Human thermoregulatory responses during serial cold-water immersions

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Human thermoregulatory responses during serial cold-water immersions. J. Appl. Physiol. 85(1): 204–209, 1998.—This study examined whether serial cold-water immersions over a 10-h period would lead to fatigue of shivering and vasoconstriction. Eight men were immersed (2 h) in 20°C water three times (0700, 1100, and 1500) in 1 day (Repeat). This trial was compared with single immersions (Control) conducted at the same times of day. Before Repeat exposures at 1100 and 1500, rewarming was employed to standardize initial rectal temperature. The following observations were made in the Repeat relative to the Control trial: 1) rectal temperature was lower and heat debt was higher (P < 0.05) at 1100; 2) metabolic heat production was lower (P < 0.05) at 1100 and 1500; 3) subjects perceived the Repeat trial as warmer at 1100. These data suggest that repeated cold exposures may impair the ability to maintain normal body temperature because of a blunting of metabolic heat production, perhaps reflecting a fatigue mechanism. An alternative explanation is that shivering habituation develops rapidly during serially repeated cold exposures, habituation; hypothermia; norepinephrine; shivering; vasoconstriction.

STUDENTS, SOLDIERS, emergency rescue teams, and others may remain outdoors for extended periods during cold weather, a condition that is often accompanied by rain, snow, and wind. Human thermoregulatory effector responses to cold act in concert to maintain normothermia and include shivering thermogenesis, which increases metabolic heat production, and peripheral vasoconstriction, which decreases body heat loss. If these adjustments are inadequate to maintain the balance between heat production and heat loss, which is often the case in cold-wet conditions because of the high thermal conductivity of water, a heat debt develops, manifested by a fall in core temperature.

Some evidence suggests that the thermoregulatory system might fatigue during prolonged cold exposures. Pugh (14, 15) provided anecdotal evidence that fatigue of shivering may have occurred in people hiking in cold-wet conditions. More quantitative evidence for shivering fatigue has been reported by Bell et al. (2) and, most recently, by Thompson and Hayward (20). Recent work has also demonstrated that smooth muscle may also exhibit characteristics of fatigue (23) and, if this occurred in vascular smooth muscle, vasoconstriction responses could be compromised. Possible mechanisms for fatigue of shivering or vasoconstriction fatigue include 1) depletion of muscle energy substrates fueling shivering metabolism and the central nervous system; 2) nonmetabolic peripheral muscle fatigue, i.e., contractile mechanism failure; and 3) central (central nervous system) or peripheral (neuromuscular junction) fatigue of muscle recruitment for shivering/vasoconstriction. No study has specifically attempted to document in a systematic manner whether thermoregulatory fatigue develops during cold exposure. This study examined whether cold-water immersions (eliciting decreases in body core temperature) repeated several times in 1 day would lead to thermoregulatory fatigue. It was hypothesized that during the second and third serial immersions, blunted shivering thermogenesis and reduced peripheral vasoconstriction would lead to a greater fall in core temperature.

METHODS

Subjects. Eight healthy men participated in this study. Physical characteristics were age, 21.3 ± 1.1 (SE) yr; height, 177.8 ± 3.0 cm; body mass, 78.8 ± 3.1 kg; body surface area, 1.96 ± 0.05 m²; peak oxygen uptake (VO₂peak), 49.5 ± 1.6 ml·kg⁻¹·min⁻¹; percent body fat, 14.2 ± 1.3%; and skinfold thickness, 2.9 ± 0.5 mm.

Preliminary testing. Body density from underwater weighing corrected for residual lung volume was measured, and percent fat was calculated according to the method of Siri (18). Mean skinfold thickness was calculated from 10 sites according to Allen et al. (1). All subjects completed an incremental cycle ergometer test to exhaustion for determination of VO₂peak. Briefly, subjects pedaled at 60 W for 2 min, and the resistance was increased 10 W every 2 min until exhaustion was achieved.

Experimental design. Subjects reported to the laboratory 1 h before their immersion. Subjects refrained from alcohol, tobacco products, medications, and exercise for 12 h before all testing. After instrumentation was completed, subjects were seated for 15 min on a platform suspended above the water to obtain preimmersion measurements. After the baseline measurements were taken, subjects were quickly lowered into stirred water (20°C) to shoulder level. On 3 separate days, designated as controls, subjects were immersed for 120 min, beginning at ~0700, 1100, and 1500. The control trials (Control) were separated by at least 1 wk, and the order was randomized. After completion of the three Control trials, subjects were then immersed three times (Repeat) during the course of 1 day, with the beginning of each immersion corresponding to the starting time (0700, 1100, and 1500) of the three Control trials. The duration of these immersions was 120 min. Preimmersion rectal temperatures (Treq) at 1100 and 1500 during Repeat were matched as closely as possible to the Treq recorded at these times during Control. To achieve this match, subjects were passively rewarmed (semirecumbent, clothed in a sweat suit, and covered by 1 woolen blanket) for 1 h after the 0700 and 1100 immersions. During minutes 10–30 of the passive rewarming period after both the 0700 and 1100 immersions, subjects received 3.57 ml/kg of hot chocolate and 16 oz of a commercial liquid food supplement (Ensure, Ross Laboratories, Columbus, OH). After the 1-h...
passive rewarming, subjects were placed in a warm shower until their $T_{re}$ matched their respective Control 1100 and 1500 preimmersion $T_{re}$. Before reimmersion, subjects were seated on the platform above the water for 15 min to obtain baseline body temperature ($T_b$) measurements.

Measurements. A thermistor inserted 10 cm past the anal sphincter measured $T_{re}$. Mean weighted skin temperature ($T_{sk}$; °C) and mean weighted heat flow ($\dot{h}_c$; W m$^{-2}$) were calculated from $T_{sk}$ and $h_c$ measurements obtained by using an integrated disk system (heat flow sensor with integral linear thermistor, Concept Engineering, Old Saybrook, CT) placed at nine skin surface sites. $T_{sk}$ was calculated (21) as follows:

$$
\dot{h}_c \text{ (W/ m}^2 \text{ )} = \frac{0.06T_{cx} + 0.17T_{cal} + 0.14T_{medial \, thigh} + 0.14T_{lateral \, thigh} + 0.14T_{chest} + 0.07T_{forearm} + 0.14T_{subscapular} + 0.07T_{hand}}{0.33S_{skin}}
$$

where $T$ is temperature. $T_{sk}$ was calculated (21) as follows:

$$
T_{sk} = 0.28h_{subscapular} + 0.14h_{forearm} + 0.08h_{triceps} + 0.22h_{cal} + 0.28h_{high}, \text{ where } H \text{ is heat flow. Mean } T_b \text{ ( } T_{sk}\text{ ) was calculated (7) as follows: preimmersion, } T_b = 0.8T_{re} + 0.2T_{sk}; \text{ during immersion, } T_b = 0.67T_{re} + 0.33T_{sk}. \text{ Tissue insulation (Iti) was measured (7) as follows: Iti } = \left( T_{re} - T_{sk} \right) / \dot{h}_c. \text{ Individual skin conductance at the site of each heat flow disk was calculated as the reciprocal of Iti. }
$$

Temperature and heat flow measurements were continuously recorded by using a computer-automated data-acquisition system.

Oxygen uptake ($V\dot{O}_2$) was measured via open-circuit spirometry by using an automated metabolic analysis system (Model 2300, Sensory Instruments, Yorba Linda, CA). Measurements were obtained during preimmersion and at minutes 5–15, 25–35, 45–55, 65–75, 85–95, and 105–115 of immersion. Metabolic heat production ($M_{\dot{Q}}$; W m$^{-2}$) was estimated from the $V\dot{O}_2$ and respiratory exchange ratio ($R$) by using the following equation (6): $M_{\dot{Q}} = 0.23(R + 0.77) \cdot (5.873)(V\dot{O}_2) \cdot (60/A_0)$, where $A_0$ is body surface area ($m^2$) derived from the DuBois and DuBois equation (6).

Body heat storage ($S_{\dot{Q}}$; W m$^{-2}$) was calculated as follows (7): $S_{\dot{Q}} = M_{\dot{Q}} - W - L - E - K - (R + C)$. where $M$ is the metabolic rate, $W$ is the work rate (0 in this experiment), $L$ is the respiratory heat losses by convection and evaporation (22), $E$ is evaporative heat loss (set at 4.1 W m$^{-2}$ in this experiment) (22), $K$ represents conductive heat loss (0 in this experiment), and $R + C$ represents dry heat loss. Cumulative body heat debt was expressed as a positive number and was defined as the total negative heat storage integrated over time. Thermal sensation (TS) was rated by using a category rating scale (26) at minutes 0, 15, 35, 55, 75, 95, and 115 of exposure.

Blood. Whole blood samples were drawn at preimmersion (minute 0) and at minutes 30, 60, 90, and 120 of immersion from an indwelling venous catheter (18 gauge) placed in a superficial forearm vein. Aliquots were centrifuged at 4°C to separate the plasma. Plasma samples were frozen at −40°C before analysis. Plasma glucose concentration was determined in duplicate by using an autoanalyzer (model 2300, Yellow Springs Instrument, Yellow Springs, OH). Plasma norepinephrine (NE) concentration was determined (9) in duplicate via high-performance liquid chromatography with electrochemical detection (model 460S, Waters).

Statistical analyses. A two-way repeated-measures analysis of variance was utilized to determine whether significant differences existed between the appropriate Control (0700, 1100, 1500) condition and the Repeat trial at the same time of day. Significant F-ratios were analyzed post hoc by using Newman–Keuls tests. The slope and intercept of each individual’s $T_{re}$ vs. change in $M_{\dot{Q}}$ (JM) relationship during immersion were determined by least-squares linear regression. Paired t-tests were used to determine whether differences in slope or intercept data existed between Control and Repeat for $T_{re}$. Data are reported as means ± SE. Significance was determined at $P < 0.05$.

RESULTS

$T_{re}$ $T_{re}$ before and during the immersions are depicted in Fig. 1. During the 0700 immersion, there were no significant differences in $T_{re}$ across time between Control and Repeat. However, during the 1100 immersion, $T_{re}$ was significantly lower at minute 120 of the Repeat trial, and there was a tendency ($P < 0.12$) for a similar effect in Repeat during the last 20 min of the 1500 immersion. The cooling rates from minute 60 to minute 120 of Control and Repeat immersions, respectively, were the following: 0700, $-0.62 ± 0.1$ and $-0.65 ± 0.1°C/h$; 1100 ($P = 0.21$), $-0.55 ± 0.1$ and $-0.74 ± 0.1°C/h$; and 1500 ($P = 0.13$), $-0.55 ± 0.1$ and $-0.73 ± 0.1°C/h$.

$T_{sk}$. There were no significant differences in $T_{sk}$ between trials at 0700, 1100, or 1500, either before or during the cold-water immersion.
Preimmersion $h_c$ was significantly higher in Repeat vs. Control before the 1100 (128 ± 7 vs. 71 ± 3 W·m$^{-2}$) and 1500 (120 ± 9 vs. 71 ± 3 W·m$^{-2}$) immersions. However, after subjects were immersed, there were no significant differences in $h_c$ between trials. $h_c$ increased to ~500 W·m$^{-2}$ at minute 5 of immersion, then fell to ~250 ± 20 W·m$^{-2}$ at 60 min of immersion. Final $I_t$ values were not different between trials at 0700 (0.06 ± 0.01 vs. 0.06 ± 0.01°C·m$^2$·W$^{-1}$), 1100 (0.06 ± 0.01 vs. 0.07 ± 0.01°C·m$^2$·W$^{-1}$), and 1500 (0.06 ± 0.01 vs. 0.07 ± 0.01°C·m$^2$·W$^{-1}$) for Control and Repeat, respectively. Skin conductance was not significantly different at 1100 between trials at any of the nine individual sites measured.

$M\dot{}$. Preimmersion $M\dot{}$ did not differ between trials at 0700, 1100, or 1500 immersions (Fig. 2). $M\dot{}$ increased ~2.5- to 3-fold after subjects were immersed, and they appeared to be shivering vigorously. During the 0700 immersion, there were no significant differences in $M\dot{}$ except at minute 75, when $M\dot{}$ was lower ($P < 0.05$) during Repeat (Fig. 2). During the 1100 and 1500 immersions, $M\dot{}$ was significantly ($P < 0.05$) lower in Repeat vs. Control.

Heat debt. Heat debt across time was similar between trials at 0700 and 1500 (Fig. 3). However, heat debt was significantly higher in Repeat at minute 115 during the 1100 immersion trial.

$T_b$ vs. $\Delta M$ relationship. The relationships between $T_b$ and the corresponding increment in $M\dot{}$ over preimmersion values (i.e., $\Delta M$, a measure of shivering thermogenesis) are presented in Table 1. During the 0700 immersion, there were no differences between trials in either the intercept or the slope of the $T_b$ vs. $\Delta M$ relationship. During the 1100 immersion, the intercept for $\Delta M$ was significantly lower in Repeat than Control, but slopes were not different between trials. During the 1500 immersion, there were no differences between trials in either the intercept or slope of the $T_b$ vs. $\Delta M$ relationship.

Plasma glucose. Preimmersion glucose concentrations were 4.7 ± 0.2 and 5.1 ± 0.1 mmol/l at 0700; 5.1 ± 0.2 and 5.8 ± 0.3 mmol/l at 1100; and 5.1 ± 0.5 and 6.6 ± 0.6 mmol/l at 1500, for Control and Repeat.
respectively. Glucose concentrations at minute 120 were 5.0 \pm 0.2 and 5.0 \pm 0.1 mmol/l at 0700; 4.9 \pm 0.2 and 4.8 \pm 0.1 mmol/l at 1100; and 4.9 \pm 0.1 and 4.8 \pm 0.1 mmol/l at 1500, for Control and Repeat, respectively.

Plasma NE. Figure 4 depicts the plasma NE concentrations during each immersion. There were no differences observed at 0700. However, at 1100 and 1500, plasma NE in Repeat vs. Control was significantly higher before immersion. NE concentrations during immersion did not differ between trials.

TS. During 0700 or 1500 immersions (Fig. 5), there were no differences in TS between trials. However, during 1100 immersion, TS was significantly higher in Repeat vs. Control, (i.e., subjects perceived the immersion as warmer).

DISCUSSION

This study investigated whether thermal balance and thermoregulatory responses during cold-water immersion would be degraded over the course of several serial immersions completed in a single day. The hypothesis was that the thermoregulatory system would become “fatigued” and unable to maintain thermal balance as effectively during subsequent exposures. No previous studies have systematically evaluated repeated cold exposure in 1 day, controlling for factors such as circadian rhythm and initial core temperature.

The principal finding of this study was that $T_{re}$ was significantly lower in Repeat vs. Control at the end of the 1100 immersion. There was also a greater heat debt in the Repeat vs. Control trial during the 1100 immersion. Even larger differences in $T_{re}$ might have been observed if the immersion had continued beyond 2 h because of the 0.2°C/h difference in cooling rate that had developed by this point. The $T_{re}$ and heat debt data from the 1500 trial were also consistent with this pattern, although differences between Control and Repeat trials did not achieve statistical significance. These observations tend to support the hypothesis and suggest that susceptibility to hypothermia may increase with repeated cold exposures completed during a single day.

The lower $T_{re}$ observed by the end of immersion in the 1100 Repeat trial appears to be due to an attenuated thermogenic response to cold and not a loss of vasoconstriction. No differences between trials in $R_{hi}$ or $I_{ti}$ suggest that peripheral heat loss was not affected by multiple cold exposures and suggest that there was no fatigue of cutaneous vascular smooth muscle or vasoconstrictor neural drive. A blunted thermogenic response was supported by $M$ and $T_b$ vs. $\Delta M$ data. The decrease in $M$ may also partially result from a delay in the onset of shivering. The intercept for the $T_{re}$ vs. $\Delta M$ relationship shifted such that the increase in $M$ during the 1100 Repeat exposure was not observed until the subjects achieved a lower $T_{re}$. Therefore, at any given $T_{re}$, $\Delta M$ was lower in the Repeat vs. Control trial at 1100.

A similar intercept shift in the shivering response has also been demonstrated after N₂ narcosis (12), anesthesia (17), hypercapnia (10), hypoglycemia (13), and an increase in $T_{sk}$ (4, 5). A leftward shift in the intercept of the $T_{re}$ vs. $\Delta M$ relationship has been interpreted as an alteration in the central reference mechanism controlling thermoregulatory effector responses (19). The subjects in the present experiments were breathing air at sea-level barometric pressure, so anesthetic effects or N₂ levels in the body do not explain the shivering suppression, nor is it likely that the subjects were hypoglycemic. Plasma glucose concentra-

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Table 1. Intercept and slope values for $T_{re}-\Delta M$ relationship

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>700</th>
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<th>1500</th>
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<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Repeat</td>
<td>Control</td>
</tr>
<tr>
<td>Intercept</td>
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<td></td>
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<td>5</td>
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<td>34.12</td>
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<tr>
<td>6</td>
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<td>33.68</td>
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<td>7</td>
<td>32.63</td>
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<tr>
<td>8</td>
<td>31.86</td>
<td>32.01</td>
<td>32.57</td>
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<tr>
<td>Mean ± SE</td>
<td>32.74 ± 0.21</td>
<td>32.68 ± 0.2</td>
<td>33.17 ± 0.26</td>
</tr>
<tr>
<td>Slope</td>
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<td>1</td>
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<td>-49.91</td>
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<tr>
<td>Mean ± SE</td>
<td>-63.97 ± 4.5</td>
<td>-69.12 ± 7.24</td>
<td>-60.71 ± 7.06</td>
</tr>
</tbody>
</table>

$T_b$, mean body temperature; $\Delta M$, change in metabolic heat production; 700, 1100, and 1500: immersion times; control and repeat, single and serial immersion trials, respectively; *repeat significantly different from control, P < 0.05.
tions were well above 2.5 mmol/l during the course of any immersion, and $T_{sk}$ values were similar between trials during all three immersion periods.

Another possible explanation for the apparent blunting of $M$ observed with serial immersion is that it represents the early development of shivering habituation. In previous studies involving cold exposures, shivering habituation has developed over the course of a number of days or weeks of repeated cold exposure (3, 8, 24). The interesting possibility arises that even as few as one or two cold exposures may be sufficient stimuli for adaptation to cold to begin. The blunting of $TS$ also suggests habituation. However, in previous investigations, cold habituation blunted the vasoconstrictor and sympathetic responses to cold (11, 16). In the present study, no blunting of plasma NE response to cold was seen, nor were there any apparent changes in the vasomotor response to cold. Studies demonstrating habituation of vasomotor and sympathetic responses to cold, however, employed cold-air exposures in contrast to the cold-water immersions used in the present experiments. Immersion may mask any changes in $T_{sk}$ because of the near matching of water temperature and $T_{sk}$. Furthermore, the large rates of heat loss may elicit maximal sympathetic responses in both acclimated and unacclimated persons. Thus, even if a relatively small number of cold-water exposures are sufficient to begin the development of metabolic and perceptual adaptations to cold, more exposures are needed for thermoregulatory effector responses to fully develop.

The effect of circadian rhythms on responses to cold has not been explored. Potentially because of a circadian rhythm effect, during the 1100 Control immersion, there was a tendency for the mean intercept, compared with the other Control values, to be higher ($P = 0.18$). And, although the mean intercept during 1100 Repeat immersion was similar to those for the 0700 and 1500 Repeat immersions, this value may, in fact, reflect a blunting of the normal circadian response at 1100 because of multiple immersions. The slope of $T_b$ vs. $\Delta M$...
was not altered, suggesting that the sensitivity of the metabolic response to a given change in body core temperature was unchanged. Further studies examining time-of-day effects on thermoregulatory responses to cold are needed.

The hypothesis of this experiment was that serial cold-water immersions, repeated over a short period, would lead to an inability of the body to thermoregulate effectively, thus increasing a person’s risk of hypothermia. Our data suggest that this in fact may be the case because individuals were unable to maintain \( T_b \) as well after being cold exposed before a subsequent cold exposure. It appears that this reduction is due to an attenuation of the metabolic heat response to the cold. However, these results may also be explained by the early development of cold habituation. Further studies are needed to determine whether the thermoregulatory system fatigues with repeated cold exposures, but the possibility that cold adaptation can develop more rapidly than was thought must be considered when experiments are designed.

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The views, opinions and/or findings in this report are those of the authors and should not be construed as official Department of the Army position, policy, or decision unless so designated by other official documentation. Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70–25 and USMRDC Regulation 70–25 on Use of Volunteers in Research.

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