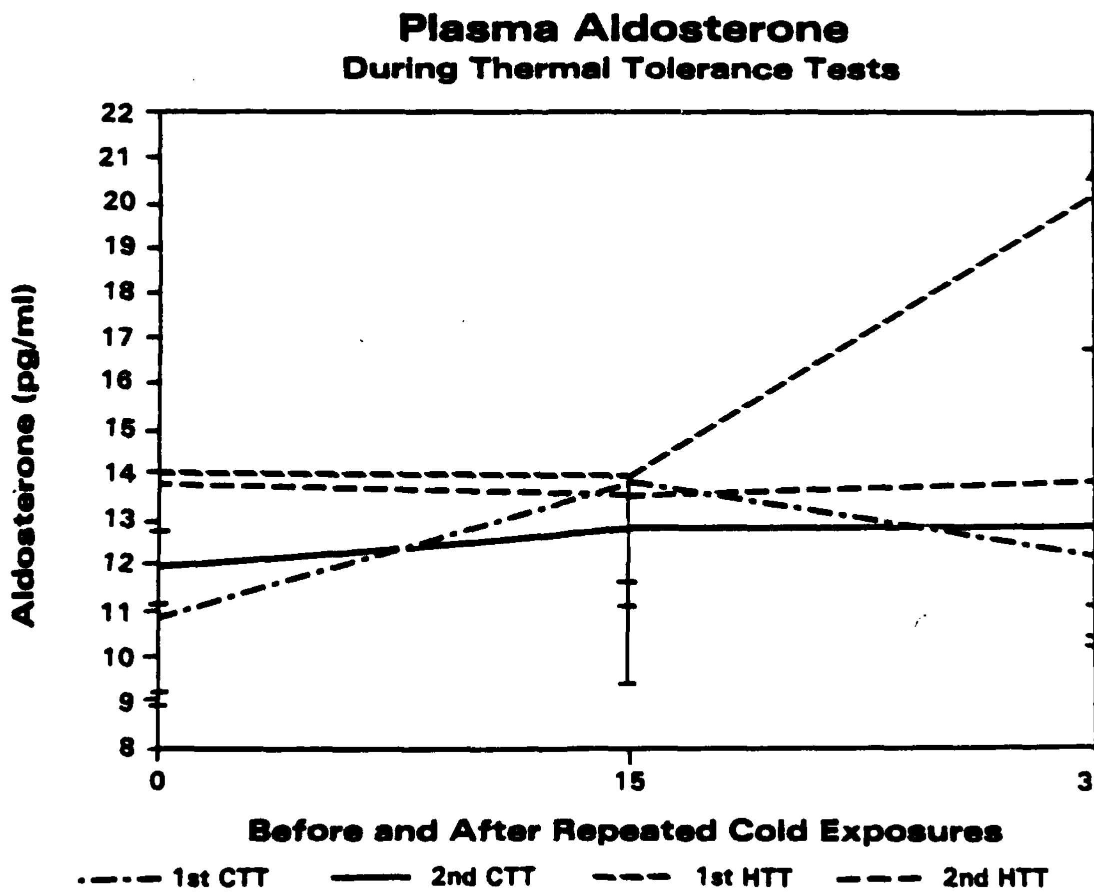

FIGURE 10

Table VI. Blood sodium (Na) and potassium (K) levels (mEq/L) prior to and following a cold or heat tolerance test before and after repeated whole body cold air exposures. Data = mean (+/- SE); * = significant difference between pre and post tolerance test values; # = significant difference between CTT & HTT values.

Variable	Test	Time	0	15	30	20
Blood	Cold	before	139.11	135.22	136.22	143.00
Na			(3.65)	(3.21)	(2.17)	(4.21)
		after	142.56	143.38	141.89	144.25
			(4.84)	(7.37)	(3.81)	(5.75)
	Heat	before	138.33	138.22	140.00	140.56
			(1.14)	(1.60)	(2.57)	(2.16)
		after	135.78	135.22	134.33	134.44
			(1.58)	(1.14)	(1.35)	(1.74)
Blood	Cold	before	4.06	4.53*#	4.39*	4.61*#
K			(.11)	(.12)	(.12)	(.13)
		after	3.98	4.51	4.68*#	4.70*#
			(.12)	(.35)	(.22)	(.20)
	Heat	before	4.01	4.10	4.18	4.11
			(.09)	(.09)	(.08)	(.11)
		after	3.87	3.96	4.00	3.86
			(.08)	(.08)	(.10)	(.05)

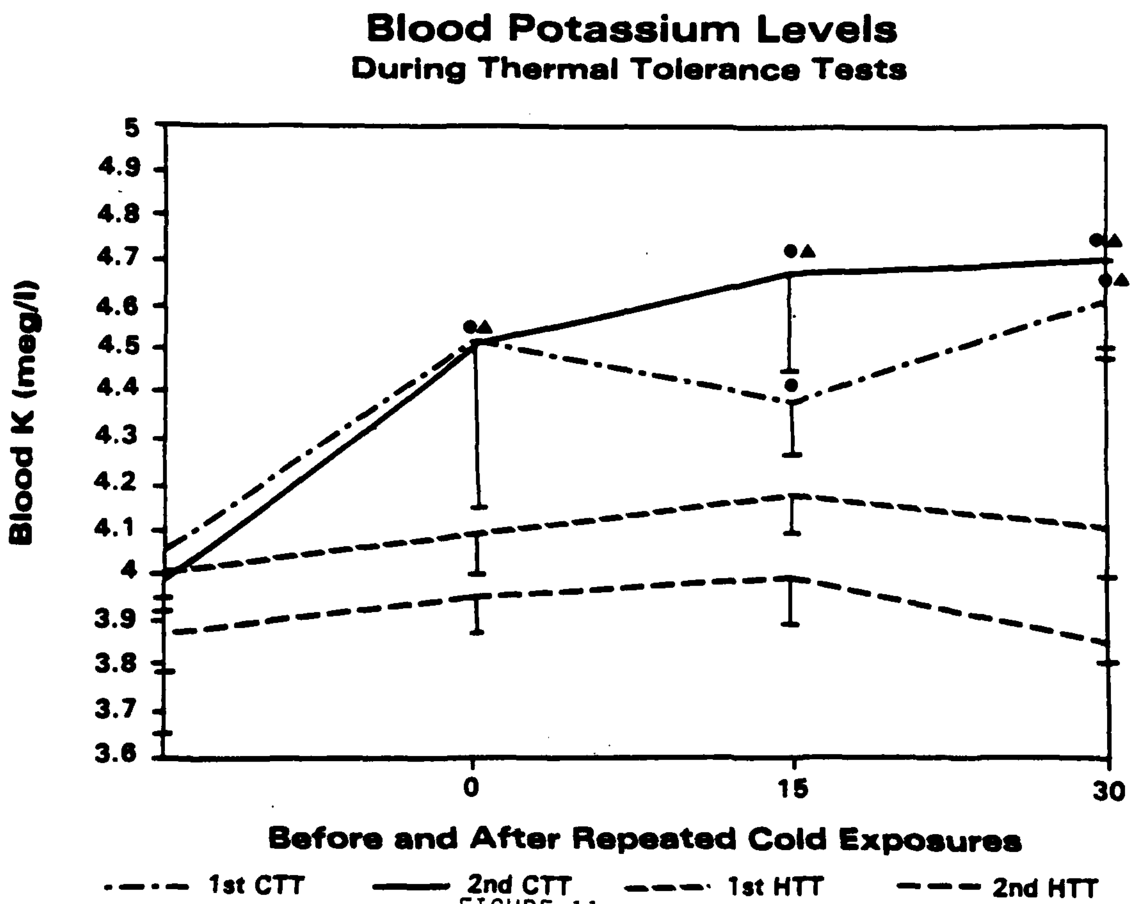
Blood Potassium Levels
During Thermal Tolerance Tests
Blood K (meg/l)
5
4.9
4.8
4.7
4.6
4.5
4.4
4.3
4.2
4.1
4
3.9
3.8
3.7
3.6
0
15
30
Before and After Repeated Cold Exposures
1st CTT
2nd CTT
1st HTT
2nd HTT

FIGURE 11

Urine flow rates during the CTTs were approximately three times the flow rates during the HTTs.

DISCUSSION

This study focused on the effects of a standardized cold tolerance test (CTT) and a standardized heat tolerance test (HTT) before and after repeated cold air exposures. The objective of this research was to assess the endocrinological and hemodynamic responses to a cold or heat tolerance test before and after repeated whole body cold air exposures. The hypothesis that repeated cold air exposures can change an individual's response to subsequent thermal tolerance tests (to either heat or cold) was confirmed.

PHYSIOLOGICAL CHANGES:

The standardized CTT and HTT, while uncomfortable for the subjects, were designed to simulate realistic environmental conditions that might be experienced outside of the laboratory. Rectal temperatures increased in the HTT but did not change significantly during the CTT. Similarly, hyperthermia is a common result of work and/or exposure to a hot environment while hypothermia is less frequently experienced in cold climates due to man's unique ability to modify his environment, e.g. adding more clothing as appropriate. As anticipated, finger skin temperatures decreased in the cold and increased in the heat; however, after 30 minutes of cold exposure during the final CTT, the finger temperature was an average of 1.3°C cooler compared to the first CTT. As noted earlier, a decrease in skin temperature following repeated cold exposures is the most frequently reported type of adaptive response to cold in man and has been described as "insulative hypothermia". This type of adaptation is generally also associated with slightly lower core temperatures. The mean rectal temperature prior to, during, and after the final CTT was an average of 0.12°C (.01) lower compared to the first CTT, although this difference did not reach statistical significance. These data would seem to suggests that after the multiple cold exposures, peripheral vasoconstriction and insulation has increased in the cold. Also, 20 minutes after the final HTT compared to the first HTT:

a) both the rectal temperature and skin finger temperature were higher (0.2°C and 3.9°C respectively); b) mean HRs during the last HTT were consistently higher; and c) MAPs were consistently lower compared to the first HTT. While these changes did not reach statistical significance, this repeated pattern may indicate that man's ability to compensate efficiently in the heat has been adversely affected. These results are in agreement with a recent report by Budd, et. al (19) who suggest that "cold exposure has an antagonistic effect on heat tolerance."

CATECHOLAMINES:

The standardized thermal tolerance tests produced acute changes in plasma catecholamine levels which were consistent with those reported in the literature (11, 20, 21, 22). Norepinephrine (NE) release is thought to originate chiefly from the adrenergic nerve endings while epinephrine (E) is secreted mainly from the adrenal glands (23). While both tests produced an increase in NE levels, this increase was greater during exposure to cold. The large rise in NE in the cold was accompanied by vasoconstriction, which resulted in elevated blood pressures and decreased skin temperatures. Conversely, the rise in E during the HTT was accompanied by increased HRs, compared with no increase in E or HR during the CTTs, and decreased blood pressures as a result of vasodilation.

Chronic cold studies on rats have demonstrated that acclimation to cold leads to an increased sensitivity of the tissues to the calorigenic effects of catecholamines, especially NE, thus exerting a sparing action on the production and/or secretion of catecholamines (23). Repeated cold exposures in man has been reported to either produce no change (20) or to show a decrease in the sympathetic nervous system (SNS) response and enhanced activity of the parasympathetic system (11). As can be seen in Figures 5 and 6, NE and E levels did not differ significantly between the first and last CTTs; however, NE and E levels increased significantly more during the final HTT compared with the first HTT. Again, these data suggest that the standardized HTT was more stressful following repeated cold exposures.

PROLACTIN:

Our results are in general agreement with recent studies that reported the serum prolactin levels decreased in response to an acute cold air exposure (24, 25, 26) and rose in response to an acute heat exposure (25). The mechanism for these changes remains unclear. While prolactin levels declined during the first CTT, no drop in plasma levels was detected during the second CTT. Prolactin rose significantly during the final HTT, where no change was detected during the first HTT. Prolactin is known to increase with stressful stimuli (27); however, no information on the effect of repeated cold exposures could be found in the literature. These results may be related to a decrease in cold stress and an increased heat stress following cold adaptation.

CORTISOL:

Previous studies have reported both increased (22, 28, 29) and decreased (30, 31) cortisol levels with cold exposure. Upon examining the Wilkerson data more closely, however, cortisol levels did not increase within the first 30 minutes of a cold exposure. Our data demonstrate that the mild cold and heat exposures experienced by the subjects in the present study were not of sufficient magnitude or duration to elevate cortisol levels. The fall in cortisol levels following the CTTs, the first of which was significant, may be a reflection of normal diurnal variations. The origin(s) of the drop during the last HTT is unclear and these results are at odds with several studies that reported elevated levels of cortisol after acute heat exposures (32, 33).

Cortisol levels are known to increase with emotional and physical discomfort and are typically monitored as an indicator of stress. The lack of rise in cortisol during this study would seem to indicate that the subjects experienced minimal discomfort and that more severe thermal exposures are necessary to elevate this adrenal cortical hormone.

ALDOSTERONE AND PLASMA RENIN ACTIVITY:

Cold exposure is known to result in hemoconcentration and decreased plasma volume (PV) as an adjustment to the circulating volume required by the smaller vascular bed. Since the hemoconcentration and decreased PV can occur even in the absence of cold-induced diuresis (34), intercompartmental shifts are believed to be involved. An increase in PRA might be predicted due to the increase in sympathetic tone and the 12-15% decrease in the plasma Na/K ratio during the CTTs. However, the PRA and aldo levels were not statistically different during the CTTs. Consequently, the urine Na and K to creat. ratios showed no significant changes in electrolyte clearance rates. While the renin-angiotensin-aldosterone system has the potential for augmenting the cold-induced elevation in BP, it has not been well studied. Our data are consistent with Hiramatsu, et al (28) who reported a significant drop in PRA after one hour of cold ($4^{o}C$) exposure; however, this fall was not significant within the first 30 minutes of exposure. Our data are consistent with the hypothesis that PRA does not contribute to the increased MAPs characteristic of acute cold exposure nor aid in the maintenance of plasma volume.

Exposure to heat induces hemoconcentration when water intake is insufficient to balance water lost in perspiration and respiration. Therefore, a rise in hormones critical for the maintenance of water and electrolyte balance would be anticipated and indeed both PRA and aldo. increased significantly during the HTTs. This response is in agreement with the literature (35, 36, 37, 38) and is consistent with the decrease in MAP associated with vasodilation.

CONCLUSIONS

1. <u>Acute Thermal Exposure Effects</u>:

a) Plasma NE levels rose dramatically (175%) during an acute exposure to a mild CTT. Vasoconstriction, as indicated by decreased finger temperatures, and increased mean arterial pressures were associated with the rise in NE levels.

b) Plasma E levels rose significantly during an acute exposure to an HTT and showed no statistically distinguishable change during an acute exposure to a CTT. The rise in E is believed to stimulate the elevation in HR, as well as vasodilation and decreased BP.

c) PRA was elevated in the heat but no change was detected in the cold, suggesting that Angiotensin II does not contribute to the general pressor effect associated with cold exposure.

2. <u>Chronic Effects of Mild Cold Exposures</u>:

a) Repeated mild cold air exposures did not significantly change E and NE responses to a CTT; however, finger skin temperature was significantly lower during the second CTT. This drop in peripheral skin temperature is indicative of "insulative" cold adaptation.

b) Following repeated cold air exposures, the NE response to a HTT increased significantly more compared to pre-exposure HTT values. In addition to elevated levels of NE, the post-cold adaptation (second) HTT differed from the pre-cold adaptation (first) HTT:

1) EP levels had not returned to pre-exposure levels 20 mins. following the second HTT, compared with no significant elevation following the first HTT.

2) MAP 20 min. after the second HTT were still elevated, compared to no significant elevation following the first HTT.

3) Prolactin levels were significantly higher during the second HTT, compared to no significant change during the first HTT.

4) Cortisol levels were significantly lower during the second HTT, compared to no significant change during the first HTT.

5) Aldosterone levels rose significantly during the first HTT and did not rise significant following the second HTT.

Taken as a group, these findings begin to confirm the hypothesis that repeated cold exposures can alter physiological responses to a standardized heat exposure. These data suggest that adaptation to cold may decrease man's ability to tolerate heat.

c) More research is needed to understand what duration and intensity of cold exposure is necessary to induce desired changes in cold tolerance, as well as how adaptation to cold affects heat tolerance and visa versa.

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FIGURE LEGENDS

<u>Figures 1 through 11</u>

CTT = Cold Tolerance Test

HTT = Heat Tolerance Test

1st = Tolerance test before repeated cold exposures

2nd = Tolerance test after repeated cold exposures

● = Significantly different ($p < 0.05$) from time 0

▲ = Significantly different between heat and cold tolerance tests

+ = Significantly different between 1st and 2nd tolerance tests

APPENDIX A. Cold tolerance test (CTT) and heat tolerance test (HTT) data

BEFORE and AFTER repeated cold air exposures.

CTT FINGER TEMPERATURES (°C)

	BEFORE --->				AFTER --->			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	19.1	13.9	10.8	15.2	22.3	10.2	7.1	16.5
2	28.6	9.8	8.2	18.9	28.1	11.3	9.9	18.3
3	25.3	11.7	9.1	18.8	27.9	10.4	8.8	17.7
4	25.4	11.4	9.0	16.6	27.4	11.0	9.1	18.8
5	33.0	16.9	11.3	24.2	32.5	9.6	8.8	26.4
6	29.0	19.2	15.9	18.4	34.6	22.0	14.0	23.2
7	30.8	15.2	13.4	25.6	32.2	11.8	10.9	27.0
8	34.0	18.7	13.1	20.8	31.8	14.1	12.8	28.8
9	35.2	22.1	18.9	33.8	35.7	21.2	16.0	31.6
10	31.6	17.2	12.7	20.8	32.3	12.3	11.9	23.7

HTT FINGER TEMPERATURES (°C)

	BEFORE --->				AFTER --->			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	28.8	39.5	39.5	28.8	33.1	39.0	40.7	34.9
2	20.8	31.3	36.0	30.2	32.6	41.4	33.8	33.8
3	31.7	39.8	40.3	33.7	28.2	40.8	39.0	32.3
4	23.4	39.0	39.0	26.2	28.0	40.7	40.6	44.7
5	34.0	38.9	38.9	34.3	30.6	40.8	39.4	29.8
6	32.2	37.7	38.0	32.8	32.4	40.1	39.4	31.9
7	30.5	40.7	40.8	27.6	32.8	38.8	39.2	33.0
8	34.5	38.2	38.5	32.1	31.3	42.4	32.8	34.7
9	32.8	41.4	40.4	30.5	34.5	39.1	38.7	35.4
10	28.8	40.2	39.8	29.9	33.7	39.7	39.1	34.9

APPENDIX A. CONT.

CTT RECTAL TEMPERATURES (^{o}C)

	BEFORE	---------->			AFTER	---------->		
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	---	---	---	---	37.6	37.4	37.4	37.2
2	37.4	37.4	37.5	37.6	36.9	36.9	36.7	36.9
3	37.7	37.4	37.4	36.9	37.4	37.1	37.1	37.0
4	36.8	37.0	37.1	36.9	37.0	36.9	37.0	37.0
5	37.9	37.7	37.9	37.8	37.2	37.1	37.4	37.6
6	37.5	37.2	37.3	37.5	37.7	37.6	37.8	37.8
7	37.9	37.8	37.9	38.1	37.3	37.3	37.5	37.7
8	37.6	37.6	37.9	38.0	37.1	37.3	37.7	37.7
9	37.7	37.3	37.4	37.7	37.7	37.7	37.8	37.7
10	37.2	37.4	37.4	37.3	37.9	37.6	37.7	37.9

HTT RECTAL TEMPERATURES (^{o}C)

	BEFORE	---------->			AFTER	---------->		
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	37.6	37.6	37.6	37.5	37.7	37.8	37.9	38.0
2	37.3	37.6	37.8	37.6	37.7	37.6	37.9	37.9
3	37.7	37.7	37.9	37.7	37.6	37.6	38.0	38.1
4	36.7	37.0	37.1	37.1	37.0	37.0	37.4	37.5
5	37.5	37.8	38.0	37.7	37.0	37.1	37.0	37.1
6	37.1	37.2	37.4	37.3	37.7	37.6	37.8	37.9
7	37.9	37.9	38.0	37.9	37.6	37.5	37.8	37.8
8	37.6	37.8	38.0	37.7	37.4	37.8	38.5	38.5
9	37.8	38.3	38.3	37.8	37.2	37.1	37.4	37.4
10	37.5	37.8	37.8	37.6	37.4	37.6	37.9	37.8

APPENDIX A. CONT.

CTT MEAN ARTERIAL PRESSURE (mmHg)

	BEFORE --->				AFTER --->			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	95	104	105	94	87	106	121	90
2	92	99	94	91	85	91	89	87
3	76	90	86	77	75	76	78	77
4	88	74	65	84	78	95	107	89
5	79	86	95	78	81	83	93	75
6	94	91	96	86	87	88	81	86
7	94	108	115	106	96	111	94	96
8	72	86	89	77	78	91	85	105
9	109	108	101	94	93	91	91	94
10	82	99	98	91	91	91	96	83

HTT MEAN ARTERIAL PRESSURE (mmHg)

	BEFORE --->				AFTER --->			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	91	87	81	94	89	81	79	84
2	93	92	86	90	96	84	71	80
3	86	78	73	78	80	69	72	84
4	63	74	65	84	87	73	69	83
5	81	69	68	69	88	81	82	75
6	89	77	75	84	86	76	81	86
7	103	82	76	101	94	80	77	79
8	76	69	69	66	85	72	64	74
9	98	87	95	102	83	68	73	85
10	90	82	80	90	89	76	76	81

APPENDIX A. CONT.

CTT HEART RATES (bpm)

	BEFORE	----------	----------	-->	AFTER	----------	----------	-->
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	72	61	70	55	67	67	74	69
2	78	70	73	76	59	66	70	59
3	68	63	61	53	74	59	57	58
4	50	70	88	71	54	62	60	55
5	52	57	51	48	49	56	51	51
6	69	96	97	56	73	66	85	73
7	78	99	64	67	61	71	85	58
8	75	79	75	75	84	78	67	78
9	81	82	82	86	88	81	103	69
10	65	66	66	64	71	65	66	59

HTT HEART RATES (bpm)

	BEFORE	----------	----------	-->	AFTER	----------	----------	-->
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	67	84	103	76	69	94	114	74
2	64	93	102	76	73	87	69	69
3	83	107	115	76	92	118	125	71
4	71	70	88	71	49	82	91	59
5	50	65	84	66	47	70	74	59
6	74	85	99	77	75	89	128	78
7	77	86	100	74	75	85	112	88
8	68	77	95	68	80	133	159	151
9	84	97	112	88	70	--	109	89
10	67	77	87	73	88	84	96	83

APPENDIX A. CONT.

CTT HEMATOCRIT (%)

	BEFORE -------->		AFTER ---------->	
TIME:	0	30	0	30
ID				
1	43	45	40	43
2	41	42	40	42
3	41	45	40	43
4	56	48	40	45
5	44	48	41	45
6	39	41	36	39
7	44	46	40	42
8	41	42	38	43
9	42	44	41	42
10	38	40	38	39

HTT HEMATOCRIT (%)

	BEFORE -------->		AFTER ---------->	
TIME:	0	30	0	30
ID				
1	41	43	37	38
2	41	42	38	39
3	43	43	40	41
4	45	46	41	42
5	41	43	38	43
6	--	--	40	42
7	45	46	42	42
8	41	40	35	38
9	44	45	37	41
10	--	47	35	35

APPENDIX A. CONT.

CTT HEMOGLOBIN (%)

	BEFORE -------->		AFTER --------->	
TIME:	0	30	0	30
ID				
1	14	15	14	15
2	21	22	14	14
3	15	12	14	16
4	15	15	14	15
5	15	16	15	15
6	--	16	--	--
7	--	--	14	15
8	14	14	14	14
9	16	16	14	14
10	--	14	13	13

HTT HEMOGLOBIN (%)

	BEFORE -------->		AFTER --------->	
TIME:	0	30	0	30
ID				
1	14	15	13	13
2	--	--	13	13
3	15	16	14	15
4	15	16	14	14
5	15	18	14	14
6	--	--	12	13
7	--	16	14	14
8	14	14	12	13
9	--	--	13	14
10	--	--	12	12

APPENDIX A. CONT.

CTT EPINEPHRINE (pg/ml)

	BEFORE				AFTER			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	75	19	17	15	21	23	107	39
2	20	29	38	33	20	20	9	24
3	12	25	35	10	81	94	83	56
4	13	10	27	18	13	11	17	43
5	59	56	140	72	15	15	58	15
6	55	71	53	61	94	94	95	128
7	15	27	15	--	15	15	15	15
8	76	46	76	82	87	94	136	129
9	15	15	15	15	--	--	--	--
10	15	15	144	94	68	52	15	55

HTT EPINEPHRINE (pg/mll)

	BEFORE				AFTER			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	11	44	43	22	33	73	70	45
2	15	25	27	15	31	34	65	51
3	14	32	44	7	21	162	167	98
4	13	56	152	--	29	30	40	34
5	58	50	105	--	21	30	100	51
6	53	114	116	75	34	102	174	74
7	--	--	--	--	51	61	53	66
8	92	90	110	57	118	196	482	241
9	--	15	30	--	--	15	--	--
10	15	127	122	23	35	37	49	44

APPENDIX A. CONT.

CTT NOREPINEPHRINE (pg/ml)

	BEFORE --->				AFTER --->			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	624	1573	1801	1553	900	1354	1430	981
2	262	948	931	713	267	785	931	570
3	341	749	920	1361	338	977	1477	1174
4	224	858	916	705	284	643	700	529
5	336	1071	1277	806	362	1293	1040	488
6	350	563	674	641	251	415	567	448
7	294	490	522	---	296	550	576	382
8	370	1196	1209	649	310	1228	1389	765
9	562	694	846	604	253	571	588	462
10	276	837	952	686	417	1040	1052	753

HTT NOREPINEPHRINE (pg/ml)

	BEFORE --->				AFTER --->			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	620	526	666	721	802	741	987	831
2	239	98	255	252	298	295	508	384
3	422	355	440	269	470	713	1151	698
4	224	227	274	305	524	562	733	408
5	255	299	460	---	264	186	407	607
6	330	306	509	384	318	499	791	579
7	339	358	480	486	423	595	762	645
8	292	235	266	360	371	574	961	420
9	389	607	656	572	369	564	543	357
10	301	225	280	336	352	267	397	441

APPENDIX A. CONT.

CTT PROLACTIN (ng/ml)

	BEFORE				AFTER			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	6	6	5	6	7	5	5	4
2	10	6	8	9	13	12	11	9
3	9	7	5	4	4	6	4	-
4	4	4	4	4	4	4	4	4
5	9	8	9	6	1	17	11	10
6	6	6	4	4	7	11	5	4
7	8	5	4	9	8	12	6	6
8	6	4	4	4	12	12	5	6
9	8	8	5	5	6	7	4	5
10	7	5	4	5	10	9	6	6

HTT PROLACTIN (ng/ml)

	BEFORE				AFTER			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	9	9	10	7	7	7	10	8
2	10	10	11	11	13	13	23	19
3	16	15	13	10	5	8	17	10
4	15	13	11	8	6	7	8	6
5	4	14	13	23	9	15	14	11
6	4	7	5	4	4	5	15	8
7	6	7	10	9	5	8	13	4
8	6	8	9	10	7	6	22	-
9	7	9	13	9	7	7	7	8
10	8	8	8	7	11	10	11	10

APPENDIX A. CONT.

CTT CORTISOL (ug/dl)

	BEFORE				AFTER			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	18.8	17.8	17.3	11.9	8.2	9.8	7.2	5.6
2	14.4	13.6	11.1	10.5	16.6	16.4	15.7	13.6
3	16.3	16.5	13.5	14.8	11.0	11.3	12.4	12.9
4	10.2	17.2	16.8	10.2	12.5	11.1	8.9	9.3
5	15.9	14.2	11.3	8.0	24.9	27.6	19.9	11.6
6	17.4	16.7	16.6	11.6	8.4	7.7	8.6	7.4
7	5.3	3.7	3.9	3.7	6.9	6.3	4.9	4.0
8	8.0	8.1	11.5	10.6	8.4	7.7	12.6	15.6
9	8.5	7.3	6.6	6.4	8.6	6.6	6.2	6.7
10	11.8	12.8	12.1	14.4	20.9	14.7	12.9	11.1

HTT CORTISOL (ug/dl)

	BEFORE				AFTER			
TIME:	0	15	30	+20	0	15	30	+20
ID								
1	18.7	17.8	16.5	13.1	15.8	12.1	12.0	11.1
2	19.7	17.0	13.3	9.5	4.5	4.9	4.8	6.5
3	30.7	12.7	10.5	8.9	13.6	11.2	12.4	14.7
4	33.8	19.8	28.6	23.4	13.1	8.7	8.7	8.9
5	13.9	11.1	14.3	22.7	18.7	14.8	18.6	22.1
6	15.8	13.1	12.7	12.5	12.1	9.1	8.9	7.4
7	8.0	5.4	5.0	4.0	13.6	13.1	11.1	9.1
8	9.8	8.0	6.3	5.2	12.2	9.0	14.1	24.4
9	7.9	7.0	7.2	6.9	6.9	5.2	5.1	4.2
10	17.3	14.1	14.0	14.2	12.1	7.9	7.8	10.2

APPENDIX A. CONT.

CTT ALDOSTERONE (pg/ml)

	BEFORE --->			AFTER --->		
TIME:	0	15	30	0	15	30
ID						
1	4.5	5.1	5.0	6.9	6.6	7.8
2	6.3	7.2	6.1	5.6	10.5	21.5
3	13.8	13.7	13.5	13.3	9.2	10.8
4	9.6	19.3	22.5	12.4	11.8	15.2
5	15.4	24.1	18.3	35.7	39.0	27.1
6	7.8	9.4	10.1	7.1	5.0	7.1
7	5.5	7.8	5.5	7.6	7.9	7.3
8	20.2	19.0	13.0	9.3	14.0	7.8
9	23.2	31.2	33.7	12.7	27.4	19.4
10	15.1	18.4	16.0	10.2	11.6	11.1

HTT ALDOSTERONE (pg/ml)

	BEFORE --->			AFTER --->		
TIME:	0	15	30	0	15	30
ID						
1	10.4	8.7	13.8	16.3	14.0	8.0
2	11.9	7.5	7.8	24.9	22.1	9.0
3	20.9	15.7	22.5	21.7	20.0	31.6
4	15.7	31.8	36.9	24.1	19.3	10.4
5	15.5	7.9	33.9	3.8	10.9	17.6
6	13.5	7.8	11.6	8.5	6.9	13.1
7	8.1	7.5	16.0	8.3	13.1	20.2
8	13.5	18.5	12.9	7.9	7.9	9.3
9	22.6	27.9	---	15.6	15.6	15.9
10	16.1	20.1	26.0	8.9	7.2	5.2

APPENDIX A. CONT.

CTT PLASMA RENIN ACTIVITY (ng/ml/h)

	BEFORE	---------------	--------------->	AFTER	---------------	--------------->
TIME:	0	15	30	0	15	30
ID						
1	0.6	0.7	0.7	1.6	1.6	1.4
2	1.5	1.1	1.2	1.9	1.5	1.6
3	1.7	1.7	1.9	3.0	2.8	3.5
4	1.8	1.4	1.3	0.8	0.7	0.7
5	4.0	2.1	2.6	5.0	3.1	2.9
6	1.7	1.6	1.7	2.1	1.7	1.7
7	0.7	0.5	0.6	0.9	0.8	0.7
8	2.5	1.8	1.6	1.5	1.1	1.2
9	2.0	1.5	1.4	2.9	2.5	2.2
10	1.5	1.5	1.3	2.7	2.0	2.1

HTT PLASMA RENIN ACTIVITY (ng/ml/h)

	BEFORE	--------------	-------------->	AFTER	---------------	--------------->
TIME:	0	15	30	0	15	30
ID						
1	0.9	1.2	2.4	1.0	1.3	2.6
2	1.1	1.1	1.7	1.7	2.0	3.2
3	4.2	4.4	8.9	3.7	6.4	18.4
4	1.6	2.8	3.8	1.2	3.5	4.3
5	1.9	3.4	5.8	2.6	4.2	6.4
6	2.8	4.1	7.4	3.2	7.9	11.6
7	1.1	1.7	2.8	1.1	2.1	4.9
8	1.4	1.1	1.4	2.1	2.2	4.2
9	2.9	6.9	9.6	1.5	2.2	5.6
10	1.4	3.1	3.6	1.4	1.4	2.4

Appendix B. Urine creatinine (creat.), and the ratio of urine chloride to creatinine (Cl/creat.), urine potassium to creatinine (K/creat.), urine sodium to creatinine (Na/creat.), and urine flow rate (UFR) prior to and following a cold or heat tolerance test before and after repeated whole body cold air exposures. Data = mean (+/- SE); # = significant difference between CTT & HTT values.

Variable	Test	Time	Pre	Post
creat. (mg/hr)	Cold	before	135.67 (26.34)	69.33 (29.47)
		after	150.90 (29.61)	72.50 (16.76)
	Heat	before	129.38 (23.31)	151.22 (40.66)
		after	157.90 (21.64)	164.00 (19.48)
Na/creat. (mEq/g)	Cold	before	0.96 (0.25)	1.38 (0.28)
		after	0.86 (0.16)	1.33 (0.32)
	Heat	before	1.12 (0.20)	0.98 (0.16)
		after	0.91 (0.11)	0.82 (0.11)
K/creat. (mEq/g)	Cold	before	0.44 (0.08)	0.46 (0.04)
		after	0.43 (0.07)	0.47 (0.06)
	Heat	before	0.50 (0.07)	0.49 (0.06)
		after	0.52 (0.10)	0.50 (0.08)
Cl/creat. (mEq/g)	Cold	before	1.11 (0.25)	1.40 (0.21)
		after	1.01 (0.17)	1.43 (0.19)
	Heat	before	1.28 (0.23)	1.11 (0.16)
		after	0.96 (0.07)	0.99 (0.11)
UFR (ml/min)	Cold	before		3.10# (0.67)
		after		3.47# (0.95)
	Heat	before		1.03 (0.25)
		after		0.96 (0.41)