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## *THE EFFECT OF HYPOXIA AND COLD AT REST ON HUMAN THERMOREGULATION*

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THE EFFECT OF HYPOXIA AND COLD AT REST ON HUMAN  
THERMOREGULATION

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## SUMMARY

### Problem

Cold is associated with altitude: the higher the altitude, the lower the temperature. As the ambient temperature decreases, oxygen consumption in humans at rest increases. Resting thermogenesis, or the ability of the body to create heat in order to maintain homeostasis, occurs in part by shivering. In some animal species (pigeons, rats, cats, dogs, and humans) shivering has been shown to be suppressed due to breathing oxygen at or below 12%. Since most U.S. Marine Corps cold-weather training occurs at altitude (2700 m) it is important to evaluate the relationship of reduced oxygen and thermogenesis. In a military environment, hypothermia will impede combat performance by rendering the hypothermic person ineffective to carry out his/her mission, and it will increase manpower demands by requiring attention from at least one other person.

### Objective

The primary objective of this investigation was to determine if exposure to moderate cold (4.4°C) and decreased oxygen (O<sub>2</sub>) tension (15% O<sub>2</sub>, simulating 2700 m) decreases the ability of the human body to shiver and to maintain core and skin temperatures at rest.

### Approach

Nine male U.S. Navy and U.S. Marine Corps personnel participated as subjects. Subjects reported to the laboratory on two separate days with at least 48 hr between the two trials. All trials were conducted at 4.4°C, 40% relative humidity while sitting at rest in a chair. The approach consisted of 15 min at room temperature (23°C) and room air (20.9% O<sub>2</sub>), cold air exposure (4.4°C) for 120 min while inhaling 20.9% O<sub>2</sub> or 15% O<sub>2</sub>, followed by 10 min at room temperature. Measurements included rectal (T<sub>re</sub>), mean-weighted skin temperatures (T<sub>sk</sub>), thermal sensation (TS), heart rate (HR), oxygen uptake ( $\dot{V}O_2$ ), electromyograms (EMGs) on left

midchest and left upper trapezius, and blood draws for hematocrit, hemoglobin, lactic acid, and cortisol.

### Results

All subjects shivered vigorously during normoxic and hypoxic cold as observed by investigators, reported in TS, and measured on EMGs. Although variables changed over time, there was no condition effect for  $T_{re}$ ,  $T_{sk}$ , TS,  $\dot{V}O_2$ , EMGs, cortisol, or plasma volume. There was no condition or time effect on HR or lactic acid.

### Conclusion

The reduction of inspired oxygen to 15% had no effect on thermoregulation in males during a resting exposure in a cold environment.

## INTRODUCTION

Cold is associated with altitude, and the higher the altitude, the lower the temperature. As the ambient temperature decreases, oxygen consumption ( $\dot{V}O_2$ ) in humans at rest increases (Feith, Hesslink, Reading, Kincaid, & Pozos, 1993; LeBlanc, 1986; Reading, Kincaid, Roberts, Hesslink, & Pozos, 1994; Robinson & Haymes, 1990; Tikuisis, Bell, & Jacobs, 1991). As cold stress increases,  $\dot{V}O_2$  and heat production rise. This rise is primarily due to shivering (Kleinebeckel & Klussmann, 1990). When hypoxia is added to cold at rest, less shivering and a lower  $\dot{V}O_2$  can occur. Controversy exists as to the threshold altitude or oxygen ( $O_2$ ) percentage at which shivering is reduced. A threshold level of 12% oxygen (simulating an altitude of 4160 m) has been proposed for reduction in shivering and  $\dot{V}O_2$  (Kottke, Phalen, Taylor, Visscher, & Evans, 1948; Blatteis, 1971).

Resting thermogenesis, or the ability of the body to create heat in order to maintain homeostasis, occurs in part by shivering. If shivering is limited, decreased, or stopped, core temperature will decline, and the person will become hypothermic and eventually die if core temperature is not restored to normal. In a military environment, hypothermia will impede combat performance by rendering the hypothermic person ineffective to carry out his/her mission, and it will increase manpower demands by requiring attention from at least one other person. Therefore, maintenance of a stable core temperature during cold exposure is of paramount importance if troops are to be battle ready.

In some animal species (pigeons, rats, cats, dogs, and humans) shivering has been shown to be suppressed due to breathing oxygen at or below 12% (Barnas & Rautenberg, 1990; Gautier & Bonora, 1992; Gautier & Bonora, 1994; Gautier, Bonora, Schultz, & Remmers, 1987; Gautier, Bonora, & Trinh, 1993; Hemingway & Birzis, 1956; Kottke et al., 1948). Shivering was not suppressed in cold acclimatized miniature pigs breathing 10%  $O_2$  (Blatteis & Gilbert, 1974).

$\dot{V}O_2$  was reported to decrease in humans, small mammals, rats, and cats while breathing at 12%  $O_2$  or lower (Blatteis & Luther, 1974; Frappell, Lanthier, Baudinette, & Mortola, 1992; Gautier, Bonora, & Remmers, 1989; Gautier & Bonora, 1992; Gautier et al., 1993; Gautier & Bonora, 1994; Giesbrecht, Fewell, Megirian, Brant, & Reemers, 1994; Hemingway & Birzis, 1956; Kottke et al., 1948).

In human studies performed on mountains, acute mountain sickness occurs at altitudes of 2000 to 3000 m (Beeley, Smith, & Oakley, 1993; Sutton, 1992). Blood oxygen saturation decreases from 96.7% at sea level to 92.0% at 3000 m (Ramirez, Agosti, Bittle, Dietz, & Colice, 1992). Nonshivering thermogenesis was decreased at 3350 to 4340 m (Blatteis & Luther, 1976). In studies using hypobaric chambers, it was reported that rectal temperature ( $T_{re}$ ) decreased 0.2°C at 2500 m and 0.3°C at 5000 m, while mean skin temperature ( $T_{sk}$ ) decreased 1.0°C at 2500 m and 2.0°C at 5000 m (Cipriano & Goldman, 1975). At rest, breathing 12%  $O_2$  for 90 min had no effect on heart rate (HR), systolic blood pressure, ventilation, respiratory exchange ratio (RER), blood lactate,  $T_{re}$ , or  $\dot{V}O_2$  (Robinson & Haymes, 1990). The mechanical reflex oscillations from a 50-g mass loaded on a human right index finger were not compromised while inhaling 10%  $O_2$  (Krause, Leiter, Daubenspeck, & Tenney, 1993), but inhibition of sympathetic nerve activity did occur (Somers, Mark, & Abboud, 1991).

Since most U.S. Marine Corps cold weather training occurs at altitude (2700 m), it is important to evaluate the relationship of reduced  $O_2$  and thermogenesis. In the present study, breathing 15%  $O_2$  was used to simulate the acute effects of an altitude of 2700 m. The laboratory is at 10 feet above sea level. The acute reaction of the low  $O_2$  (simulating 2700 m) was compared with normal room air at sea level. The purpose of this investigation was to determine if exposure to moderate cold (4.4°C) and decreased  $O_2$  tension (15%  $O_2$ ) decreases the ability of the human body to shiver and to maintain  $T_{re}$  and  $T_{sk}$  at rest.

## **METHODS**

Nine male U.S. Navy and U.S. Marine Corps personnel participated as subjects after being briefed and signing voluntary consent forms according to NAVHLTHRSCHCENINST 6500.2. The subjects physical characteristics were ( $\pm$  SD): weight  $83.3 \pm 13.1$  kg, height  $180.1 \pm 7.1$  cm, and percent fat  $15.1 \pm 5.5\%$ . All measurements and methods were approved by the Naval Health Research Center and the Navy Medical Research and Development Command committees for the protection of human subjects.

### Medical Screening

Subjects were informed of the nature, purpose, and potential risks of the experimental procedures, and they signed informed consent and Privacy Act Statements. All subjects underwent medical screening, which included a medical history questionnaire, body composition assessment, and clearance to participate by a medical officer. Height and weight were determined by standard methods. Body density was determined using the three sites equation proposed by Jackson and Pollock (1978). Siri's equation (1961) was used to determine relative body fat.

### Experimental Protocol

Subjects reported to the laboratory on two separate days with at least 48 hr between the two trials. The influence of circadian rhythms on body temperature was controlled by conducting each test at the same time of day as proposed by Hagan and Horvath (1978). Experimental conditions were presented to each subject in a counterbalanced-blind design. All trials were conducted at  $4.4^{\circ}\text{C}$ , 40% relative humidity while sitting at rest in a chair. The testing protocol consisted of 15 min at room temperature ( $23^{\circ}\text{C}$ ) and room air (20.9%  $\text{O}_2$ ), cold air

exposure (4.4°C) for 120 min while inhaling 20.9% O<sub>2</sub> (N) or 15% O<sub>2</sub> (H), followed by 10 min at room temperature (23°C) and room air (20.9% O<sub>2</sub>).

Upon arrival at the laboratory, body weight was recorded. Each subject then inserted a rectal thermistor to a depth of 20 cm. Skin thermistors were placed on the right side of the body on the biceps, chest, front mid thigh, and back mid calf. Electrodes for electromyograms (EMGs) were placed on the left pectoralis major and the left upper trapezius. An HR telemetry system was placed around the torso at chest level. A heparinized catheter was placed in a brachial vein in the antecubital space. During the test, each subject wore shorts, T-shirt, socks, and tennis shoes.

### Measurements

A polar Vantage XL monitor (Polar USA, Inc.; Stamford, CT) was used to determine HR.  $T_{re}$  was measured using sterile disposable Sher-I-Temp® thermistors. Skin temperatures were measured using silver skin thermocouples. A Grant 1200 series (12-bit) Squirrel Meter/Logger was used to record core and skin temperatures. An ME3000P data recording device (Woodway, Inc., Minneapolis, MN) was used to record and store EMGs. The median power frequency (MPF) and root mean square (RMS) were calculated from the EMGs. A 9-point thermal sensation scale (TS) (Bedford, 1936) was used to determine how cold the subject felt (8 extremely hot, 4 neutral, 0 extremely cold).

$\dot{V}O_2$  and carbon dioxide production ( $\dot{V}CO_2$ ) were determined using open-circuit spirometry. Expired gas was collected for 2 min in a Collins 100-L plastic bag (Warren E. Collins; Braintree, MA) connected to a two-way valve. Expired gas was analyzed for O<sub>2</sub> and carbon dioxide (CO<sub>2</sub>) using S-3A/I oxygen and CD-3A CO<sub>2</sub> analyzers (Ametek; Pittsburgh, PA), respectively. Expired gas volume was measured using a 120 l Tissot. Blood pressure was measured using a manual sphygmomanometer and stethoscope. Blood samples were used to

determine hematocrit, hemoglobin, lactic acid, and cortisol. Percent plasma volume was calculated from hematocrit and hemoglobin values (Young, Muza, Sawka, & Pandolf, 1987).

Throughout the study, HR,  $T_{re}$ , and skin temperatures were recorded every min.  $T_{sk}$  was calculated as:  $0.35 (T_{chest} + T_{biceps}) + 0.15 (T_{thigh} + T_{calf})$ , using the techniques proposed by Ramanathan (1964), as adapted by Mitchell and Wyndham (1969). Exhaled gas, EMG, and blood were measured after 15 min of rest prior to exposure (baseline) and at min 30, 60, 90, and 120 of cold exposure. Blood was drawn before exposure and taken 10 min postexposure. After baseline measurements were completed, the subject remained in the chair and was wheeled into the cold chamber. The subject remained in the cold for 120 min. After the cold exposure, the subject was wheeled out of the chamber and remained seated until the last measurement was taken.

#### Statistical Analysis

Data were analyzed using repeated-measures analysis of variance. The alpha level was set at 0.05. When significant differences occurred, a Neumann-Kuels post hoc analysis was used to determine where differences occurred.

## **RESULTS**

All subjects shivered vigorously during normoxic and hypoxic cold as observed by investigators, reported in thermal sensations, and measured on EMGs. No differences occurred between hypoxic and normoxic conditions. Although variables changed over time, there was no condition effect for  $T_{sk}$ ,  $T_{re}$ , EMG,  $\dot{V}O_2$ , or TS. There was no condition or time effect on HR.

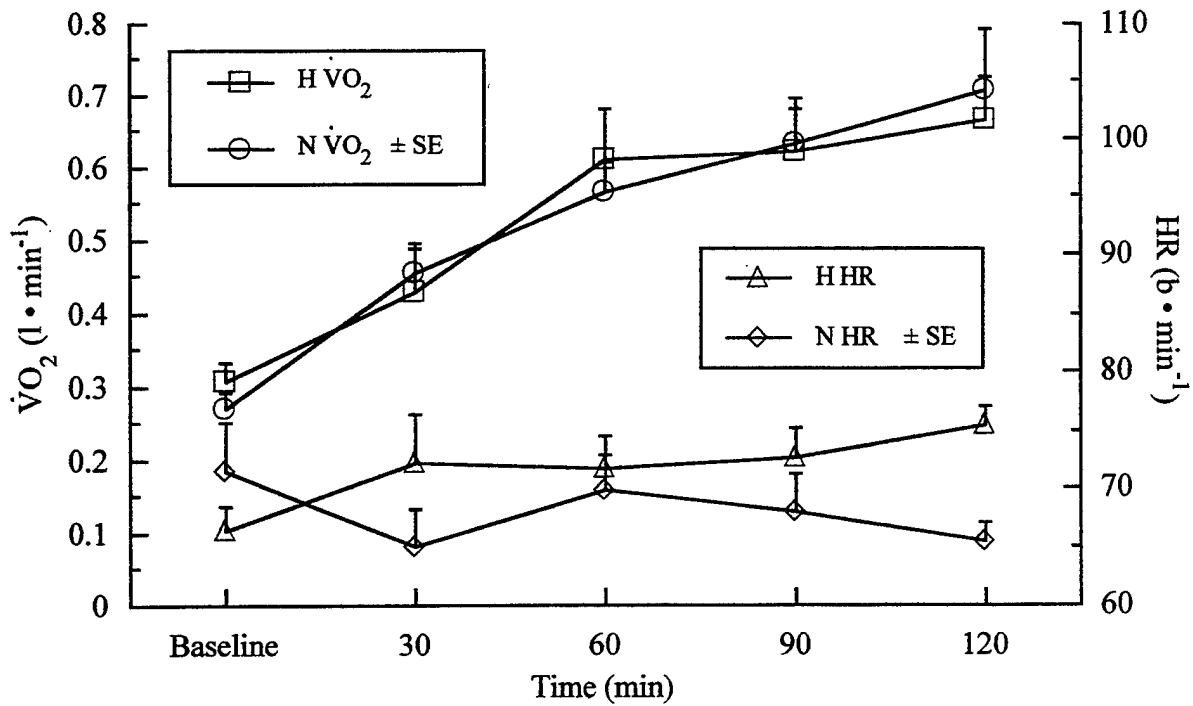


Figure 1. Oxygen consumption and heart rate for H vs. N inspired oxygen.

In both conditions,  $\dot{V}O_2$  (Figure 1) increased progressively ( $0.307 \pm 0.08$  to  $0.664 \pm 0.18$   $l \cdot min^{-1}$  in hypoxia and  $0.268 \pm 0.07$  to  $0.706 \pm 0.26$   $l \cdot min^{-1}$  in normoxia) during the 120-min cold exposure.

There was no difference between conditions for TS. TS decreased from 4.6 to 1.3 in hypoxia and from 4.5 to 1.6 in normoxia (Figure 2). Analysis of  $T_{re}$  (Figure 3) revealed no differences between the conditions. A gradual decrease over time did occur.  $T_{re}$  decreased  $0.31^{\circ}\text{C}$  from  $37.05 \pm 0.40$  to  $36.74^{\circ}\text{C} \pm 0.41$  during hypoxia, and it decreased  $0.35^{\circ}\text{C}$  from  $37.06 \pm 0.30$  to  $36.71^{\circ}\text{C} \pm 0.42$  during normoxia. Analysis of  $T_{sk}$  (Figure 4) revealed no differences between the conditions. A gradual decrease over time in both conditions did occur.  $T_{sk}$  decreased  $13.01^{\circ}\text{C}$  from  $31.86 \pm 0.56$  to  $18.85^{\circ}\text{C} \pm 2.15$  during hypoxia, and it decreased  $12.84^{\circ}\text{C}$  from  $31.90 \pm 1.01$  to  $19.06^{\circ}\text{C} \pm 2.74$  during normoxia.

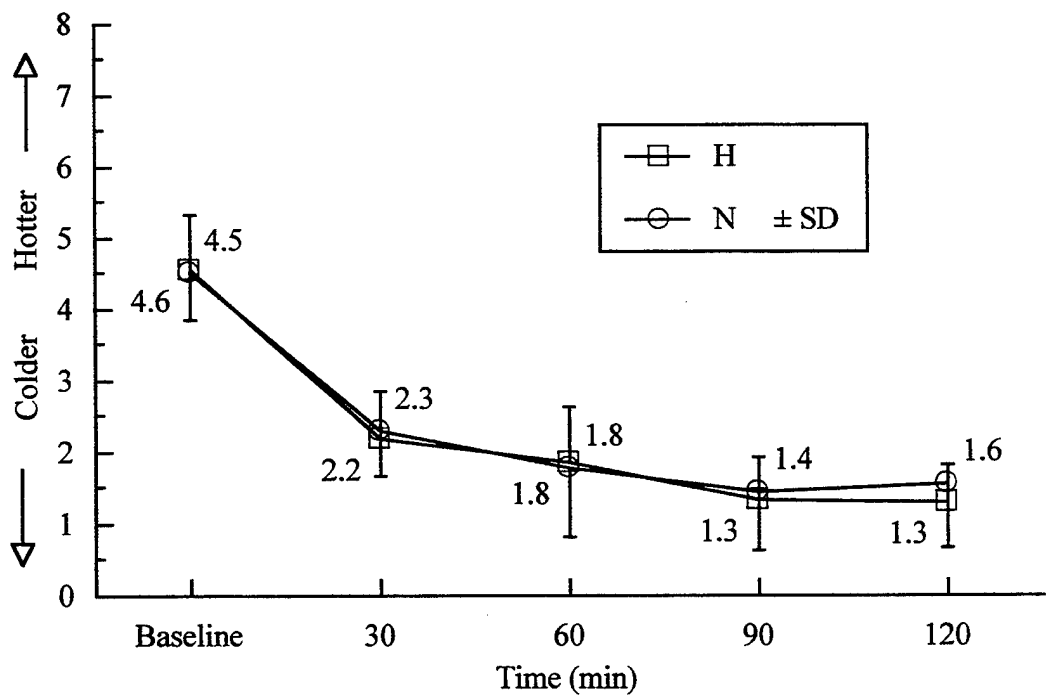


Figure 2. Thermal sensation for H vs. N inspired oxygen.

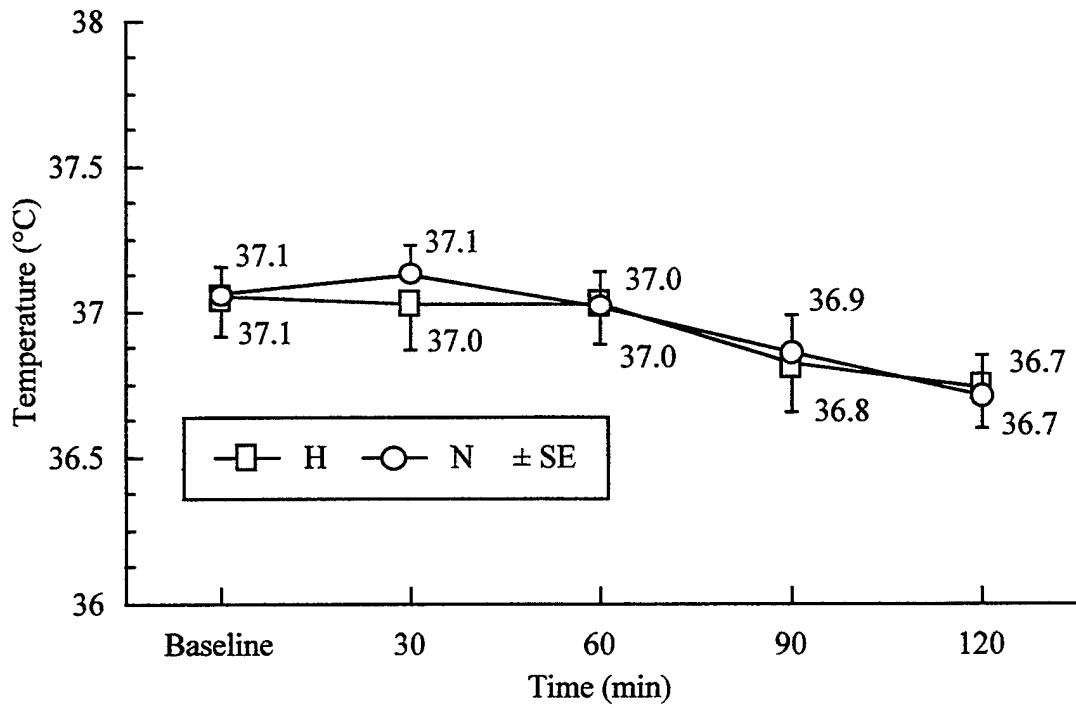


Figure 3. Core temperature for H vs. N inspired oxygen.

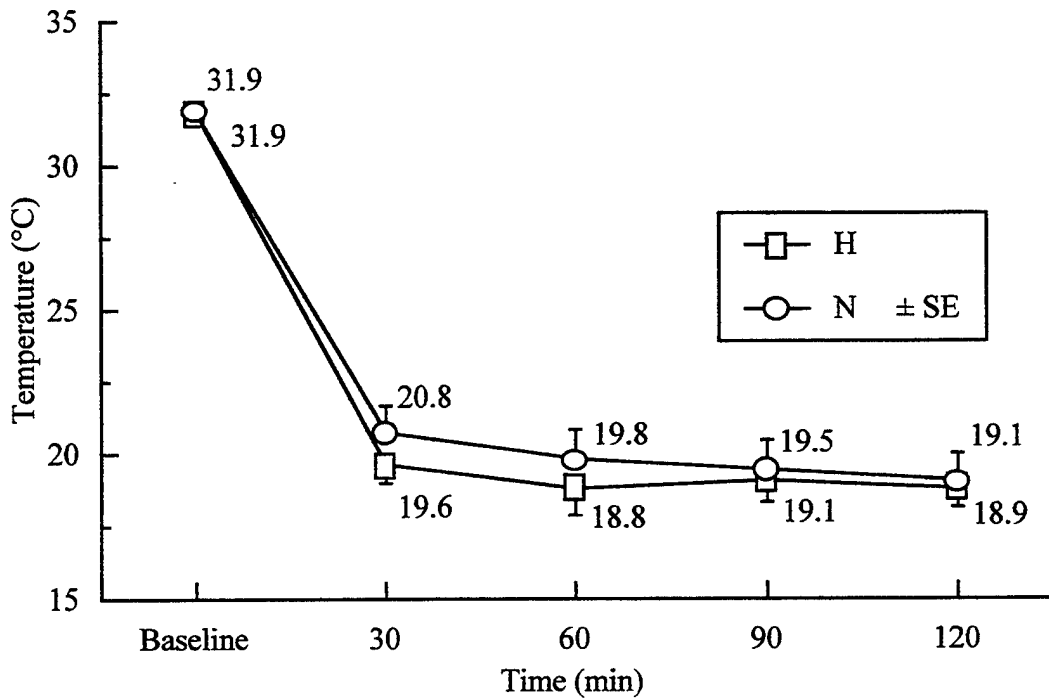


Figure 4. Mean skin temperature at rest for H vs. N inspired oxygen.

### EMG Analysis

There was no condition effect in RMS or MPF. A gradual increase in RMS over time did occur in both conditions. Table 1 shows RMS and MPF values for both pectoralis major (pec) and trapezius (trap) muscles.

Table 1.

Average ( $\pm$  SD) RMS ( $\mu$ V) and MPF (hz) Values for H and N.

Parameter	Baseline	30	60	90	120
Pec RMS H	11.7 $\pm$ 6.3	45.7 $\pm$ 28.1	58.1 $\pm$ 35.6	65.7 $\pm$ 53.1	70.2 $\pm$ 80.0
Pec RMS N	13.0 $\pm$ 7.3	36.3 $\pm$ 33.2	44.2 $\pm$ 20.5	58.1 $\pm$ 51.6	42.1 $\pm$ 21.7
Trap RMS H	12.6 $\pm$ 17.3	41.9 $\pm$ 33.9	44.0 $\pm$ 33.9	59.8 $\pm$ 39.7	56.9 $\pm$ 44.3
Trap RMS N	8.7 $\pm$ 4.0	19.2 $\pm$ 12.8	29.5 $\pm$ 17.4	46.7 $\pm$ 49.1	48.7 $\pm$ 41.7
Pec MPF H	34.2 $\pm$ 7.3	55.3 $\pm$ 12.6	51.2 $\pm$ 9.0	54.6 $\pm$ 9.6	53.2 $\pm$ 12.1
Pec MPF N	32.2 $\pm$ 8.1	49.2 $\pm$ 14.1	58.0 $\pm$ 11.7	55.1 $\pm$ 10.0	55.6 $\pm$ 9.7
Trap MPF H	52.3 $\pm$ 17.5	66.0 $\pm$ 14.1	65.1 $\pm$ 10.9	67.5 $\pm$ 11.4	65.0 $\pm$ 12.8
Trap MPF N	47.2 $\pm$ 15.1	61.0 $\pm$ 11.0	67.2 $\pm$ 13.7	64.1 $\pm$ 9.8	63.7 $\pm$ 10.2

There was no condition effect for percent plasma volume change, cortisol, or lactic acid. Percent plasma volume change decreased over 120 min in both conditions ( $-11.6 \pm 4.9\%$  in hypoxia and  $-9.5 \pm 8.9\%$  in normoxia). Cortisol increased over 120 min from  $8.4 \pm 2.3$  to  $14.6 \pm 3.3$  mg  $\cdot$  dl $^{-1}$  in hypoxia and  $10.9 \pm 3.8$  to  $14.1 \pm 4.5$  mg  $\cdot$  dl $^{-1}$  in normoxia. Lactic acid did not change over time.

## DISCUSSION

It has been proposed that breathing oxygen at concentrations of 12% or lower will have profound effects on human thermoregulation during a prolonged cold stress (Blattesis, 1971; Kottke et al., 1948 ). Within the military environment, exposure to altitudes of 2700 to 3000 m is routine, but exposure to altitudes in excess of 3000 m is much less common. Therefore, the question involves the role of exposure to moderate altitude (reduced oxygen tension) and its effect on thermoregulation in humans.

Exercise thermogenesis could be expected to override any decrement in shivering thermogenesis, so this study did not include an exercise component. The cold stress was sufficient to cause an increase in shivering thermogenesis (sevenfold increase in RMS in the pectoralis muscle), but the reduction in inspired oxygen was not large enough to reduce the shivering thermogenesis. Cold-induced vasoconstriction occurred during the initial exposure (within 30 min) and continued at a stable rate for the duration of the exposure. The increase in thermogenesis was not sufficient to maintain the core temperature since the trend was downward over the duration of the exposure.

The subjects in this study were in an artificial situation (sitting quietly in a cold environment while lightly dressed) so the decrease in core temperature might not be a factor if normal thermal protective clothing were worn. It is evident that the reduction of inspired oxygen to 15% had no effect on an individual during a resting exposure in a cold environment. Therefore, thermoregulation during military missions conducted at altitudes up to 10000 feet will not be adversely affected by the reduction in inspired oxygen.

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