SYMPOSIUM / SYMPOSIUM

Exertional fatigue and cold exposure: mechanisms of hiker's hypothermia

Andrew J. Young and John W. Castellani

Abstract: Participants in prolonged, physically demanding activities in cold weather are at risk of a condition known as "hiker's hypothermia". During exposure to cold weather, the increased gradient favoring body heat loss to the environment must be balanced by physiological responses, clothing, and behavioral strategies that conserve body heat stores, or else body temperature will decline. The primary human physiological responses elicited by cold exposure are shivering and peripheral vasoconstriction. Shivering increases thermogenesis and replaces body heat losses, while peripheral vasoconstriction improves thermal insulation of the body and retards the rate of heat loss. A body of scientific literature supports the concept that prolonged and (or) repeated cold exposure, fatigue induced by sustained physical exertion, or both together can impair shivering and vasoconstrictor response to cold. The mechanisms accounting for this thermoregulatory impairment are not clear, but the possibility that changes in blood glucose availability or sympathetic responsiveness to cold due to exertion and fatigue merit further research.

Key words: thermoregulation, shivering, thermal balance, vasoconstriction.

Résumé : Par temps froid, les participants à des activités physiques de longue durée s'exposent à souffrir de « l'hypothermie du randonneur ». Afin de contrer une éventuelle chute de la température corporelle, l'organisme doit compenser par des actions physiologiques, par des ajustements de la tenue vestimentaire et par des stratégies comportementales les pertes de chaleur corporelle causées par les plus forts gradients de température. Les deux premières lignes de défense physiologique mises en branle chez l'humain par temps froid sont le frisson et la vasoconstriction périphérique. Le frisson augmente la thermogenèse pour couvrir les pertes de chaleur encourues et la vasoconstriction périphérique améliore l'isolation thermique de l'organisme pour en diminuer la perte de chaleur. D'après de nombreuses observations scientifiques, il semble que l'exposition prolongée ou répétée au temps froid et la fatigue résultant de l'activité physique prolongée peuvent indépendamment ou concurremment modifier les mécanismes de réaction au froid que sont le frisson et la vasoconstriction périphérique. On ne connaît pas bien les mécanismes à la base de cette défaillance en thermorégulation, mais nous pensons que les variations de la disponibilité du glucose ou la réactivité du système nerveux sympathique au froid causées par l'activité physique et la fatigue devraient faire l'objet d'autres études scientifiques.

Mots-clés : thermorégulation, frisson, équilibre thermique, vasoconstriction.

[Traduit par la Rédaction]

Introduction

Persons engaged in outdoor activities during cold weather are at risk of accidental hypothermia. Pugh (Pugh 1964) was the first to document what is often referred to as "hiker's hypothermia" in a case study of 7 hypothermia casualties (4 fatal) that occurred among contestants of a competitive hill walking event. Pugh concluded that the casualties resulted because individuals became too fatigued to sustain exercise at a sufficiently high enough metabolic rate to offset the rate of heat loss in the cold ambient conditions. This simple heat balance mechanism is illustrated in Fig. 1, which shows core temperatures of hikers during an 8 h walk during cold, wet, and windy weather (Ainslie et al. 2002). As shown, core temperatures first increased and then remained level until subjects stopped walking for a rest (denoted in the figure by the asterisk), during which core temperatures declined; when exercise was resumed, core temperatures began increasing again (Ainslie et al. 2002). However, our laboratory's research over the past 8 years suggests that accumulating physiological effects of sustained exertion and (or) cold exposure can lead to an impairment of the thermoregulatory responses to cold. The purpose of this paper is to review the results of those studies and other relevant reported findings that could contribute to a better understanding of physiological mechanisms affecting susceptibility to accidental hypothermia during outdoor activities in cold weather.

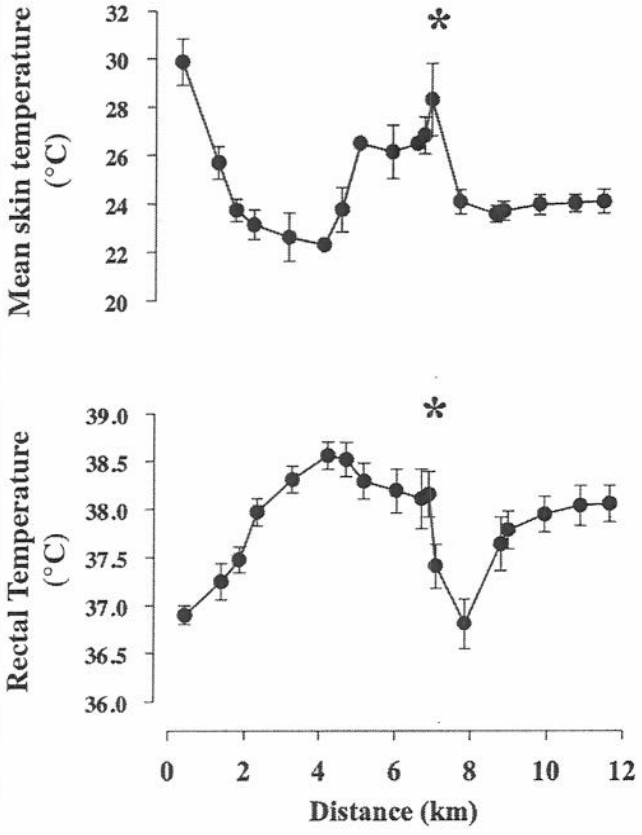
Received 24 May 2006. Accepted 16 March 2007. Published on the NRC Research Press Web site at apnm.nrc.ca on 18 June 2007.

A.J. Young[1] and J.W. Castellani. US Army Research Institute of Environmental Medicine, Kansas St., Natick, MA 01760-5007. USA.

[1]Corresponding author (e-mail: andrew.young@na.amedd.army.mil).

 doi:10.1139/H07-041

Fig. 1. Core (rectal, $n = 11$) and mean weighted skin temperatures (four sites, $n = 10$; mean ± standard error (SE)) of hikers during an 8 h walk during cold, wet, and windy weather. The asterisk indicates the beginning of a 30 min rest/lunch break, following which the subjects resumed walking. (Reproduced from Ainslie et al. 2002. Physiological and metabolic responses to a hill walk. J. Appl. Physiol. **92**: 179–187, with permission).



Thermal balance in the cold

When humans are exposed to the cold, the first and most effective responses elicited for defending body temperatures involve behavioral strategies such as wearing warmer clothing or remaining in heated shelters. However, when those behavioral strategies do not effectively prevent body heat loss, 2 major physiological responses act to maintain thermal balance (Toner and McArdle 1996; Young et al. 1996). Peripheral vasoconstriction decreases peripheral blood flow, thereby reducing convective heat transfer between the body's core and shell, effectively increasing insulation and conserving body heat. Second, muscular shivering increases metabolic heat production. The effectiveness of these responses for maintaining normal body temperature during cold exposure varies among individuals (Young et al. 1996), primarily as a result of differences in body surface area, body mass, and the distribution of fat and nonfatty body tissues about the body (Toner and McArdle 1996), as well as, to a lesser extent, differences in aerobic fitness, acclimatization, age, and sex (Young et al. 1996).

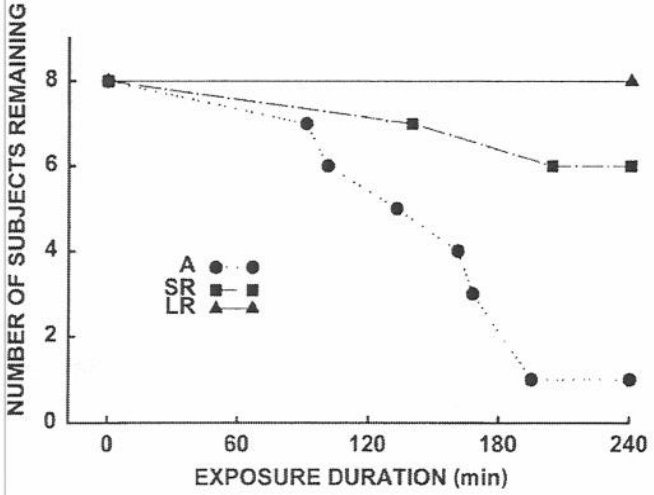
Exercise also affects thermal balance during cold exposure, depending on a complex interaction among factors related to exercise intensity, environmental conditions, and mode of activity. Physical activity or exercise can increase metabolic heat production even more than shivering, so voluntarily increasing activity can increase heat production sufficiently to obviate the need for shivering. However, exercise also increases conductive and convective heat loss from the skin by 2 mechanisms. Limb movement during exercise disrupts the stationary boundary layer of air or water that develops at the skin surface in a still environment, and this movement tends to reduce insulation. More important, exercise increases blood flow to the skin and muscles thereby facilitating convective heat transfer from the central core to peripheral shell. Thus, while metabolic heat production increases progressively as exercise intensity increases, so too does heat loss, and the influence of these competing effects on overall thermal balance will be further modulated by anthropomorphic factors. A detailed examination of human thermoregulatory responses associated with exposure to environmental extremes and exercise is available elsewhere (Sawka and Young 2006).

Exertion, fatigue, and impaired thermoregulation

The first experimental observation suggesting that a thermoregulatory response, namely shivering, could exhibit an impairment possibly reflecting a fatigue of that response was reported by Thompson and Hayward (Thompson and Hayward 1996). Those authors reported that during a 5 h walk at a constant pace in a controlled experimental environment that simulated hiking in cold, rainy conditions, they observed 1 subject who, having maintained stable metabolic rate and core temperature for the first 3 h of exposure, exhibited a progressive decline in metabolic rate and core temperature over the final 2 h, despite the fact that the walking pace remained unchanged throughout (Thompson and Hayward 1996). The authors concluded that the decline in metabolic rate exhibited by this subject reflected a decrease in shivering, since the subject maintained the same walking pace. They concluded that this decrease in shivering was evidence of a fatigue or exhaustion of shivering responses. However, since the effect was only observable in 1 of the 5 subjects, and decreases in muscular activity besides shivering might account for a decline in overall metabolic rate without a change in walking pace, the authors' conclusions remained speculative.

Consequently, our laboratory investigated how physiological responses to cold were affected by fatigue associated with more prolonged, chronic physical exertion. Responses to cold were measured in 8 men who had completed an arduous 9-week military training course, throughout which participants perform very strenuous physical activity, and daily sleep is limited to about 4 h (Young et al. 1998). During this training course, daily energy expenditures averaged 4100 kcal (17.2 MJ) per day, but daily energy intakes averaged only about 3300 kcal (13.8 MJ) per day, and there were many periods when energy expenditures were much higher and intakes lower. The subjects in this study completed a standardized experimental cold air exposure within 2 h after finishing the regimen (no rest), which was then repeated following a short (48 h) recovery period for rest and refeeding, and again a third time following 16 weeks of recovery. Our experiments demonstrated that cold tolerance

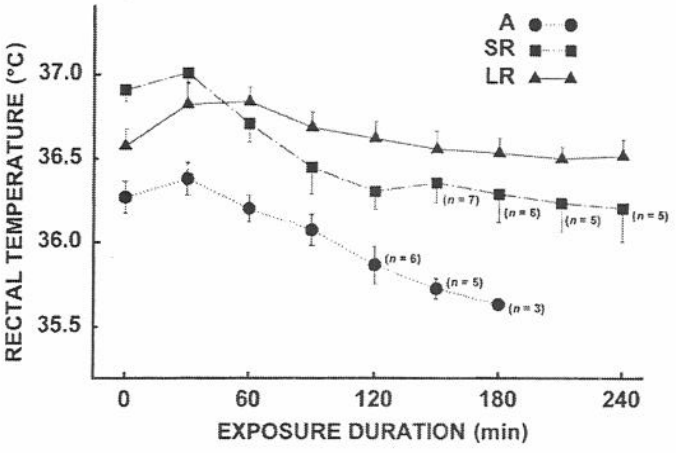
Fig. 2. Cold tolerance as indicated by attrition of test subjects during 4 h cold exposure experiments conducted immediately (<2 h) after 61 d of exhaustive activity, sleep deprivation, and negative energy balance (trial A) and again after short (48 h, trial SR) and long (16 weeks, trial LR) rest and recovery. Each point represents the number of subjects still remaining exposed to cold (of the 8 who began the exposure experiment) as a function of exposure duration (from Young et al. 1998)).



(see Fig. 2) and ability to maintain normal body temperature (see Fig. 3) during cold exposure were compromised during the trial performed without rest and remained compromised even after 48 h of recovery. While the magnitude and duration of stress experienced during recreational hiking are certainly less severe than those experienced by the subjects in this study, the experimental observations of the effects of such severe stress do provide insight regarding mechanisms that may operate, albeit perhaps more subtly, to impair thermoregulation during hiking and other physical activities performed in cold conditions.

Two factors appeared to account for the impaired capability to defend thermal balance exposed to cold in chronically fatigued and underfed persons. First of all, the 10% body weight loss observed during the training course, which included both fat and nonfatty tissue, would reduce tissue insulation and compromise body heat conservation during both the first and second trials by mechanisms discussed in detail elsewhere (Toner and McArdle 1996). Undoubtedly, reduced tissue insulation accounts for the observation (Young and Castellani 2001) that the steady-state skin temperatures of these subjects reached a plateaue at a higher level during the first 2 trials than the third trial when body mass had recovered. However, there was also evidence that alterations in normal physiological responses to cold may have contributed to impaired maintenance of thermal balance. Shivering responses appeared blunted (Young et al. 1998), and the vasoconstrictor response developed more slowly (Young and Castellani 2001) during the cold-exposure trial performed immediately after subjects had completed the exhaustive training course, compared with trials completed after rest and recovery. In addition, the sympathetic nervous response to cold appeared less pronounced during that first trial but not after 48 h rest and recovery (Young et al. 1998). These experiments demonstrated that the combined

Fig. 3. Rectal temperature (mean ± SE) during cold exposures conducted immediately (<2 h) after 61 d of exhaustive activity, sleep deprivation, and negative energy balance (trial A) and again after short (48 h, trial SR) and long (16 week, trial LR) rest and recovery (from Young et al. 1998).



effects of exertional fatigue, negative energy balance, and sleep loss compromised thermoregulation during cold exposure, but the relative importance of those individual factors could not be determined because of the multistressor nature of the conditions that subjects experienced and the lack of investigator control over those conditions.

A subsequent study reported by Castellani et al. (Castellani et al. 2003) replicated Young et al.'s (Young et al. 1998) observations that the effects of exertional fatigue, negative energy balance, and sleep loss, in combination, impaired cold-induced shivering. Therefore, we undertook a series of experiments using more controlled conditions to examine potential mechanisms accounting for impaired thermoregulation in hiker's hypothermia. To determine whether shivering responses to cold exhibited signs of fatigue, metabolic heat production was measured during 2 h cold-water immersions conducted 3 times in a single day (2 h rewarming intervening) and compared with metabolic heat production measured during a single immersion completed at the same time of day (Castellani et al. 1998). As shown in Fig. 4, metabolic heat production was lower during the serial immersions than when only a single immersion was completed at that same time of day, suggesting that the shivering response did indeed exhibit a fatigue during prolonged or repeated activation (Castellani et al. 1998). We hypothesized that this "shivering fatigue" was attributable to fatigue of the large muscle groups engaged in shivering, and we reasoned that it might be the mechanism by which acute and chronic exercise impairs shivering. However, studies designed to directly test the hypothesis that muscle fatigue associated with physical exertion, independent of sleep and dietary restriction effects, would impair cold-induced shivering have, so far, been inconclusive (Castellani et al. 1999, 2001).

However, experimental data have been collected that appear to confirm the suggestion that exertional fatigue is a primary factor that can impair vasoconstrictor responses to cold. In 1 study (see Fig. 5), skin surface heat flow was greater, skin temperatures tended to be higher, and rectal temperatures fell more and faster during cold (5 °C air) ex-

Fig. 4. Metabolic heat production during cold-water immersion at different times of the day (0700, panel A; 1100, panel B; and 1500, panel C). During Control (bullet), only a single immersion per day was completed, whereas during Repeat (open circle), 3 immersions were completed serially in a single day. Asterisk indicates time-dependent difference between Control and Repeat, and pound symbol indicates main effect with Repeat lower than Control ($P < 0.05$) (from Castellani et al. 1998).

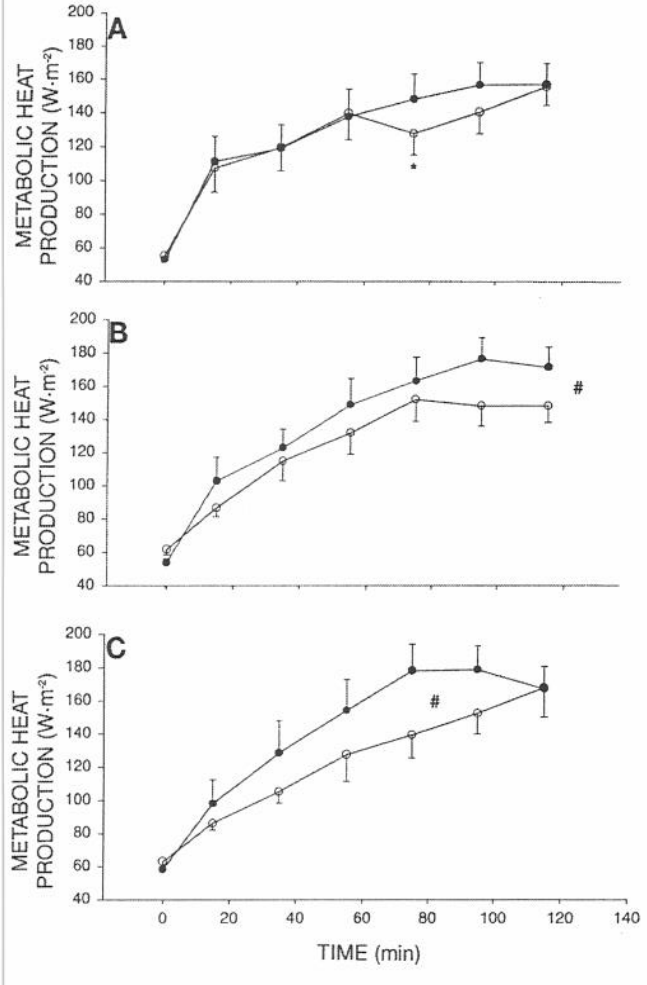
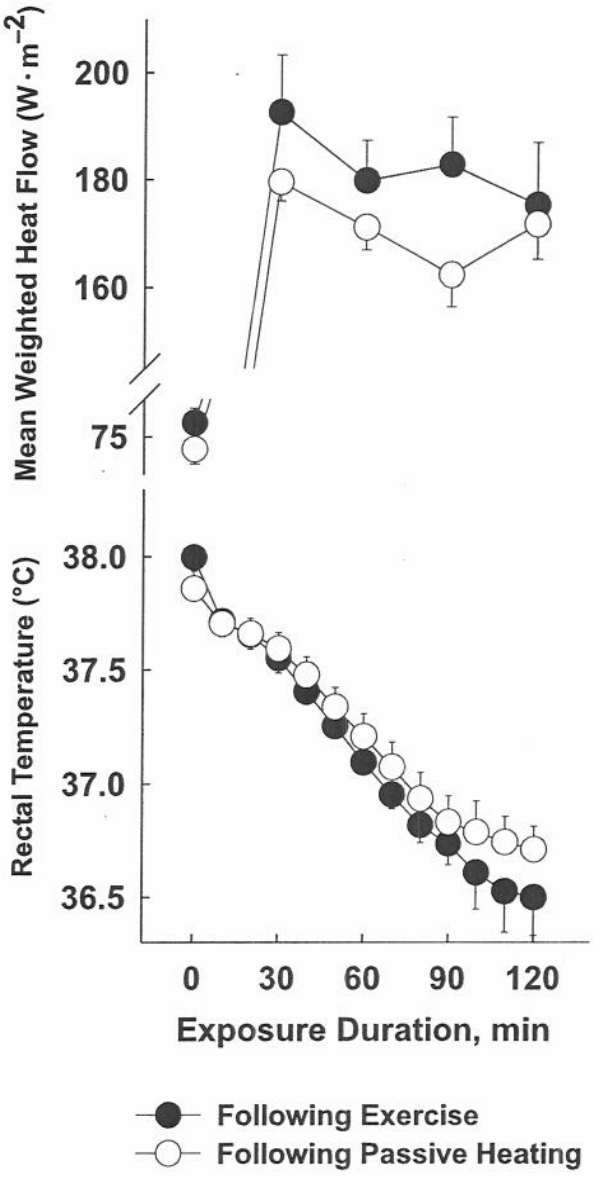


Fig. 5. Skin surface heat flow and rectal temperature (mean ± SE) of men resting in cold air following exercise or passive heating to a similar preimmersion rectal temperature (from Castellani et al. 1999).



posure preceded by 60 min of aerobic-type exercise compared with when cold exposure was preceded by passive heating of subjects until they achieved the same preimmersion rectal temperature (Castellani et al. 1999). Since the experimental conditions employed allowed sleep deprivation and energy substrate availability to be ruled out as significant influences, those findings were interpreted as evidence for an impairment of cold-induced vasoconstrictor response induced by exertional fatigue (Castellani et al. 1999). However, because the possibility that exercise-induced hyperemia persisted during cold exposure following exercise and accounted for the greater heat loss, rather than impaired vasoconstriction, a follow-on study was conducted to rule that out. A similar impairment of the vasoconstrictor response to cold was observed following several days of severe physical exertion compared with cold exposures completed when subjects were physically rested (Castellani et al. 2001). In those experiments, the evidence for impaired vasoconstriction during cold exposure was observed while the subjects were exercising at a fixed intensity in the cold, so any effects of exercise-induced hyperemia should have been similar for all trials. Also, experimental controls were again in place to obviate sleep deprivation and energy substrate levels as influential factors. Thus, it seems reasonable to conclude that some other mechanism related to exertional fatigue acts to impair vasoconstrictor response to cold.

The specific fatigue-related physiological mechanisms by which thermoregulatory responses to cold become impaired following severe physical exertion remain unidentified. One possibility is that exercise-induced depletion of energy substrates impairs thermoregulation. Ainslie et al. (2003) observed that men completing a 21 km, self-paced walk in mountainous terrain sustained lower core temperatures when energy intake was severely restricted (616 kcal, 2.6 MJ) than during trials in which energy intake was significantly higher

(3019 kcal, 12.6 MJ). However, a direct effect of dietary energy restriction to impair shivering and metabolic heat production during cold exposure seems unlikely. Research (Haman et al. 2002, 2004; Young 1990; Young et al. 1989) has generally shown that exercise-associated depletion of peripheral energy stores is an unlikely explanation for the impaired shivering responses that we have reported. Further, while severe depletion of circulating energy substrate (i.e., blood glucose) has been shown to impair shivering (Gale et al. 1981), this too has been ruled out as a factor in the experimental observations of shivering fatigue that we have reported (Castellani et al. 1998, 2001, 2003; Young et al. 1998). Ainslie et al. (2003) speculated that lower blood glucose during the restricted energy intake trials of their hill-walking study might have caused an increase in peripheral blood flow, facilitating heat loss, compared with trials when energy intake was high but presented no data to support that speculation. Therefore, the possibility that energy substrate depletion, in particular blood glucose, modulates impaired vasoconstrictor responses to cold associated with exertional fatigue cannot be dismissed.

There are some data to suggest that a more viable mechanism mediating impaired thermoregulatory responses to cold following sustained physical exertion and environmental stress involves a blunting of sympathetic nervous activation in response to cold. Young et al. (1998) reported that, besides showing signs of impaired thermoregulatory responses to cold, soldiers who had just completed a prolonged period of exhaustive physical exertion with inadequate rest also exhibited elevated basal levels of circulating norepinephrine, but smaller increments in circulating norepinephrine during cold exposure than when they were exposed to cold in rested conditions (Young et al. 1998). Sympathetic nervous system release of norepinephrine is the primary mediator of cold-induced vasoconstriction through stimulation of alpha-adrenoreceptors in the cutaneous vasculature (Frank et al. 1996, 2000). Age-related decreases in the body temperature threshold for onset of sympathetic nervous response to cold, the magnitude of associated norepinephrine release, and the magnitude of the resulting vasoconstrictor response to cold have all been reported and are thought to account for the impairments in temperature regulation known to develop with aging (Frank et al. 2000; Grassi et al. 2003). Therefore, a reasonable working hypothesis to explain hiker's hypothermia and the impairment of thermoregulatory responses to cold with sustained overexertion is that with chronic sympathetic nervous activation, the capacity for further activation in response to an added cold stimulus may be limited and (or) adrenergic receptors involved in modulating cold-induced vasoconstriction could become downregulated by chronic sympathetic activation.

Summary

Our research suggests that the ability to increase insulation by reducing peripheral blood flow in response to cold exposure may become impaired following exercise. It remains unclear whether this effect is due to a fatigue of the vasoconstrictor response to cold perhaps associated with blood glucose changes, central or peripheral nervous mechanisms, or both. The shivering response to cold appears to be resistant to the effects of several hours or even several days of exhaustive exercise, but when extremely high levels of exertion are sustained for many weeks, shivering does become impaired.

Acknowledgements

This paper summarizes Dr. Young's presentation at the annual meeting of the Canadian Society of Exercise Physiologists on 10 November 2005 in Gatineau, Quebec. The views, opinions, and (or) findings contained in this report are those of the authors and should not be construed as an official Department of the Army position, policy, or decision unless designated by other official documentation. Approved for public release; distribution is unlimited.

References

Ainslie, P.N., Campbell, I.T., Frayn, K.N., Humphreys, S.M., Maclaren, D.P., and Reilly, T. 2002. Physiological and metabolic responses to a hill walk. J. Appl. Physiol. **92**: 179–187. PMID: 11744658.

Ainslie, P.N., Campbell, I.T., Frayn, K.N., Humphreys, S.M., MacLaren, D.P.M., and Reilly, T. 2003. Physiological, metabolic, and performance implications of a prolonged hill walk: influence of energy intake. J. Appl. Physiol. **94**: 1075–1083. PMID: 12571136.

Castellani, J.W., Young, A.J., Sawka, M.N., and Pandolf, K.B. 1998. Human thermoregulatory responses during serial cold-water immersions. J. Appl. Physiol. **85**: 204–209. PMID: 9655776.

Castellani, J.W., Young, A.J., Kain, J.E., Rouse, A., and Sawka, M.N. 1999. Thermoregulation during cold exposure: effects of prior exercise. J. Appl. Physiol. **87**: 247–252. PMID:10409582.

Castellani, J.W., Young, A.J., Degroot, D.W., Stulz, D.A., Cadarette, B.S., Rhind, S.G., et al. 2001. Thermoregulation during cold exposure after several days of exhaustive exercise. J. Appl. Physiol. **90**: 939–946. PMID:11181604.

Castellani, J.W., Stulz, D.A., Degroot, D.W., Blanchard, L.A., Cadarette, B.S., Nindl, B.C., et al. 2003. Eighty-four hours of sustained operations alter thermoregulation during cold exposure. Med. Sci. Sports Exerc. **35**: 175–181. PMID:12544652.

Frank, S.M., el-Gamal, N., Raja, S.N., and Wu, P.K. 1996. alpha-adrenoceptor mechanisms of thermoregulation during cold challenge in humans. Clin. Sci. (Lond.), **91**: 627–631. PMID:8942402.

Frank, S.M., Raja, S.N., Bulcao, C., and Goldstein, D.S. 2000. Age-related thermoregulatory differences during core cooling in humans. Am. J. Physiol. Regul. Integr. Comp. Physiol. **279**: R349–R354. PMID:10896899.

Gale, E.A.M., Bennett, T., Green, J.H., and MacDonald, I.A. 1981. Hypoglycaemia, hypothermia and shivering in man. Clin. Sci. **61**: 463–469. PMID:7026128.

Grassi, G., Seravalle, G., Turri, C., Bertinieri, G., Dell'Oro, R., and Mancia, G. 2003. Impairment of thermoregulatory control of skin sympathetic nerve traffic in the elderly. Circulation, **108**: 729–735. doi:10.1161/01.CIR.0000081769.02847.A1. PMID: 12885757.

Haman, F., Peronnet, F., Kenny, G.P., Massicotte, D., Lavoie, C., Scott, C., et al. 2002. Effect of cold exposure on fuel utilization in humans: plasma glucose, muscle glycogen, and lipids. J. Appl. Physiol. **93**: 77–84. PMID:12070189.

Haman, F., Peronnet, F., Kenny, G.P., Doucet, E., Massicotte, D., Lavoie, C., et al. 2004. Effects of carbohydrate availability on sustained shivering I. Oxidation of plasma glucose, muscle gly-

cogen, and proteins. J. Appl. Physiol. **96**: 32–40. PMID: 12949018.

Pugh, L.G.C. 1964. Deaths from exposure on Four Inns walking competition, March 14–15, 1964. Lancet, **13**: 1210–1212. PMID:14132670.

Pugh, L.G.C.E. 1966. Accidental hypothermia in walkers, climbers, and campers: report to the Medical Commission on Accident Prevention. BMJ, **1**: 123–129. PMID:5901570.

Sawka, M.N., and Young, A.J. 2006. Physiological systems and their responses with exposure to heat and cold. *In* ACSM's advanced exercise physiology textbook. Lippincott, Williams & Wilkins, Baltimore. pp. 535–580.

Thompson, R.L., and Hayward, J.S. 1996. Wet-cold exposure and hypothermia: thermal and metabolic responses to prolonged exercise in rain. J. Appl. Physiol. **81**: 1128–1137. PMID:8889744.

Toner, M.M., and McArdle, W.D. 1996. Human thermoregulatory responses to acute cold stress with special reference to water immersion. *In* Handbook of physiology: section 4: environmental physiology. Oxford University Press for the Amercian Physiological Society, New York. pp. 379–397.

Young, A.J. 1990. Energy substrate utilization during exercise in extreme environments. *In* Exercise and sports sciences reviews. 18th ed. Williams and Wilkens, Baltimore, Md. pp. 65–117.

Young, A.J., and Castellani, J.W. 2001. Exertion-induced fatigue and thermoregulation in the cold. Comp. Biochem. Physiol. A Mol. Integr. Physiol. **128**: 769–776. PMID:11282320.

Young, A.J., Sawka, M.N., Neufer, P.D., Muza, S.R., Askew, E.W., and Pandolf, K.B. 1989. Thermoregulation during cold water immersion is unimpaired by low muscle glycogen levels. J. Appl. Physiol. **66**: 1809–1816. PMID:2732173.

Young, A.J., Sawka, M.N., and Pandolf, K.B. 1996. Physiology of cold exposure. *In* Nutritional needs in cold and in high-altitude environments. National Academy Press, Washington, D.C. pp. 127–147.

Young, A.J., Castellani, J.W., O'Brien, C., Shippee, R.L., Tikuisis, P., Meyer, L.G., et al. 1998. Exertional fatigue, sleep loss, and negative energy balance increase susceptibility to hypothermia. J. Appl. Physiol. **85**: 1210–1217. PMID:9760307.