WHOLE-BODY COOLING FOLLOWING EXERCISE-INDUCED HYPERTHERMIA: BIOPHYSICAL CONSIDERATIONS

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ABSTRACT

This thesis examined the effect of differences in body surface area-to-lean body mass ratio (A_D/LBM) on core temperature cooling rates during cold water immersion (2°C, CWI) and temperate water immersion (26°C, TWI) following exercise-induced hyperthermia (end-exercise rectal temperature of 40°C).

Individuals with a High A_D/LBM (315 cm^2/kg) had a ~1.7-fold greater overall rectal cooling rate relative to those with Low A_D/LBM (275 cm^2/kg) during both CWI and TWI. Further, overall rectal cooling rates during CWI were ~2.7-fold greater than during TWI for both the High and Low A_D/LBM groups.

Study findings show that A_D/LBM must be considered when determining the duration of the immersion period. However, CWI provides the most effective cooling treatment for EHS patients irrespective of physical differences between individuals.

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PART ONE: EMPIRICAL AND THEORETICAL CONSIDERATIONS

CHAPTER I: INTRODUCTION

1.1 Introduction

The majority of exertional heat stress casualties occur in military operations, industrial work and sporting events where the potential combination of high ambient air temperatures, elevated relative humidity, insulative clothing and physical exertion can result in core temperature increases to 40.0°C or higher (Hales, Khogali, Fawcett, & Mustafa, 1987; Yaqub & Al Deeb, 1998). When the rate of heat loss (through skin vasodilatation and sweating) does not match the rate of metabolic heat production, uncompensable heat stress occurs, thereby increasing body temperature and the risk of heat related injury (Parsons, 2003; Webb, 1995). Common heat illnesses include heat cramps, heat syncope, heat exhaustion and exertional heat stroke (Casa, McDermott, et al., 2007; Eichner, 1998). Some predisposing factors such as dehydration, poor physical fitness or lack of heat acclimation can increase the incidence of heat illnesses (Armstrong, Crago, Adams, Roberts, & Maresh, 1996). It is import to note that heat illnesses can also occur when the environment is relatively cool (Casa, McDermott, et al., 2007).

The most severe form of heat injury, exertional heat stroke (EHS), is defined as a rectal temperature (T_{re}) greater than 40.0°C and is accompanied by multiple organ system failure, circulatory collapse, confusion, disorientation, irrational behaviour, hyperventilation, vomiting, diarrhea and most frequently, central nervous system dysfunction (Armstrong et al., 2007; Casa, Armstrong, Kenny, O'Connor, & Huggins, 2012; Casa, McDermott, et al., 2007; Epstein & Roberts, 2011; Murphy, 1984; Yaqub & Al Deeb, 1998). The underlying pathophysiology of EHS occurs when internal organ tissue temperatures rise above critical levels, damaging cell

membranes and disrupting cell energy systems, giving rise to a characteristic clinical syndrome which includes organ dysfunction and cell death (Armstrong et al., 2007). The The incidence rate for EHS can be as high as 1 in 1000 at some athletic events, with some events having more than 10,000 or more participants, with the ensuing potential for medical staff to be treating 10 or more cases (Casa, McDermott, et al., 2007). According to Casa et al. (2007), most deaths due to EHS occur 12 hours to 1 week following EHS. Further, the time to treatment upon recognition of EHS will determine the amount of time the victim is severely hyperthermic, and consequently the degree of damage observed during recovery (Casa, Kenny, & Taylor, 2010; Casa, McDermott, et al., 2007; Gaffin, Gardner, & Flinn, 2000; Hubbard et al., 1977).

The severity of EHS is directly related to the duration of core temperature above critical levels (Armstrong et al., 2007; de Galan & Hoekstra, 1995; Hubbard et al., 1977; Smith, 2005). For example, Hubbard et al. (1977) demonstrated that the time core temperatures were elevated above 40.4°C in hyperthermic mice following both passive heat stress and exercise determined the mortality rate. Therefore, rapid on-site cooling of individuals with EHS to a near resting core temperature is paramount to their survival and to minimize heat related injury (Armstrong et al., 2007; Casa, Armstrong, Ganio, & Yeargin, 2005; Casa et al., 2012; Casa, McDermott, et al., 2007; Proulx, Ducharme, & Kenny, 2003). As such, core cooling guidelines for the treatment of EHS patients state that cooling modalities must achieve a rectal temperature cooling rate exceeding 0.10ºC/min when cooling begins immediately and should be no less than 0.15ºC/min if cooling is delayed (Casa, McDermott, et al., 2007).

Several methods have been suggested for the treatment of EHS, including evaporative techniques such as fanning and water sprays, direct application of ice the body, continuous water dousing and whole-body water immersion (Hadad, Rav-Acha, Heled, Epstein, & Moran, 2004; Smith, 2005). The current literature suggests that cold water immersion (CWI) < 10°C is the gold standard treatment for EHS (Casa, McDermott, et al., 2007). This treatment modality has a proven clinical track record with 100% survivability if the cooling is initiated within 5 minutes (Casa et al., 2010). Cold water immersion using 2°C water has been shown to produce some of the highest rectal cooling rates (0.35°C/min), especially during the second degree drop (note: the first and second degree cooling rate simply reflect the change in core temperature measured for the first and second degree Celsius drop in core temperature subsequent to the start of immersion) in core temperature (0.50°C/min) as compared with other methods, and two times greater than that of warmer water (Casa, McDermott, et al., 2007; Proulx et al., 2003). For example, according to whole-body heat loss in a study by Proulx et al. (2003), data showed that water immersion at 2°C provided the greatest rate of heat loss, as the heat gained during prior exercise in the heat was fully eliminated after 5.4 min of immersion following 2°C ice-water immersion as compared to warmer water temperatures (7.9, 10.4 and 13.1 min of immersion in 8, 14 and 20°C water, respectively). The effectiveness of circulated CWI is mainly attributed to high levels of conductive and convective heat loss between the skin surface and water, where the colder the water, the greater the skin-water thermal gradient to facilitate heat transfer (Proulx et al., 2003).

Despite the proven clinical benefits of CWI, some experts continue to argue against its use in the treatment of EHS patients. The premise of their argument is that when peripheral circulation is viable (patient is not under circulatory collapse), temperate water immersion (TWI, 26°C) should be employed as it minimizes patient discomfort and the adverse effects (cold shock response, elevated shivering and marked vasoconstriction reducing core cooling rate, cold injury, etc.) associated with CWI while at the same time providing comparable core cooling rates to that of CWI (Casa et al., 2010; Taylor, Caldwell, Van den Heuvel, & Patterson, 2008). It has been demonstrated that rapid core cooling rates during TWI can be achieved by minimizing the skin-water temperature gradient, thereby inducing a less powerful vasoconstrictor response and consequently, promoting enhanced central heat transport to the skin surface by lengthening the convective pathway between the perfused skin and water (Casa et al., 2010; Taylor et al., 2008).

It is important to note that the evidence in support of the aforementioned argument is primarily based on a study by Taylor et al. (2008) who showed that 26°C temperate water provided similar esophageal cooling rates to that measured in 14°C water (0.71 and 0.88 °C/min for 26 and 14°C water immersion, respectively), rapid enough to cool esophageal temperature from 39.5 to 37.5°C in under 3 minutes (2.91 min for 26°C and 2.16 min at 14°C). Taylor et al. (2008) concluded that TWI could provide sufficient cooling to protect the central nervous system and that the cooling time difference between cold and temperate water immersion would not have any meaningful clinical or physiological implications, questioning the need to use CWI in the treatment of EHS.

Of particular concern is the fact that conclusions by the authors regarding the benefits of temperate versus cold water immersion were based on esophageal temperature and not rectal temperature, which provides a more accurate measurement of deep visceral temperature. Further, it is well established that esophageal temperature cooling rates far exceed rectal temperature cooling rates (Gagnon, Lemire, Jay, & Kenny, 2010). Indeed, Taylor et al. (2008) reported a rectal temperature cooling rate of only 0.10ºC/min during 26°C TWI, at least 3 times lower than the rate (0.35ºC/min) measured by Proulx et al. (2003) during 2ºC CWI. Literature suggests that rectal temperature measurement is the only reliable and valid index of core temperature that can be practically used in emergency situations (Armstrong et al., 2007; Casa, Becker, et al., 2007; Casa et al., 2010; Moran & Mendal, 2002). In addition, the risk of adverse outcomes in EHS patients is related to the duration of visceral organ hyperthermia (Armstrong et al., 2007) and the length of time that core temperature remains above critical values for cell damage is an important determinant of survival from EHS (Hubbard et al., 1977).

In the studies directed at the evaluation of temperate versus cold water immersion for the treatment of EHS, the effects of physical characteristics were not considered. Furthermore, current cooling guidelines of EHS patients do not consider the influence of physical characteristics between individuals, particularly in regards to differences in body size, shape, and composition. However, EHS occurs in athletic, recreational and occupational activities where individual physical characteristics vary significantly. Although, according to Taylor et al. (2008), TWI is more than adequate to provide rapid and effective heat removal to safe core temperature levels in keeping

with the current minimum cooling guidelines (rectal temperature cooling rate of 0.10°C/min), this may not be the case for some individuals whose body composition differs greatly from those participants tested in previous studies pertaining to the evaluation of cold vs. temperate water immersion (Casa et al., 2010).

Previous studies with normothermic individuals have demonstrated that individuals with greater body mass typically demonstrate a smaller decrease in core temperature during CWI (White, Ross, & Mekjavic, 1992). It is also known that physical characteristics such as body surface area-to-body mass ratio (A_D/M) directly influence core cooling rates during CWI in normothermic individuals (Kollias et al., 1974; McArdle, Magel, Gergley, Spina, & Toner, 1984), where individuals with a greater surface area per unit body mass show faster core temperature decreases (Anderson, 1999). Differences in core cooling rates between normothermic males and females have also been found to be related to differences in lean body mass (LBM) (Anderson, Ward, & Mekjavic, 1995). Furthermore, studies show that the rate of core temperature decay is inversely associated with high levels of tissue insulation (i.e., subcutaneous fat) and cold-induced vasoconstriction (Baker & Daniels, 1956; Sloan & Keatinge, 1973). However, it remains unclear whether the pattern of response is similar when CWI is used in the treatment of individuals rendered hyperthermic by prolonged exercise in the heat. Further, no studies have evaluated the effects of physical characteristics on core cooling rates during 26°C TWI.

Differences in heat distribution (i.e., elevated core and muscle tissue) and deep (muscle) and peripheral (skin) blood flow associated with exercise-induced hyperthermia

have been shown to elevate the core-to-skin and the skin-to-water thermal gradients, consequently minimizing the insulatory effect of muscle and adipose tissue by heat loss during CWI (Lemire et al., 2008; Scott, Ducharme, Haman, & Kenny, 2004). study by Lemire et al. (2008), it was demonstrated that a ~10% difference in body adiposity did not influence core cooling rates during water immersion at 8°C following exercise-induced hyperthermia (end exercise T_{re} of 39.5°C) despite significant differences in A_D/M between the High (22.3 ± 4.3%) and Low (12.9 ± 1.9%) fat groups.

In a more recent study, Lemire et al. (2009) examined core cooling rates between males and females matched for A_D/M during 2°C CWI following exercise-induced hyperthermia (end exercise T_{re} = 39.5°C) and found that core temperature cooling rates in females were ~1.7 times faster compared to males (0.22 ± 0.07 vs. 0.12 ± 0.03 °C/min, respectively). Females also had a higher body fat percentage than males, despite a faster core cooling rate. Due to the fact that A_D/M and body adiposity did not influence rectal cooling rates, the greater cooling rates in females was attributed to differences in LBM (Lemire, Gagnon, Jay, & Kenny, 2009; Xu, Castellani, Santee, & Kolka, 2007). Since LBM has been shown to influence tissue insulation during cold stress and the fact that body surface area directly influences heat exchange from the surface of the body (Anderson, 1999), the authors surmised that body surface area-to-lean body mass ratio (A_D/LBM) could better explain differences in core cooling rate. This was further supported by a secondary analysis where a significant correlation (r = 0.70, P = 0.001) independent of sex was observed

between rectal cooling rate and A_D/LBM. The authors stated that future studies were required to demonstrate that this relationship holds true across a wide spectrum of body body surface area-to-lean body mass ratios.

1.2 Rationale and statement of the problem

To date, there remains a paucity of information on the influence of body surface area-to-lean body mass ratio (A_D/LBM) on core temperature cooling rates during water immersion following exercise-induced hyperthermia. Further, current cooling guidelines in the treatment of hyperthermic individuals using water immersion do not consider physical characteristics. Lastly, it is debated as to whether cold water immersion (2°C, CWI) is necessary in the treatment of EHS patients and questions remain as to the efficacy of temperate water immersion (26°C, TWI) when considerable physical differences between individuals (i.e., A_D/LBM) exist. Therefore, it is important to ascertain the influence of differences in A_D/LBM on core temperature cooling rates during both CWI and TWI following exercise-induced hyperthermia.

1.3 Purpose

The purpose of this study was to evaluate the effect of differences in body surface area-to-lean body mass ratio (A_D/LBM) on core temperature cooling rates during cold water immersion (2°C, CWI) and temperate water immersion (26°C, TWI) following exercise-induced hyperthermia (end-exercise core temperature of 40°C).

1.4 Objectives

1) To examine the effect of differences in body surface area-to-lean body mass ratio (A_D/LBM) on core temperature cooling rates during cold water immersion (2°C, CWI) and temperate water immersion (26°C, TWI) following exercise-induced hyperthermia.

2) To examine if cold water immersion (2°C, CWI), as compared with temperate water immersion (26°C, TWI), can provide more efficient cooling (i.e., faster core temperature cooling rates) and minimize the effect of body surface area-to-lean body mass ratio (A_D/LBM) on core temperature cooling rates and immersion times.

In order to fulfill these objectives, a study was performed which compared the core cooling responses of individuals with a High A_D/LBM (315 cm^2/kg, n =10) and a Low A_D/LBM (275 cm^2/kg, n =10) during cold water immersion (2°C, CWI) and temperate water immersion (26°C, TWI) following exercise-induced hyperthermia to a rectal temperature of 40.0°C.

1.5 Hypotheses

We evaluated the hypothesis that individuals with a High A_D/LBM (315 cm^2/kg) would have higher core cooling rates compared to individuals with a Low A_D/LBM (275 cm^2/kg). Furthermore, we examined the hypothesis that core cooling rates during temperate water immersion (26°C, TWI) would be lower in comparison to cold water immersion (2°C, CWI) and that cold water immersion (2°C, CWI) would minimize variations in core cooling rates and immersion times attributed to differences in A_D/LBM.

1.6 Relevance

Advancing our understanding of the influence of physical characteristics such as body surface area-to-lean body mass ratio (A_D/LBM) on whole-body cooling rates during both cold water immersion (2°C, CWI) and temperate water immersion (26°C, TWI) following exercise-induced hyperthermia is an important step in both understanding and reducing the risk of heat-related injuries. By understanding the interplay between A_D/LBM and core cooling rates during both CWI and TWI, we can provide recommendations as to the optimal treatment that should be employed in the treatment of EHS patients, irrespective of physical differences that may exist between individuals. Additionally, the results may have practical implications for the development and advancement of health and safety guidelines as they relate to the treatment of EHS.

1.7 Delimitations and limitations

Participants recruited for this study were physically active males between the ages of 18-45 years, with no history of respiratory, metabolic or cardiovascular disease, and not currently on medication related to these conditions. Therefore, the results of this study will not be applicable to children, the elderly, sedentary or morbidly obese individuals, or to individuals with any of the above conditions. Participants were not subjected to a heat acclimation procedure prior to each experiment and therefore, it is assumed that participants had a similar degree of heat acclimation. Lastly, participants were rendered hyperthermic through exercise in the heat and, therefore, comparisons to individuals suffering from classic heat stroke are not valid.

CHAPTER II: REVIEW OF LITERATURE

2.1 Human thermoregulation

2.1.1 Principles of thermoregulation

The body's ability to thermoregulate around a core temperature of approximately approximately 37.0°C independent of environmental conditions, physical work or exercise exercise levels is vital to survival (Webb, 1995). The narrow core temperature limits in in which the body can operate is regulated in fine balance between heat production and heat loss mechanisms to the environment (Kenny & Journeay, 2010). It is important to understand that the amount of heat storage or heat loss is directly related to body temperature (Brooks, 2005). The process of maintaining constant core temperature (heat balance) is achieved through a dynamic equilibrium as a result of the body responding to both internal and external conditions with autonomic effector responses (Parsons, 2003).

The anterior hypothalamus controls physiological thermal balance through feedback from central and peripheral thermoreceptors (Brooks, 2005; Werner, 1980, 1981). Warm and cold thermosensitive neurons found in the hypothalamus, brain stem and spinal cord transmit information to the preoptic region of the hypothalamus (PO/AH) (Cooper, 2002). Blood temperature is measured directly from the hypothalamus, while skin temperature is measured from thermoreceptors just under the skin. Thermoreceptors are also located in deeper tissue such as muscles, visceral organs and major blood vessels in the body (Brooks, 2005). Temperature changes sensed by the PO/AH result in appropriate effector heat production or heat loss responses based on the magnitude of the thermal disturbance, such as cutaneous vasodilation/vasoconstriction or sweating/shivering (Werner, 1980, 1981).

Human thermal balance can be represented by the heat balance equation (Parsons, 2003):

$M-W = (K + C + R + E_{sk}) + (C_{res} + E_{res}) + S$

M = rate of metabolic heat production.
W = rate of mechanical work.
K = rate of conductive heat exchange.
C = rate of convective heat exchange from skin.
R = rate of radiative heat exchange from skin.
E_{sk} = rate of evaporative heat loss from skin.
C_{res} = rate of convective heat exchange from respiration.
E_{res} = rate of evaporative heat exchange from respiration.
S = rate of body heat storage.

(All units are $W \cdot m^2$)

The heat balance equation can determine if there will be a positive, negative or zero rate of body heat storage (S). Gains or losses in body heat storage (S) are determined through imbalances between rates of metabolic heat storage ($M \pm W$) and heat loss mechanisms (i.e., R+C+K-E). In conditions where heat loss equals the rate of metabolic heat storage, the rate of body heat storage will be zero and core temperature will remain at a steady-state. In conditions where metabolic heat storage exceeds the rate of heat loss, a positive rate of body heat storage is achieved and core temperature will increase. On the contrary, when heat loss exceeds metabolic heat storage, body temperature will decrease due to a negative rate of body heat storage.

When the rate of heat loss or heat gain cannot be matched, uncompensable cold or heat stress occurs. Further, if decreases or increases in temperature are left

untreated in uncompensable conditions, life threatening levels of hypothermia and hyperthermia can develop (Parsons, 2003).

2.1.2 Heat exchange

The main means of heat exchange with the surrounding environment are conduction, convection, radiation and evaporation at the skin surface and the lungs (Wilmore & Costill, 2004). Conduction is defined as heat exchange through direct contact with another object. The magnitude of heat exchange between two objects in direct contact will be dictated by the amount of surface area in contact, the temperature of the objects, as well as the specific heat capacity of the objects. Convection is defined as heat exchange as a result of movement of a medium such as gas or liquid from a high to low thermal gradient, such as the gradient between the skin and the moving air or water in the surrounding environment. As air or water moves over the skin surface and gains heat, it is replaced by colder air or water, thus enhancing the heat loss due to an elevated temperature gradient between the skin surface and the external environment. Radiation is defined as heat exchange with the environment through electromagnetic waves such as ultraviolet, visible infrared and microwaves. Infrared waves are the most important when considering heat balance (Brooks, 2005). Radiation provides much more heat exchange in an outdoor environment than an indoor environment by comparison. Evaporation is defined as the transfer of heat from the evaporation of a liquid, such as sweat from the skin surface to the surrounding air. Evaporation in thermoregulation is regarded only as a heat loss mechanism as no heat can be gained through evaporation. In environmental conditions where evaporation is possible, evaporation is often the most powerful means of heat dissipation during exercise (Parsons, 2003).

2.1.3 Thermoregulatory responses

The primary thermoregulatory responses to actively attain heat balance through heat dissipation to the environment are increased cutaneous vasodilation and increased sweat rate (Benzinger, 1969; Hammel, 1968; Hardy, 1961). Both these responses increase based on changes in core and skin temperature (Bligh, 2006) and the change in response for a given change in core or skin temperature is known as the sensitivity (Gagge & Gonzales, 1996). The evaporation of sweat has a high potential for heat loss due to its high latent heat of vaporization (2427 J/g of sweat) at 30°C (Wenger, 1972). There are two types of sweat glands found in the body; aprocrine (armpits and pubic regions) and eccrine (2-4 million glands distributed all over the body). However, it is the eccrine glands that are largely responsible for thermoregulation (Parsons, 2003). Sweat glands are primarily affected by cholinergic activity, but are also affected by adrenergic agonists (Shibasaki, Wilson, & Crandall, 2006). During heat stress, sweat rate is affected by both the number of sweat glands activated as well as the sweat output per gland. It is also important to note that there are also noticeable differences in sweat rate between and within body segments (Kondo et al., 1998). Main factors determining the effectiveness of sweating as a heat loss mechanism include sweat rate and the ability of the ambient environment to remove the sweat through vaporization (Kenny & Journeay, 2010; Parsons, 2003). The higher the dry bulb temperature, the more water vapour the environment can potentially hold. Therefore, the higher the relative humidity of the air at a given temperature (ASHRAE, 1989), the higher the water vapour pressure in the air and

consequently, a reduction in the amount of water vapour that can be effectively taken up by the air (Parsons, 2003). This means that even though sweat rate is very high, not all sweat can be evaporated if it cannot be taken up by the environment, leading to impaired heat loss, which in turn creates increased potential for developing heat related injuries (Wyndham, Morrison, & Williams, 1965).

Increased vasodilation, coupled with increased skin blood flow during exercise heat stress, is important to maintain heat balance. Cutaneous vasodilation is a redistribution of regional blood flow to the skin and is the only controllable means by which heat can be transferred from within the body core to the skin surface, where it can be exchanged with the environment (Hammel, 1968; Hardy, 1961). At rest, the skin receives ~500 ml or 5-10% of cardiac output in thermoneutral environments. However, under heat stress, skin blood flow can increase up to 8 liters per minute or ~50-70% of cardiac output (Charkoudian, 2003; Kenney & Johnson, 1992). This increase in skin blood flow distribution during heat stress places increased work on the cardiovascular system, as there is competition for cardiac output between active muscles and skin blood flow for thermoregulation. The opposite occurs during cold stress, where vasoconstriction occurs to minimize heat loss at the skin surface. Vasodilation and vasoconstriction share the same adrenergic pathways, therefore skin blood flow at the skin surface is the balance between the vasoconstrictor and vasodilator systems (Brooks, 2005). The main purpose of regulating skin blood flow is to increase or decrease skin temperature to maintain the optimal level of dry heat exchange with the environment (Gagge & Gonzales, 1996). Skin blood flow is stimulated mainly through increases or decreases in core temperature beyond a core temperature onset threshold

(Kenney & Johnson, 1992). Vasodilation is also affected my mean and local skin temperatures, which alter the onset threshold and sensitivity of the response (Wissler, In conditions where environmental temperature exceeds skin temperature, increased skin blood flow will not serve to increase dry heat loss, but rather minimize dry heat gain by decreasing the temperature gradient between the skin and the environment (Gagge & Gonzales, 1996).

2.1.4 Exercise and thermoregulation

Humans are at most 30% efficient in performing external work (Joyner & Coyle, 2008) and consequently, the rest of the metabolic energy (70% or higher) required to perform this work is liberated as heat. At the start of exercise, there is a rapid increase in metabolic heat production (10-20 times normal) which will attain steady-state after approximately five minutes and remain in this state for the duration of exercise, if the mechanical efficiency and external workload (intensity) are kept constant (Kenny, Webb, Ducharme, Reardon, & Jay, 2008). Heat loss responses do not immediately match the rate of metabolic heat production (Webb, 1995). Consequently, there is a pronounced increase in body heat storage at the start of exercise (Kenny et al., 2009; Kenny et al., 2008). As exercise progresses, muscle temperature increases and heat propagates throughout the body by conduction and convection (Hammel, 1968; Hardy, 1961).

During exercise in the heat, core temperature and skin temperature rise above threshold levels for heat loss responses to be activated, leading to increased cutaneous

vasodilation and increased skin blood flow. The purpose of this is to redirect warm blood from exercising muscles to the skin surface where heat transfer with the external environment can occur (Hammel, 1968; Hardy, 1961). Sweat rate also increases to elicit the evaporation of sweat (Sawka, Wenger, & Pandolf, 1996). In addition, an increased cardiac output is needed to maintain blood pressure at a level high enough to sustain both skin and muscle perfusion during exercise.

Environmental conditions such as the ambient temperature and relative humidity, as well as exercise intensity and physical characteristics of the human body dictate how long it takes for the rate of heat loss to match the rate of metabolic heat production (Kenny et al., 2008). This will only occur if the heat loss capacity of the individual in a given environment can offset the rate of metabolic heat production, also termed a compensable heat stress environment. Conversely, if an individual's heat loss mechanisms are unable to match the rate of metabolic heat production, core temperature will continue to rise at a magnitude based on the difference between the two rates, which leads to uncompensable heat stress. Uncompensable heat stress can be dangerous because core temperature will continue to rise unless the individual adjusts the exercise intensity or the environmental conditions are changed to offset the positive rate of body heat storage. Uncompensable heat stress will ultimately lead to dangerous elevations in core temperature and severe heat illnesses, such as exertional heat stroke, can develop. In the absence of any heat dissipating mechanisms, core body temperature could increase at a rate as high as ~1°C every 5 minutes (Nadel, Wenger, Roberts, Stolwijk, & Cafarelli, 1977).

2.1.5 Post-exercise thermoregulation

At the cessation of exercise, the residual heat stored in the body during the bout must be lost in order for core temperature to return to baseline levels. However, have shown that core temperatures remain elevated for durations greater than 60 minutes post-exercise, indicating a compromised thermoregulatory response following dynamic exercise (Kenny et al., 2006; Kenny & Niedre, 2002; Thoden, Kenny, Reardon, Jette, & Livingstone, 1994). Although core temperature remains elevated post-exercise, studies have also shown that local skin blood flow and sweating responses are attenuated to near pre-exercise levels during the early stages of recovery (Gagnon, Jay, Reardon, Journeay, & Kenny, 2008; Kenny & Journeay, 2010; Kenny & Niedre, 2002). These attenuated thermoregulatory responses post-exercise are a result of mainly non-thermal factors such as central command, mechanoreceptors and baroreceptors (Journeay, Carter, & Kenny, 2006; Kenny & Journeay, 2010).

Post-exercise, there is a reduction in mean arterial pressure (MAP) leading to post-exercise hypotension (PEH) (Halliwill, 2001; Kenney & Seals, 1993). Hypotension develops as a result of increased vascular conductance (CVC) of up to 30% (Halliwill, 2001), increasing blood flow to vasodilated regions and augmenting venous blood pooling in previously active muscles (Kenney & Seals, 1993). The degree of MAP reduction post-exercise also depends on the type of recovery and body position. In the upright seated posture, there is increased blood pooling in the lower extremities in comparison to a supine position. During inactive recovery, there

is less venous return from the muscle pump mechanism, leading to a more significant drop in MAP as compared to active (low intensity exercise) or passive (device assisted; no exercise) recoveries (Halliwill, 2001).

During exercise in the heat, the combined effect of lost plasma volume (due to sweating and failure to replace fluid losses) and increased blood volume in vasodilated areas, reduce central venous pressure and cardiac filling pressure. As a result of these combined effects, cardiac output often remains increased post-exercise and hypotension develops due to the fact that the drop in systemic vascular resistance is not offset by increased cardiac output (Halliwill, 2001).

2.2 Heat illnesses

2.2.1 Predisposing factors for heat illnesses

Heat illnesses can develop in conditions where the environmental and metabolic heat load exceed the body's physological capacity to dissipate heat. Heat illnesses are more prevalent in hot, humid environments or when high insulative or non-permeable clothing or athletic equipment is worn (Armstrong et al., 2010; Howe & Boden, 2007). There are factors that mitigate the occurrence of heat illnesses, such as some medications (i.e., those affecting sweat production or skin blood flow), dehydration, sleep deprivation, sunburn or damage to the skin, obesity, low physical fitness and low levels of heat acclimation (Barrow & Clark, 1998). Certain populations are generally more susceptible to heat illneses, such as the elderly, children, or those with medical conditions that inhibit their thermoregulatory ability (Howe & Boden, 2007). In heathy, active individuals, heat illnesses can also occur when the

environment is relatively cool due to high levels of metabolic heat production (exceeding heat loss mechanisms) sustained over a long period of time (Casa, McDermott, et al., 2007). In some individuals, high levels of motivation or unwillingness to quit during physical activity or athletic competition contribute to an increased incidence of heat illnesses (Howe & Boden, 2007).

2.2.2 Heat illnesses

Heat illnesses have varying degrees of recognizable symptoms. Common heat illnesses include heat cramps, heat exhaustion, heat syncope and, the most severe, heat stroke. Heat cramps are caused by dehydration, electrolyte imbalances, muscle fatigue and symptoms often include painful skeletal muscle spasms (Eichner, 1998). Heat syncopy, also known as orthostatic syncopal episode, occurs after the cessation of exercise or work in the heat. This occurs as a result of reduced blood plasma volume (due to dehydration) and post-execise vasodilation (Eichner, 1998). Heat exhaustion is most common amongst an active population and is characterized by the inability to continue exercise in the heat, and may or may not involve collapse. Heat exhaustion typically involves heavy sweating, dehydration, sodium loss and energy depletion (Binkley, Beckett, Casa, Kleiner, & Plummer, 2002). In some cases, the only way to distinguish heat exhaustion from heat stroke is by measuring rectal temperature (Armstrong et al., 1996; Casa, 1999a, 1999b).

Heat stroke is the severest form of heat illness and is defined as a core temperature exceeding 40.0°C (Armstrong et al., 2007; Casa, McDermott, et al., 2007; Parsons, 2003). Consequences of body temperature elevated to this extent can have serious consequences

including multiple organ system failure, circulatory collapse and death (Armstrong et al., 2007). Symptoms associated with heat stroke include decreased blood pressure, increased heart rate, hyperventilation, vomiting, diarrhea, convulsions, delirium and most frequently, central nervous system dysfunction (Armstrong et al., 2007; Casa et al., 2012; Casa, McDermott, et al., 2007; Epstein & Roberts, 2011; Murphy, 1984; Yaqub & Al Deeb, 1998). Heat stroke can be a result of classical models, or exertional means through exercise. Classical heat stroke is commonly seen is children and the elderly during heat waves (in the absence of exercise), whereas exertional heat stroke (EHS) can occur very rapidly and is usually caused by endogenous heat production (Eichner, 1998).

The underlying pathophysiology of EHS occurs when internal organ tissue temperatures rise above critical levels, damaging cell membranes and disrupting cell energy systems, giving rise to a characteristic clinical syndrome which includes organ dysfunction and cell death (Armstrong et al., 2007). The incidence rate for EHS can be as high as 1 in 1000 at some athletic events, with some events having more than 10,000 or more participants, with the ensuing potential for medical staff to be treating 10 or more cases (Casa, McDermott, et al., 2007). According to Casa et al. (2007), most deaths due to EHS occur 12 hours to 1 week following EHS.

It is important to note that the severity of EHS is directly related to the duration of visceral organ hyperthermia above critical levels (Armstrong et al., 2007; de Galan & Hoekstra, 1995; Hubbard et al., 1977; Smith, 2005). For example, Hubbard et al. (1977) demonstrated that the time core temperatures were elevated above 40.4°C in hyperthermic

mice, following both passive heat stress and exercise determined the mortality rate. Fortunately, the survival rate for EHS in humans is even better if the duration of severe hyperthermia is <30 min (Casa, McDermott, et al., 2007). Therefore, as delays in the treatment of EHS patients influence the prognosis during recovery, rapid on-site cooling of hyperthermic individuals to a near normal resting core temperature is paramount to their survival and to minimize heat related injury (Armstrong et al., 2007; Casa et al., 2005; Casa et al., 2012; Casa, McDermott, et al., 2007; Proulx et al., 2003).

2.3 Treatment of heat illnesses

2.3.1 Cooling modalities

There are a multitude of treatment modalities used in the treatment of heat illnesses (Casa, McDermott, et al., 2007; Hadad et al., 2004; McDermott et al., 2009; Smith, 2005). These methods can be organized into four categories: 1) evaporative cooling measures (i.e, fanning, spraying, effects of clothing etc.), 2) wet towels and ice packs on the chest, neck, axilla and groin area, 3) combination of dousing with water and fanning and 4) whole-body water immersion (Casa, McDermott, et al., 2007).

Current guidelines for the treatment of EHS state that any treatment modality should achieve a rectal cooling rate of at least 0.10°C/min if treatment begins immediately and cool the hyperthermic victim back to near normal resting core temperature levels within 30 minutes (Casa, McDermott, et al., 2007). Further, a treatment modality with a rectal cooling rate of 0.15°C/min should be employed

when treatment is delayed longer than 20-30 minutes after collapse (Casa, McDermott, et al., 2007). It is important to note that current cooling guidelines do not take into account variations in physical characteristics between individuals; particularly with regards to differences in body size, shape, and composition.

An extensive and critical review by McDermott et al. (2009) of the available research on whole-body cooling for the treatment of exertional hyperthermia concluded that cold water immersion (2-10°C) provided the most efficient cooling. Further, a review by Casa et al. (2007) emphasized that the fastest core cooling rates have been shown to be with 2°C CWI (Casa, McDermott, et al., 2007). Based on the fact that CWI has produced the highest core cooling rates to date and has a proven clinical track record, CWI (<10°C) is currently viewed as the 'gold standard' treatment for hyperthermic individuals (Casa, McDermott, et al., 2007).

An important paradigm in the treatment of EHS patients is, "cool first; transport second (Casa et al., 2010)". This is based on the premise that immediate rapid cooling is the most important aspect to treating EHS patients. It has been advocated that in circumstances where CWI cannot be used, then the next best available cooling modality should be used (cold showers, rotating ice/wet towels etc.) in the interim until CWI can be employed (Casa et al., 2010). When CWI is not possible, it is advised that cooling should be done while transporting the victim to a more optimal cooling facility where CWI can take place (Casa et al., 2010).

2.3.2 Cold water immersion

The use of circulated CWI has been shown to produce some of the highest cooling rates with the fastest recorded during 2°C ice water immersion (0.35°C/min; 1ºC every 3 minutes), especially during the second degree drop (note: the first and second degree cooling rate simply reflect the change in core temperature measured for the first and second degree Celsius drop in core temperature subsequent to the start of immersion) in rectal temperature (0.50°C/min) (Proulx et al., 2003). The effectiveness of CWI is primarily due to the heat transfer properties of water. Water has a thermal conductivity (630.5 $mW/m^2/°K$) that is approximately 24 times greater than air (26.2 $mW/m^2/°K$). Water also has high specific heat capacity (4.18 J/g/°K) relative to air (1.02 J/g/°K). The density of water is 0.99 g/cm^3 whereas the density of air is only 0.0012 g/cm^3, resulting in a ~3500 times greater volume- specific heat capacity of water relative to air, making it an ideal medium for cooling applications (Casa, McDermott, et al., 2007; McDonald, Goode, Livingstone, & Duffin, 1984; Smith, 2005).

When a hyperthermic victim is immersed in cold water, heat is dissipated rapidly from the skin surface to the surrounding water due to the large thermal gradient between the water and the skin surface. When the water is circulated, the water movement aids in maintaining this high temperature gradient between the skin and water. Therefore, the colder the water, the greater the potential for heat loss at the surface of the skin (Casa et al., 2010; Proulx et al., 2003). For example, the skin-water temperature gradient during 2°C immersion was 1.8, 2.5 and 2.6 times that of

8,14 and 20°C water, respectively (Proulx et al., 2003). These rates are approximately 2 times greater than that of warmer water temperatures (Proulx et al., 2003). Furthermore, according to whole-body heat loss, data showed that the heat gained during prior exercise in the heat was fully eliminated after 5.4 minutes of immersion following the 2°C ice water immersion as compared to warmer water temperatures (7.9, 10.4 and 13.1 minutes of immersion in 8, 14 and 20°C water respectively) (Proulx et al., 2003). This data by Proulx et al. (2003) clearly demonstrates immersion in 2°C water provides the most effective treatment in eliminating heat from exercise-induced hyperthermia.

Cold water immersion is currently used during many athletic, military and industrial settings. The use of CWI at the Falmouth Road Race in Falmouth, Massachusetts holds a 100% survival rate for the approximately 400 EHS victims in the 37 year history of the race (Casa et al., 2010). Other events in which CWI has been utilized include the Peachtree Road Race and the New York Marathon (Casa et al., 2010). The United States Military (Marine Corps) at Parris Island has adopted CWI as a treatment for EHS, and many NCAA and NFL football teams are more frequently adopting this modality. Many industries, such as mining, use CWI effectively as it is readily available (Casa et al., 2010). Desirable features of CWI include the minimal requirements for equipment and space, the ease of set up and cost effectiveness, making CWI applicable in a broad range of situations. All that is needed is a Rubbermaid tub, ice, and water, with the use of rectal core temperature monitoring as a standard.

Despite the proven clinical benefits of CWI, its use has been questioned due to the fact that sudden immersion of normothermic individuals in cold water can invoke powerful cold shock responses (potentially lethal responses including hyperventilation, cardiac arrhythmias, elevated blood pressure, reduced cerebral blood flow etc.), vasoconstriction, intense shivering, discomfort and an increased risk of hypothermia during prolonged exposure (Casa et al., 2012; Casa et al., 2010; Taylor et al., 2008). However, Proulx et al. (2003) clearly demonstrated that during CWI in hyperthermic individuals, an abundant skin blood flow is not essential for the body to cool as the temperature gradient between the skin and water is so great (7.7°C). Further, cold shock responses and shivering were seldom observed during 2°C CWI (Casa et al., 2010; Proulx et al., 2003; Proulx, Ducharme, & Kenny, 2006). In addition, safe cooling limits have been proposed in order to minimize the risk of hypothermia following CWI in the treatment of hyperthermic individuals (Proulx et al., 2006). On the basis of the heat loss data by Proulx et al. (2006), a decrease of only 1.5°C in T_{re} during the immersion in 2°C water, resulted in the elimination of 100% of the heat gained during exercise without causing hypothermia. As a result, it was proposed that cooling the core temperature of hyperthermic subjects to a rectal temperature between 37.8°C (during immersion in water >10°C) and 38.6°C (during immersion in water <10°C), can eliminate the heat gained during exercise without causing hypothermia (Proulx et al., 2006). Lastly, discomfort should not be a deterrent to providing the best treatment for EHS victims given the life threatening

nature of EHS. In life threatening situations, comfort becomes a secondary consideration (Casa et al., 2010; Casa, McDermott, et al., 2007).

2.3.3 Temperate water immersion

It has recently been demonstrated that temperate water immersion (26°C, TWI) provided near similar overall core cooling rates to that measured in much cooler water conditions and they concluded on this basis that TWI can be used to reduce the undesirable effects of CWI (i.e., cold shock response and elevated shivering response, etc.), while maintaining patient comfort (Casa et al., 2010; Taylor et al., 2008). This argument is based on a study by Taylor et al. (2008) who showed that following a heat stress protocol (semi-recumbent cycling in the heat while wearing a water perfused suit) to an esophageal temperature of 39.5°C, participants cooled in under 3 minutes during both temperate (26°C: 2.91 min, 0.71°C/min) and cold water (14°C: 2.16 min, 0.88°C/min) and surmised that the time difference in cooling between cold and temperate water (only 45 seconds) would not have any meaningful physiological or clinical implications, and questioned the need to use CWI in the treatment of EHS. It is important to mention however that Taylor et al. (2008) clearly advocated that TWI should not be employed in cases where EHS victims are under circulatory collapse (i.e., when peripheral circulation is not viable). It is also important to note that the basis for this argument is in the field, where core temperature monitors are not available to monitor high-risk individuals during cooling, therefore risk minimization takes priority over comfort (Taylor, Caldwell, Van Den Heuvel, & Patterson, 2009).

The rapid core cooling rates observed during TWI were said to be achieved by minimizing the skin-water temperature gradient, thereby inducing a less powerful vasoconstrictor response and consequently promoting enhanced central heat transport skin surface by lengthening the transcutaneous convective pathway between the skin water (Casa et al., 2010; Taylor et al., 2008). According to Taylor et al. (2008), TWI provides a 115% greater convective heat transfer to the skin compared with CWI based on linear extrapolation of actual skin temperatures (cold: 21.2°C and temperate: 26.8°C) to predict skin blood flow, assuming that maximal flow occurs at a skin temperature of ~42°C and minimal flow occurs at ~10°C.

The conclusions made by Taylor et al. (2008) regarding the benefits of TWI were solely based on esophageal temperature and not rectal temperature, which have different temporal responses and fundamentally represent different physiological structures and/or regions. It is well established that core cooling rates based on esophageal temperature far exceed those rates measured by rectal temperature (Gagnon et al., 2010). In addition, rectal temperature provides a more accurate measure of deep visceral temperature, whereas esophageal temperature is more representative of cardiac tissue temperature and provides a better estimate of central nervous system (or brain) temperature (Gagnon et al., 2010). Although TWI (0.71°C/min) had similar esophageal cooling rates to CWI (0.88°C/min), rectal cooling rates were only 0.10°C/min and 0.18°C/min during temperate (26°C) and cold (14°C) water immersion, respectively. In fact, the rectal core cooling rates

observed by Taylor et al. (2008) were 3.5 times slower (0.35°C/min) than previously repored by Proulx et al. (2003).

It is important to note that Taylor et al. (2008) did not consider that while a shorter shorter immersion time is necessary to drop esophageal temperature to 37.5ºC, a significant residual heat storage (~50% of heat accumulated during exercise) remains in the deeper tissues and is paralleled by a corresponding elevation of rectal temperature of ~39-39.5ºC (Casa et al., 2010; Proulx et al., 2003). As the risk of adverse outcomes in EHS patients is related to the duration of visceral organ hyperthermia (Armstrong et al., 2007) and the length of time that core temperature remains above critical values for cell damage is an important determinant of survival from EHS (Hubbard et al., 1977), questions remain as to the efficacy of TWI in emergency situations where rectal temperature may exceed 40°C, as it may take a considerable amount of time for rectal temperature to decrease below critical levels. Based on results from Taylor et al. (2008), TWI is more than adequate to provide rapid and effective heat removal to safe core temperature levels in keeping with the current minimum cooling guidelines (rectal temperature cooling rate of 0.1°C/min). However, this may not be the case for some individuals whose body composition differs significantly from the average population tested in the previous studies directed at the evaluation of cold vs. temperate water immersion (Casa et al., 2010).

2.4 Physical characteristics

2.4.1 Physical characteristics and thermoregulation

Physical characteristics play an important role in thermoregulation, especially influencing core temperature responses during heat stress (Anderson, 1999; Havenith, 2001b). The human body can be divided into two main compartments; the core and (Stolwijk & Hardy, 1966). The shell compartment consists of the skin and subcutaneous fat while the core compartment consists of the muscles and viscera. The sum of each compartment determines body mass, body composition and body surface area (Anderson, 1999).

The average specific heat capacity of the human body is ~3.470 kJ/kg/°C and the heat storage capacity of the body can be represented by body mass (Geddes & Baker, 1967). The specific heat of the human body is defined as the amount of energy required to increase 1 kg of body weight by 1°C. In theory, the greater the mass, the greater the amount of heat that can be lost or gained from the body before there are changes to core body temperature (Anderson, 1999; Havenith, 2001b). This applies to both cold and heat stress. The body's heat storage capacity is also dictated by body composition, as each tissue in the body has its own specific heat capacity (Anderson, 1999). Therefore, different relative amounts of fat mass (adipose tissue) and lean body mass (body mass-fat mass; i.e. muscle tissue) can affect the body's heat capacity. Muscle tissue is mainly composed of water, which possesses a high heat storage capacity relative to other tissues. Body fat has a lower specific heat capacity

compared with lean body mass and therefore, individuals with higher amounts of fat mass will show a greater change in core temperature for a given change in body heat content (Anderson, 1999). Fat and lean body mass also possess different thermal conductivities (Anderson, 1999). For example, during heat stress, high levels of adipose tissue can potentially act as a barrier to heat loss (Havenith, Coenen, Kistemaker, & Kenney, 1998; Havenith, Luttikholt, & Vrijkotte, 1995) and during cold stress, these high levels of adipose tissue, combined with vasoconstricted muscle tissue, reduce core temperature decay due to insulative effects (Keatinge, 1960; Park, Pendergast, & Rennie, 1984; Veicsteinas, Ferretti, & Rennie, 1982).

Body surface area is a major determinant in heat exchange between the body and the environment. The greater the area exposed between the skin and the external environment, the greater the potential for heat exchange (Gagge & Gonzales, 1996). Larger individuals, both in height and diameter, have a greater potential for dry and evaporative heat exchange in comparison to smaller individuals. During heat stress, individuals with a larger surface area have lower core temperatures (Havenith et al., 1998; Havenith et al., 1995). However, during cold stress, the larger surface area available for exchange in bigger individuals is often counterbalanced by their greater body mass (Anderson, 1999). In many studies, the body surface area-to-mass ratio (A_D/M) explains core temperature variations amongst individuals in both heat and cold stress (McArdle, Magel, Gergley, et al., 1984; McArdle, Magel, Spina, Gergley, & Toner, 1984; Shapiro, Pandolf, Avellini, Pimental, & Goldman, 1980). However, this has not always been the case because some larger individuals, possessing both a large body surface area and body mass, demonstrated a lower core

temperature increase in the heat due to their large surface area and high heat capacity (Havenith, 2001a).

2.4.2 The influence of physical characteristics during water immersion

It has been demonstrated that when normothermic individuals are immersed in cold water, those with greater body mass typically demonstrate a smaller decrease in core temperature (White et al., 1992). It has also been shown that body surface area-to-body mass ratio (A_D/M) directly influences core cooling rates during CWI in normothermic individuals (Kollias et al., 1974; McArdle, Magel, Gergley, et al., 1984), whereby a greater surface area is available per unit body mass is associated with a greater rate of core temperature cooling (Anderson, 1999). Differences in core cooling rates between normothermic males and females have also been shown to be related to differences in lean body mass (Anderson et al., 1995). Furthermore, studies have shown that the rate of core temperature decay is inversely associated with high levels of tissue insulation (i.e., subcutaneous fat) and cold-induced vasoconstriction (Baker & Daniels, 1956; Sloan & Keatinge, 1973). However, differences in tissue blood flow and tissue heat content during exercise in the heat can alter the body's physiological responses during subsequent CWI (Proulx et al., 2003).

Differences in heat distribution (i.e., elevated core and muscle tissues) and deep (muscle) and peripheral (skin) blood flow associated with exercise-induced hyperthermia have been shown to elevate the core-to-skin and the skin-to-water thermal gradients, consequently minimizing the insulatory effect of muscle and

adipose tissue by increasing dry heat loss during CWI (Lemire et al., 2008; Scott et al., 2004). Therefore, the pattern of response of the influence of physical characteristics on core temperature cooling rates may not be similar to the same extent when hyperthermic individuals (rendered hyperthermic by prolonged exercise in the heat) are immersed in cold water. In fact, some evidence suggests that this pattern of response is different in hyperthemic individuals. However, this concept has only been recently investigated and is not well understood (Lemire et al., 2008; Lemire et al., 2009).

In a study by Lemire et al. (2008), it was demonstrated that a ~10% difference in body adiposity did not influence core cooling rates during water immersion at 8°C following exercise-induced hyperthermia (end-exercise T_{re} of 39.5°C), despite significant differences in A_D/M between the High (22.3 ± 4.3%) and Low (12.9 ± 1.9%) fat groups. It was suggested that the elevated skin blood flow induced by exercise in the heat reduced the advantage that a greater adipose tissue insulation would otherwise provide in normothermic individuals immersed in cold water (Lemire et al., 2008).

In a more recent study, Lemire et al. (2009) examined core cooling rates of both males and females matched for A_D/M during 2°C CWI following exercise-induced hyperthermia (end exercise T_{re} = 39.5°C). Males and females were matched for A_D/M to eliminate some apparent physical differences between sexes, as females typically have a larger A_D/M than males (McArdle, Magel, Gergley, et al., 1984). Lemire et al. (2009) found that core temperature cooling rates in females were ~1.7- fold faster compared to males (0.22 ± 0.07 vs. 0.12 ± 0.03 °C/min, respectively). Females also had a higher body fat percentage

than males, despite a faster core cooling rate. Due to the fact that A_D/M and body adiposity did not influence rectal cooling rates, the greater cooling rates in females were attributed to differences in lean body mass (Lemire et al., 2009; Xu et al., 2007). Since LBM has been show to influence tissue insulation during cold stress and that body surface area directly influences conductive heat exchange from the surface of the body (Anderson, 1999), the authors surmised that A_D/LBM could better explain differences in core cooling. Although the study by Lemire et al. (2009) was not designed to specifically evaluate the influence of A_D/LBM, a secondary analysis demonstrated a key observation. When male and female participants were pooled into a single group, a significant correlation ($r = 0.70$, $P = 0.001$) independent of sex was observed between rectal cooling rate and A_D/LBM. Lemire et al. (2009) indicated that future research was needed to confirm this relationship across a wide spectrum of body surface area-to-lean body mass ratios.

PART TWO: METHODS AND RESULTS OF THESIS

Water immersion in the treatment of exertional hyperthermia: physical determinants

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ABSTRACT

Purpose: We examined the effect of differences in body surface area-to-lean body mass ratio (A_D/LBM) on core temperature cooling rates during cold water immersion (CWI, 2°C) and temperate water immersion (TWI, 26°C) following exercise-induced hyperthermia. **Methods:** Twenty male participants were divided into 2 groups; High (315.6 ± 7.9 cm^2/kg, n=10) and Low (275.6 ± 8.6 cm^2/kg, n=10) A_D/LBM. On two separate occasions, participants ran on a treadmill in the heat (40.0°C, 20% relative humidity) wearing an impermeable rain suit until rectal temperature reached 40.0°C. Following exercise, participants were immersed up to the nipples (arms remained out of the water) in either a cold (2ºC) or temperate (26ºC) circulated water bath until rectal temperature returned to 37.5ºC. **Results:** Overall rectal cooling rates were significantly different between experimental groups (High vs. Low A_D/LBM, P = 0.005) and between immersion conditions (CWI vs. TWI, P < 0.001). Individuals with a High A_D/LBM had a ~1.7-fold greater overall rectal cooling rate relative to those with Low A_D/LBM during both CWI (High: 0.27 ± 0.10 vs. Low: 0.16 ± 0.10°C/min) and TWI (High: 0.10 ± 0.05 vs. Low: 0.06 ± 0.02°C/min). Further, overall rectal cooling rates during CWI were ~2.7-fold greater than during TWI for both the High (CWI: 0.27 ± 0.10 vs. TWI: 0.10 ± 0.05 °C/min) and Low (CWI: 0.16 ± 0.10 vs. TWI: 0.06 ± 0.02°C/min) A_D/LBM groups. **Conclusion:** We show that individuals with a Low A_D/LBM have a reduced rectal cooling rate and take longer to cool than those with a High A_D/LBM during both CWI and TWI. However, CWI provides the most effective cooling treatment irrespective of physical differences.

Key words: cold water immersion; temperate water immersion; core temperature cooling rates; exertional heat stroke.

INTRODUCTION

Exertional Heat Stroke (EHS) is a medical condition that occurs when core temperature exceeds 40.0°C (3, 8, 32) and can lead to circulatory failure, multi-organ dysfunction and most commonly central nervous system dysfunction (10). Early recognition of EHS and the rapid on-site cooling of the individual with EHS to a near normal resting core temperature is paramount to their survival and to minimize heat related injury (3, 6, 8). Effective cooling modalities in the treatment of EHS must achieve a rectal temperature cooling rate exceeding 0.1-0.2ºC/min when cooling begins immediately and should be no less than 0.15ºC/min if cooling is delayed (8).

Cold water immersion (CWI) < 10°C is considered the gold standard treatment for EHS patients (8) and circulated ice-water immersion (2ºC) has been shown to provide some of the highest rectal temperature cooling rates (0.35ºC/min), especially for the second degree drop (note: the first and second degree cooling rate simply reflect the change in core temperature measured for the first and second degree Celsius drop in core temperature subsequent to the start of immersion) in core temperature (0.50ºC/min) (24). Despite the proven clinical benefits of CWI, Taylor et al. (28) recently showed that temperate water immersion (TWI) at 26°C provided near similar overall core cooling rates to that measured in much cooler water

temperature conditions (24) and they concluded on this basis that TWI should be used to reduce the undesirable effects of CWI (i.e., cold shock response and elevated shivering response, etc.) while maintaining patient comfort. While they showed that TWI resulted in esophageal cooling to 37.5°C in less than 3 min, they failed to consider the fact that a significant residual body-heat load remained in the visceral organs as evidenced by a correspondingly elevated rectal temperature of ~39-39.5ºC.

It is well established that physical characteristics such as adiposity, lean body mass, body surface area and body surface area-to-mass ratio (A_D/M) influence core cooling responses in previously resting normothermic individuals during CWI (1, 2, 4, 15, 16, 20, 23, 29, 31). However, it is unclear whether the pattern of response is similar when CWI is used in the treatment of individuals rendered hyperthermic by prolonged exercise in the heat. Some insight may be gleaned by recent reports showing that lean body mass, and not body adiposity is an important factor affecting cooling rates during CWI (21, 22). However, the one study (22) showing that differences in LBM was an important factor in determining core cooling rates in hyperthermic individuals during CWI was based on a comparison between males and females, whereby females demonstrated a ~1.7-fold greater rectal cooling rate during CWI relative to their male counterparts despite being matched for A_D/M and having a greater body adiposity. In a secondary analysis, a significant correlation, ($r = 0.70$, $P = 0.001$) was observed between rectal cooling rates and body surface area-to-lean body mass ratio (A_D/LBM) when pooled data from male and females were examined. The authors surmised that A_D/LBM may be a key factor affecting whole-body cooling rate during the treatment of hyperthermic individuals using water immersion (22).

Therefore, the purpose of this study was to evaluate the effect of differences in A_D/LBM on core temperature cooling rates during cold water immersion (2°C, **CWI**) and temperate water immersion (26°C, **TWI**) following exercise-induced hyperthermia (end-exercise rectal temperature of 40°C). We evaluated the hypothesis that individuals with a High (315.6 cm^2/kg) A_D/LBM would have greater core cooling rates compared to individuals with a Low (275.6 cm^2/kg) A_D/LBM. Furthermore, we examined the hypothesis that core cooling rates during TWI would be lower in comparison to CWI, and that CWI would minimize variations in core cooling rates and immersion times attributed to differences in A_D/LBM.

METHODS

Ethical approval

The current experimental protocol was approved by the University of Ottawa Health Sciences and Science Research Ethics Board, in accordance with the Declaration of Helsinki. Written informed consent was obtained from all volunteers prior to their participation in the study.

Experimental design

Twenty adult males (18-35 years of age) volunteered for one preliminary and two experimental sessions. Participants were healthy, physically active (exercised for a minimum of 30-minutes 3 times per week at a moderate intensity), non-smoking

and free of any known cardiovascular, metabolic and respiratory diseases. During the preliminary session, training history, body height, mass, and density, as well as maximum maximum oxygen uptake were determined. Training history was assessed by having the participants quantify their physical activity levels using the quantitative (3 month) and seven day physical activity recall questionnaires proposed by Kohl et al. (19). Maximum oxygen uptake (VO_{2max}) was determined by indirect calorimetry (MOXUS system, Applied Electrochemistry, Pittsburgh, PA, USA) during a progressive incremental treadmill exercise protocol in thermoneutral (22°C, 30% relative humidity) conditions (5). Body height was determined using a stadiometer (model 2391, Detecto, Webb City, MO, USA), while body mass was measured using a digital high-performance weighing terminal (IND560, Mettler Toledo Inc., Mississauga, ON, CANADA). Body surface area was subsequently calculated from the measurements of body height and mass (9). Body density was measured using the hydrostatic weighing technique, and used to calculate body fat percentage (27). Lean body mass was calculated from the difference between body mass and absolute fat mass. Participants were then divided into High (315.6 ± 7.9 cm^2/kg, n = 10) or Low (275.6 ± 8.6 cm^2/kg, n = 10) body surface area-to-lean body mass ratio (A_D/LBM) groups. Participant's physical characteristics are presented in Table 1.

Experimental Protocol

All experimental sessions were at the same time of day for a given participant and were separated by a minimum of 48 hours. The participants were asked to drink 500 mL of water the night prior to, as well as the morning of each experimental session and to limit

food consumption 2 hours prior to each experimental session. Participants were asked to refrain from ingesting alcohol, caffeine and non-steroidal anti-inflammatory drugs as well as exercising 24 hours prior to experimentation. Upon arrival at the laboratory, participants inserted a temperature probe in their rectum, voided their bladder and weighed themselves nude. Participants then changed into standardized athletic clothing (shorts and running shoes) and subsequently sat quietly for a 20-min instrumentation period at an ambient room temperature of 23°C. Following instrumentation, the participant entered a thermal chamber (Can-Trol Environmental Systems Ltd, Markham, ON, CANADA) regulated at 40.0°C, 20% relative humidity where they remained seated resting for an additional 20-min. Thereafter, participants donned a nylon rain poncho covering the entire upper body and head in order to minimize evaporative heat loss and accelerate the heating process. Participants were then required to run on a treadmill (Desmo HP, Woodway, Waukesha, WI, USA) at ~65% of their pre-determined VO_{2max} until rectal temperature (T_{re}) reached 40.0ºC or until volitional fatigue.

Following the cessation of exercise, participants donned neoprene boots (DuPont, Wilmington, DE, USA) and after 5 minutes, were transferred and immersed in an upright seated position with their legs extended to the nipples (arms and hands out of the water for safety reasons) in a circulated water bath (S-110-SL, Whitehall Manufacturing), City of Industry, CA, USA) maintained at either 2°C (cold water immersion, **CWI**) or 26°C (temperate water immersion, **TWI**). Participants remained in the water bath until T_{re} decreased to 37.5°C. Participants were then removed from

the water bath and remained in an upright seated posture while they were towel dried. To ensure the safety of each participant, T_{re} was monitored for 30-minutes or until T_{re} returned within 0.5°C of baseline resting values. After the completion of the trial, a nude body weight measurement was completed to assess fluid loss.

Instrumentation

Esophageal temperature (T_{es}) and T_{re} were measured using general purpose thermocouple temperature probes (Mon-a-therm General Purpose Temperature Probe, Mallinckrodt Medical Inc., St-Louis, MO, USA). The rectal temperature probe was inserted approximately 15 cm past the anal sphincter. The esophageal temperature probe was inserted 40 cm past the entrance of the nostril while the participants sipped water (100-300 mL) through a straw. Skin temperature and dry heat exchange was measured at 9 sites using T-type (copper/constantan) thermocouples integrated into heat flow sensors (Concept Engineering, Old Saybrook, CT, USA) attached to the skin with surgical tape (3M™,Transpore™, St. Paul, MN, USA). Mean skin temperature (MT_{sk}) and mean dry heat loss (H_D) were subsequently calculated using a 9 point weighting of the regional proportions determined by Hardy and Dubois (13). These were as follows: forehead 9.39%, upper arm 9.39%, upper back 11.75%, chest 11.75%, lower back 11.75%, abdomen 11.75%, quadriceps 12.75%, hamstring 12.75%, and front calf 8.72%. Since the head, chest, upper back, upper arm and forearm were not entirely immersed during water immersion, they were not used to calculate MT_{sk} and H_D (24). As such, the following weightings were used to calculate mean skin temperature ($MT_{sk\text{-}im}$) and dry heat loss ($H_{D\text{-}im}$) during water immersion: lower back

20.35%, abdomen 20.35%, quadriceps 22.09%, hamstring 22.09%, and front calf 15.12%. Temperature data were collected using a HP Agilent data acquisition module (model 3497A) at a rate of one sample every 15 seconds and simultaneously displayed and recorded in spreadsheet format on a personal computer with LabVIEW software (Version 7.0, National Instruments, TX, USA). Heart rate was measured continuously using a heart rate monitor (Model FS1, Polar Electro Oy, Kempele, Finland) in combination with a coded transmitter. Heart rate was recorded every 5 minutes during the experimental trials. Measurements of nude body weight were obtained prior to and following each experimental trial using a digital high performance weighing terminal (IND560, Mettler Toledo Inc., Mississauga, ON, Canada). Results were recorded to the nearest 0.01 kg.

Data Analysis

For each trial, T_{re}, T_{es} and MT_{sk} values during the rest period were averaged over the last 5-min. The rates for whole-body heating during exercise [change in (Δ) temperature / exercise time] and core cooling during water immersion (Δ temperature / immersion time) were calculated for both T_{re} and T_{es}. The core cooling rates were calculated from start-immersion temperature to end-immersion temperature for both T_{re} and T_{es}. In addition, the core cooling rates for the first (start immersion temperature - 1°C) and second degree Celsius [(start immersion temperature - 1°C) - 1°C] reductions in temperature were also calculated for T_{re} and T_{es}. The time to reach a temperature of 39.5, 39.0, 38.5, 38.0, 37.5°C during immersion as well as the time

to reach the nadir following immersion was calculated for T_{re} and T_{es}. During the immersion period, $MT_{sk\text{-}im}$ and $H_{D\text{-}im}$ were calculated in minute averages. Segmental linear regression analysis was conducted in order to analyze the break point (lag) period (in minutes) at which core temperature (T_{re} and T_{es}) decreased following the start of immersion. The two slope method was employed using Graph Pad Prism software v5.0 (GraphPad Software Inc., La Jolla, CA, USA).

Statistical Analysis

All analyses were performed using the statistical software package SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA). Physical characteristics of the two experimental groups (High and Low A_D/LBM) were analyzed using independent sample t-tests. A 2x2 mixed model Analysis of Variance (ANOVA) was used to analyze the data between groups (levels: High and Low A_D/LBM) and between conditions (levels: 2°C and 26°C) for the following dependent variables: core temperatures (T_{re} and T_{es}), MT_{sk}, and heart rate (time points: rest, start-exercise, end-exercise, start-immersion, end-immersion and nadir). Further, exercise and immersion times, weight loss, heating rates (T_{re} and T_{es}), cooling rates (overall, first and second degree decrease in T_{re} and T_{es}), segmental regression at the start of immersion and the time to reach T_{re} and T_{es} nadir during recovery following immersion were also analyzed employing this method. A three-way mixed model ANOVA was used to analyze $MT_{sk\text{-}im}$ and $H_{D\text{-}im}$ during the immersion period. The analysis was conducted using repeated factors of time (i.e., levels: 0, 1, 2, 3, 4, 5, 6 min etc. to last common point at end immersion) and water temperature (levels: 2°C and 26°C) and the non-repeated factor of

A_D/LBM (Levels: High and Low A_D/LBM). Similar analysis was conducted with the time to reach a core temperature of 39.5, 39.0, 38.5, 38.0 and 37.5°C during immersion for both T_{re} and T_{es}. The level of statistical significance was set at 0.05 and alpha level was adjusted during multiple comparisons in order to maintain the rate of Type I error at 5% during the Holm–Bonferroni *post hoc* analysis.

RESULTS

Physical characteristics

By design, there were significant differences between groups for A_D/LBM ($P < 0.001$). There were also significant differences in lean body mass ($P = 0.001$) and % body fat ($P = 0.039$) between groups. No differences were found in terms of body mass ($P = 0.256$), absolute fat mass ($P = 0.217$), body surface area ($P = 0.302$), body surface area-to-mass ratio ($P = 0.174$) or relative maximum oxygen consumption ($P = 0.920$) between groups (Table 1).

Exercise Period

There were no differences between groups or conditions in resting T_{re}, T_{es}, MT_{sk} and HR prior to the start of exercise (all $P > 0.05$; Table 2). No differences were observed in the exercise time taken to reach the end-exercise T_{re} of 40.0°C between groups ($P = 0.836$) and between conditions ($P = 0.638$). Exercise times were similar between groups for both the CWI (High A_D/LBM: 41.4 ± 10.0 min vs. Low A_D/LBM:

41.9 ± 10.0 min) and TWI (High A_D/LBM: 43.6 ± 6.3 vs. Low A_D/LBM: 41.7 ± 8.5 min) conditions. As such, the rate of T_{re} increase (heating rate) was similar between groups (P = 0.661) and between conditions (P = 0.432). Similarly, no differences in the rate of T_{es} was measured between groups (P = 0.933) and between conditions (P = 0.543) (Table 3). Exercise also resulted in similar T_{re} increases from rest for both groups (P = 0.795) and conditions (P = 0.573). Increases in T_{re} during the CWI trial were 2.96 ± 0.34°C vs. 3.02 ± 0.16°C and increases during the TWI trial were 3.03 ± 0.38°C vs. 3.03 ± 0.17°C for the High and Low A_D/LBM groups respectively. Similarly for T_{es}, increases in temperature during exercise were similar for both groups (P = 0.595) and conditions (P = 0.678). Increases in T_{es} during the CWI trial were 3.43 ± 0.56°C vs. 3.12 ± 0.64°C and increases during the TWI trial were 3.17 ± 0.58°C vs. 3.24 ± 0.63°C for the High and Low A_D/LBM groups respectively. End-exercise MT_{sk} was similar between groups (P = 0.161) and between conditions (P = 0.700) (Table 2). End-exercise heart rate was elevated above resting values to a similar magnitude for both groups (P = 0.874) and treatment conditions (P = 0.057) (Table 2).

Immersion Period

Core temperature (T_{re} and T_{es}) remained significantly elevated above baseline resting levels prior to the start of immersion. There were no differences in the core temperature response between groups (T_{re}, P = 0.248; T_{es}, P = 0.384) and conditions (T_{re}, P = 0.712; T_{es}, P = 0.481) at the start of immersion (Table 2). No differences in pre-immersion heart rate were observed between groups (P = 0.742) or treatment conditions (P = 0.209) (Table 2). Water immersion resulted in similar decreases in T_{re} for both groups (P = 0.243) and

conditions (P = 0.845). Decreases in T_{re} during CWI were 2.50 ± 0.23°C vs. 2.58 ± 0.19°C and decreases during TWI were 2.51 ± 0.34°C vs. 2.60 ± 0.05°C for the High and Low A_D/LBM groups respectively. This was expected given that exit temperature was defined as T_{re} = 37.5°C. However, differences in the decrease in T_{es} were observed between conditions (P < 0.001) but not between groups (P = 0.627), with a greater T_{es} decrease observed during CWI. Decreases in T_{es} during CWI were 4.02 ± 1.19 vs. 4.12 ± 0.89°C while decreases during TWI were 2.60 ± 0.41 vs. 2.76 ± 0.55°C for the High and Low A_D/LBM groups respectively. Immersion times were significantly different between groups (*P* = 0.001) and treatment conditions (*P* < 0.001). Immersion times during the 2°C trial were 11.1 ± 5.4 min vs. 19.7 ± 7.7 min for the High and Low A_D/LBM groups respectively. Further, immersion times during the 26°C trial were 29.3 ± 14.5 min vs. 52.1 ± 20.7 min for the High and Low A_D/LBM groups respectively. The time (in min) taken to cool to a T_{re} of 39.5°C, 39.0°C, 38.5°C, 38.0°C and 37.5°C are presented in Figure 1. Responses were significantly different between groups (all P < 0.05) as well as conditions (all P < 0.05), where the time taken to reach the aforementioned temperature points was less during CWI compared to TWI; and individuals with a Low A_D/LBM taking longer to reach all temperature points relative to those with a High A_D/LBM.

Overall T_{re} cooling rates were significantly different between groups (P = 0.005) as well as conditions (P < 0.001). Greater T_{re} cooling rates were observed during CWI relative to TWI; and individuals with a Low A_D/LBM had slower overall T_{re} cooling rates compared to those with a High A_D/LBM. Similar differences were

observed during first degree T_{re} cooling rates between groups ($P = 0.006$) as well as conditions ($P = 0.001$). In contrast, no differences in second degree T_{re} cooling rates were were measured between groups ($P = 0.136$). However, second degree T_{re} cooling rates were different between conditions ($P < 0.001$), with faster second degree T_{re} cooling rates observed during CWI (Table 3).

Overall T_{es} cooling rates were significantly different between groups ($P = 0.002$) and conditions ($P < 0.001$) with faster T_{es} cooling rates observed during CWI relative to TWI; and individuals with a Low A_D/LBM having slower overall T_{es} cooling rates compared to those with a High A_D/LBM (Table 3). Further, differences in first degree T_{es} cooling rates were observed between conditions ($P < 0.001$). While a difference between groups ($P = 0.001$) was measured for the CWI condition ($P < 0.001$) there were no differences between groups for the TWI condition ($P = 0.786$). Significant differences in second degree T_{es} cooling rates were measured between conditions ($P < 0.001$) but responses did not differ between groups ($P = 0.067$).

The break point (lag) period (in minutes) at which T_{re} started to decrease following the start of immersion was significantly different between groups ($P = 0.002$), with a greater lag time observed in the Low A_D/LBM group. However, no differences were found in the lag time at the start of immersion between conditions ($P = 0.855$). The T_{re} lag period during CWI was 2.34 ± 2.43 min vs. 5.85 ± 2.80 min for the High and Low A_D/LBM groups, respectively. The lag period during TWI was comparable to CWI (3.16 ± 1.55 min vs. 4.74 ± 2.64 min for High and Low A_D/LBM groups, respectively). In contrast, no differences in T_{es} break point

were measured between groups (P = 0.163) or conditions (P = 0.935). The T_{es} lag period during CWI was 0.96 ± 1.48 min vs. 1.48 ± 0.38 min for the High and Low A_D/LBM groups, respectively with similar responses measured in the TWI condition (1.02 ± 0.70 min vs. 1.48 ± 1.33 min for High and Low A_D/LBM groups, respectively).

There was no difference in MT_{sk} prior to the start of immersion between groups (P = 0.760) and conditions (P = 0.177) (Table 2). Reductions in $MT_{sk\text{-}im}$ became gradually less as a function of time (P < 0.001) and no differences between groups were observed (P = 0.094), however differences were found between conditions (P < 0.001) where $MT_{sk\text{-}im}$ was lower during CWI after the first minute of immersion.

At the start of immersion, there was a marked increase in $H_{D\text{-}im}$ followed by gradual reduction as a function of time throughout the immersion period (P < 0.001). No differences in $H_{D\text{-}im}$ were observed between groups (P = 0.826). Conversely, differences in $H_{D\text{-}im}$ were found between conditions (P < 0.001), where $H_{D\text{-}im}$ was higher during CWI relative to TWI (Figure 2). When $H_{D\text{-}im}$ was averaged over the entire immersion period (minute averages), there were no differences between groups (P = 0.137), however there were differences between conditions (P < 0.001), where the average $H_{D\text{-}im}$ was higher during CWI. Average $H_{D\text{-}im}$ for the 2°C trial was 1217.9 ± 406.1 W/m^2 vs. 969.6 ± 238.9 W/m^2 for the High and Low A_D/LBM groups

respectively. Further, average $H_{D\text{-}im}$ during the 26°C trial was 471.8 ± 213.6 W/m^2 vs. 392.8 ± 180.5 W/m^{2}for the High and Low A_D/LBM groups respectively.

Post-immersion Period

No differences in T_{re} were observed between groups (P = 0.839) and conditions (P = 0.202) at the end of immersion. This was expected given that exit temperature was defined as a T_{re} of 37.5°C. The corresponding changes in T_{es} were different between conditions such that T_{es} at end of immersion during CWI was significantly lower (P < 0.001). However, T_{es} was similar between groups (P = 0.244) at the end of immersion. Heart rate at the end of immersion was similar between groups (P = 0.387) but was lower during TWI as compared to CWI (P = 0.010) but not different between groups (Table 2).

There were no differences in the T_{re} nadir following immersion between groups (P = 0.259), however differences were found between conditions (P < 0.001), whereas the T_{re} nadir following CWI was lower (Table 2). Although the T_{re} nadir between groups was similar, the time (in min) to reach the T_{re} nadir was significantly different between groups (P = 0.037) and conditions (P < 0.001). During both CWI and TWI, the time to reach T_{re} nadir was greater for the Low relative to the High A_D/LBM groups, however, the time to reach T_{re} nadir for both groups were reduced in the TWI condition (CWI: 20.1 ± 7.9 min vs. 13.9 ± 6.7 min and TWI: 8.3 ± 6.5 min vs. 4.9 ± 4.8 min). Similarly, T_{es} nadir was different between conditions (P < 0.001), however no differences between groups (P = 0.727) were observed.

Changes in body mass as assessed pre- and post-trial were similar between groups (P = 0.346) and conditions (P = 0.284). The change in body mass during the 2°C trial was 1.38

± 0.31 kg vs. 1.59 ± 0.51 kg for the High and Low A_D/LBM groups respectively. A similar magnitude of change was observed during the 26°C trial, where reductions in body mass were 1.53 ± 0.30 kg vs. 1.61 ± 0.34 kg for the High versus Low A_D/LBM groups, respectively.

DISCUSSION

In accordance with our hypothesis, we show that A_D/LBM influences core cooling rates during both CWI and TWI following exercise-induced hyperthermia (T_{re} of 40°C). Individuals with a High A_D/LBM had a ~1.7-fold greater overall rectal cooling rate relative to those individuals with a Low A_D/LBM during both CWI and TWI. Further, overall rectal cooling rates during CWI were ~2.7-fold faster than during TWI for both the High and Low A_D/LBM groups. Further, the time-to-reach a rectal temperature of 39.5, 39.0, 38.5, 38.0 and 37.5°C was greater in the low versus high A_D/LBM group with CWI producing the fast cooling times for both groups relative to TWI.

Death related to EHS is preventable through early recognition and rapid on-site cooling with cold water immersion (3, 6, 8). Growing evidence suggests that CWI (i.e., < 10°C) is the most efficacious treatment modality for EHS patients (8) with 2°C ice-water immersion yielding some of the highest overall cooling rates, especially for the second degree decrease in core temperature (24). This treatment modality has a proven clinical track record with 100% survivability if the cooling is

initiated within 5 minutes (7). The effectiveness of CWI is mainly attributed to high levels of conductive and convective heat loss between the skin surface and water, where the colder the water, the greater the skin-water thermal gradient to facilitate heat transfer (24). Despite the proven clinical benefits of CWI, some experts continue to argue against the use of CWI in the treatment of EHS patients (28). The premise of their argument is that when peripheral circulation is viable (patient is not under circulatory collapse), a temperate water bath of ~26°C should be employed (7, 28), as it minimizes patient discomfort and the potential adverse effects (cold shock response, elevated shivering and marked vasoconstriction reducing core cooling rate, cold injury, etc.) associated with CWI while at the same time providing comparable core cooling rates to that of CWI (7, 28). Their findings have led to the misguided conclusion that temperate water immersion should be employed in the treatment of hyperthermic victims.

It is important to note that the evidence in support of the aforementioned argument is primarily based on a study by Taylor et al. (28) who showed that temperate water (26°C) provided similar esophageal cooling rates to that measured in 14°C cold water (0.71 and 0.88 °C/min for 26 and 14°C water immersion, respectively) based on the time it took to reduce esophageal temperature to 37.5°C. However, the authors failed to consider that while esophageal temperature was reduced to 37.5°C in less than 3 minutes, a significant amount of residual heat remained in the deep visceral organs as evidenced by a corresponding rectal temperature of ~39-39.5°C at that time (7). From a clinical perspective, employing TWI would have a detrimental effect on the survival of EHS patients as the length of time core temperature remains above critical values is the main criteria determining the survival of

individuals with EHS (3, 14). Our study clearly demonstrates that CWI provides rectal cooling rates that far exceed TWI by ~2.7-fold for individuals in both the High and Low A_D/LBM groups. This is consistent with findings of Proulx et al. (24), who reported that rectal cooling rates during 2°C CWI (0.35°C/min) were almost two times greater than during water temperatures of 8, 14 and 20°C (0.19, 0.15 and 0.19°C/min, respectively). Further, overall esophageal cooling rates were significantly greater during CWI as compared with TWI for both the High and Low A_D/LBM groups. Our results demonstrate that CWI cools both rectal and esophageal temperature more rapidly than during TWI. From a clinical perspective, a more rapid attenuation of both visceral (represented by rectal temperature) and central nervous system (represented by esophageal temperature) is critical to maximizing the chances of surviving exertional heatstroke (3, 12, 26, 30).

Our results support the suggestion by Lemire et al. (22) that A_D/LBM may be an important physical determinant of whole-body cooling rate during water immersion in hyperthermic individuals. This is evidenced by our observation that individuals with a High A_D/LBM had a ~1.7-fold greater overall rectal cooling rate relative to those with Low A_D/LBM during both CWI and TWI. Moreover, we show that differences in A_D/LBM are more pronounced with a warmer water immersion temperature, as there was an 8.6 min immersion time difference between groups during CWI (11.1 ± 5.4 vs. 19.7 ± 7.7 min for High and Low A_D/LBM, respectively) and a 22.8 min difference between groups during TWI (29.3 ± 14.5 vs. 52.1 ± 20.7 min for High and Low A_D/LBM, respectfully). These results provide strong support

to the previous suggestions (7) that CWI can minimize variations in core cooling caused by large differences in physical characterisitics.

The differences in core temperature cooling rates observed between the High and Low A_D/LBM groups can be largely explained by differences in LBM as a significant (~13 kg) difference in LBM between High (63.29 kg) and Low (75.96 kg) groups was observed. It is important to note that there were no differences between groups in body surface area or A_D/M. While a ~ 7% (High: 20.24 ±7.64 % vs. 13.26 ± 6.31 %) difference in body adiposity was observed between High and Low A_D/LBM groups, previous studies show that moderate differences in adiposity do not affect core cooling rates in hyperthermic individuals (21, 22). Regardless, we show that core cooling rates were greater in the High A_D/M group despite a greater adiposity. In light of marked differences in LBM between groups, it is likely that differences in core cooling rate between groups are attributed to differences in the residual heat load in muscle. Previous studies show that a significant residual heat load remains in muscle tissue following dynamic exercise in the heat (17, 18). For example, Kenny et al. (18) demonstrated that only 53% of the heat stored during 60 min of exercise was dissipated after 60 min of recovery, with the majority of residual heat stored in muscle tissue. This is supported in part by our observation of a greater lag time in the decrease in rectal temperature at the start of immersion in individuals with a Low A_D/LBM relative to individuals with a High A_D/LBM.

Practical considerations

Current guidelines of the treatment of EHS patients suggest that cooling modalities must achieve a rectal temperature cooling rate exceeding 0.1-0.2ºC/min when cooling begins immediately and should be no less than 0.15ºC/min if cooling is delayed (8). Our results suggest that CWI effectively surpasses this standard even in the presence of large physical differences, achieving overall rectal cooling rates of 0.27 and 0.16°C/min for the High and Low A_D/LBM groups, respectively. On the other hand, rectal cooling rates during TWI were markedly lower at 0.10 and 0.06°C/min for individuals with a High and Low A_D/LBM, respectfully. It is noteworthy that individuals with a High A_D/LBM just met the minimum cooling guidelines of 0.1°C/min while individuals in the Low A_D/LBM group fell short of this lower limit. Taken together, our findings clearly demonstrate that TWI cannot provide sufficient cooling to meet the current cooling guidelines for individuals of all body morphologies, especially when treatment is delayed and cooling modalities with higher core cooling rates (0.15ºC/min) are recommended.

An important consideration when employing CWI is ensuring that rectal temperature is measured continuously during the immersion period in order to prevent excessive overcooling. Previous studies show that there is a marked afterdrop in core temperature following CWI when hyperthermic individuals are immersed in cold water to near resting temperatures (11, 24, 25). This core temperature afterdrop has been attributed primarily to the fact that the heat lost during immersion is greater

than the heat gained during exercise (11, 25). Further, there is a delayed response of conductive and convective heat transfer from the periphery to the core during CWI (11). In (11). In order to avoid excessive afterdrop following CWI, safe cooling limits have been been proposed whereby individuals should be removed from the water bath when T_{re} reaches 38.6°C to ensure the removal of 100% of the heat gained by exercise while reducing the risk of hypothermia (11, 25). With respect to the latter, we observed a similar nadir (after-drop T_{re} of 36.3 and 36.0°C for individuals with a High and Low A_D/LBM, respectfully) to that reported by Proulx et al. (24) following 2°C CWI (35.7°C). Thus, we confirm the previous recommendations (11, 25) that a similar exit temperature be used irrespective of physical differences.

Summary

In summary, we show that individuals with a High A_D/LBM had a ~1.7-fold greater overall rectal cooling rate compared with those with a Low A_D/LBM during both CWI and TWI following exercise-induced hyperthermia. Furthermore, overall rectal cooling rates were ~2.7-fold greater during CWI compared with TWI for both the High and Low A_D/LBM groups. Taken together, we show that individuals with a Low A_D/LBM have a reduced rectal cooling rate and take longer to cool than those with a High A_D/LBM during both CWI and TWI. However, CWI provides the most effective cooling treatment for all EHS patients irrespective of physical differences as it minimizes the time patients remain severly hyperthermic.

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Table 1. Physical characteristics for the High (n = 10) and Low (n = 10) A_D/LBM groups.

	High A_D/LBM	**Low A_D/LBM**
Age (years)	29 ± 9	29 ± 7
$VO_{2\ max}$ (ml/kg/min)	56.31 ± 7.42	55.93 ± 9.02
Height (cm)	179.9 ± 7.6	181.5 ± 7.5
Weight (kg)	80.65 ± 15.72	88.35 ± 13.53
A_D (m^2)	2.00 ± 0.21	2.09 ± 0.18
A_D/M (m^2)	251.56 ± 23.37	238.85 ± 16.18
Body Fat (%)	20.24 ± 7.64	13.26 ± 6.31*
Fat Mass (kg)	17.35 ± 9.57	12.39 ± 7.69
LBM (kg)	63.29 ± 6.65	75.96 ± 6.92 *
A_D/LBM (cm^2/kg)	315.57 ± 7.91	275.58 ± 8.59 *

Values are mean ± standard deviation (SD). $VO_{2\ max}$ = maximum oxygen uptake, A_D = body surface area, A_D/M = body surface area-to-body mass ratio, LBM = lean body mass, A_D/LBM = body surface area-to-lean body mass ratio.*, indicates values significantly different between groups (High vs. Low A_D/LBM; $p < 0.05$).

Table 2. Rectal temperature, esophageal temperature, mean skin temperature and heart rate for the High and the Low A_D/LBM groups during both cold (2°C) and temperate (26°C) water immersion.

	CWI (2°C)		TWI (26°C)	
	High A_D/LBM	**Low A_D/LBM**	**High A_D/LBM**	**Low A_D/LBM**
Rectal Temperature (°C)				
Rest	36.84 ± 0.26	36.86 ± 0.23	36.75 ± 0.31	36.86 ± 0.24
Start Exercise	36.94 ± 0.29	36.98 ± 0.22	36.84 ± 0.26	36.95 ± 0.21
End Exercise	39.90 ± 0.11	40.00 ± 0.09	39.87 ± 0.20	39.97 ± 0.09
Start Immersion	39.97 ± 0.22	40.05 ± 0.21	39.99 ± 0.33	40.08 ± 0.05
End Immersion	37.47 ± 0.03	37.47 ± 0.04	37.48 ± 0.02	37.48 ± 0.03
Nadir	36.32 ± 0.50	35.97 ± 0.88	37.24 ± 0.17 †	37.19 ± 0.17 †
Esophageal Temperature (°C)				
Rest	36.79 ± 0.24	36.66 ± 0.17	36.67 ± 0.38	36.67 ± 0.16
Start Exercise	36.85 ± 0.29	36.80 ± 0.23	36.72 ± 0.30	36.67 ± 0.23
End Exercise	40.26 ± 0.41	39.92 ± 0.57	39.86 ± 0.53	39.91 ± 0.77
Start Immersion	39.97 ± 0.32	39.52 ± 0.56	39.59 ± 0.40	39.70 ± 0.67
End Immersion	35.95 ± 1.14	35.40 ± 0.77	37.00 ± 0.32 †	36.94 ± 0.49 †
Nadir	35.14 ± 0.89	35.04 ± 0.66	36.87 ± 0.37 †	36.81 ± 0.48 †
Skin Temperature (°C)				
Rest	34.94 ± 0.54	35.28 ± 0.53	34.65 ± 1.00	35.27 ± 0.22
End Exercise	37.46 ± 0.42	37.35 ± 0.51	37.59 ± 0.56	37.11 ± 0.65
Start Immersion	37.51 ± 0.53	37.63 ± 0.54	37.69 ± 0.45	37.71 ± 0.56
End Immersion	10.25 ± 3.72	9.25 ± 3.04	26.85 ± 1.22 †	26.19 ± 1.50 †
Heart Rate (bpm)				
Rest	68.70 ± 9.75	70.20 ± 8.24	68.40 ± 6.70	72.70 ± 9.33
End Exercise	185.30 ± 12.38	180.60 ± 13.77	183.60 ± 11.62	189.90 ± 9.42
Start Immersion	144.10 ± 5.26	142.50 ± 12.12	146.50 ± 7.12	145.50 ± 12.76
End Immersion	86.88 ± 8.90	79.90 ± 16.07	76.75 ± 12.75 †	73.80 ± 12.72 †

Values are mean ± standard deviation (SD). *, indicates values significantly different between groups (High vs. Low A_D/LBM; $p < 0.05$). †, indicates values significantly different between conditions (2 vs. 26°C; $p < 0.05$).

Table 3. Rectal and esophageal heating and cooling rates (°C/min) for the High and Low A_D/LBM groups during both cold (2°C) and temperate (26°C) water immersion.

	CWI (2°C)		TWI (26°C)	
	High A_D/LBM	**Low A_D/LBM**	**High A_D/LBM**	**Low A_D/LBM**
Rectal Temperature (°C/min)				
Heating Rate	0.07 ± 0.02	0.08 ± 0.02	0.07 ± 0.01	0.08 ± 0.02
Overall Cooling Rate	0.27 ± 0.10	0.16 ± 0.10 *	0.10 ± 0.05 †	0.06 ± 0.02 *†
First Degree Cooling Rate	0.23 ± 0.12	0.11 ± 0.06 *	0.11 ± 0.04 †	0.08 ± 0.04 *†
Second Degree Cooling Rate	0.32 ± 0.12	0.26 ± 0.16	0.17 ± 0.11 †	0.10 ± 0.06 †
Esophageal Temperature (°C/min)				
Heating Rate	0.08 ± 0.02	0.08 ± 0.03	0.08 ± 0.02	0.08 ± 0.03
Overall Cooling Rate	0.40 ± 0.11	0.24 ± 0.10 *	0.11 ± 0.05 †	0.06 ± 0.03 *†
First Degree Cooling Rate	0.56 ± 0.15	0.28 ± 0.07 *	0.29 ± 0.05 †	0.28 ± 0.12 †
Second Degree Cooling Rate	0.70 ± 0.23	0.47 ± 0.18	0.32 ± 0.10 †	0.27 ± 0.15 †

Values are mean ± standard deviation (SD). *, indicates values significantly different between groups (High vs. Low A_D/LBM; $p < 0.05$). †, indicates values significantly different between conditions (2 vs. 26°C; $p < 0.05$).

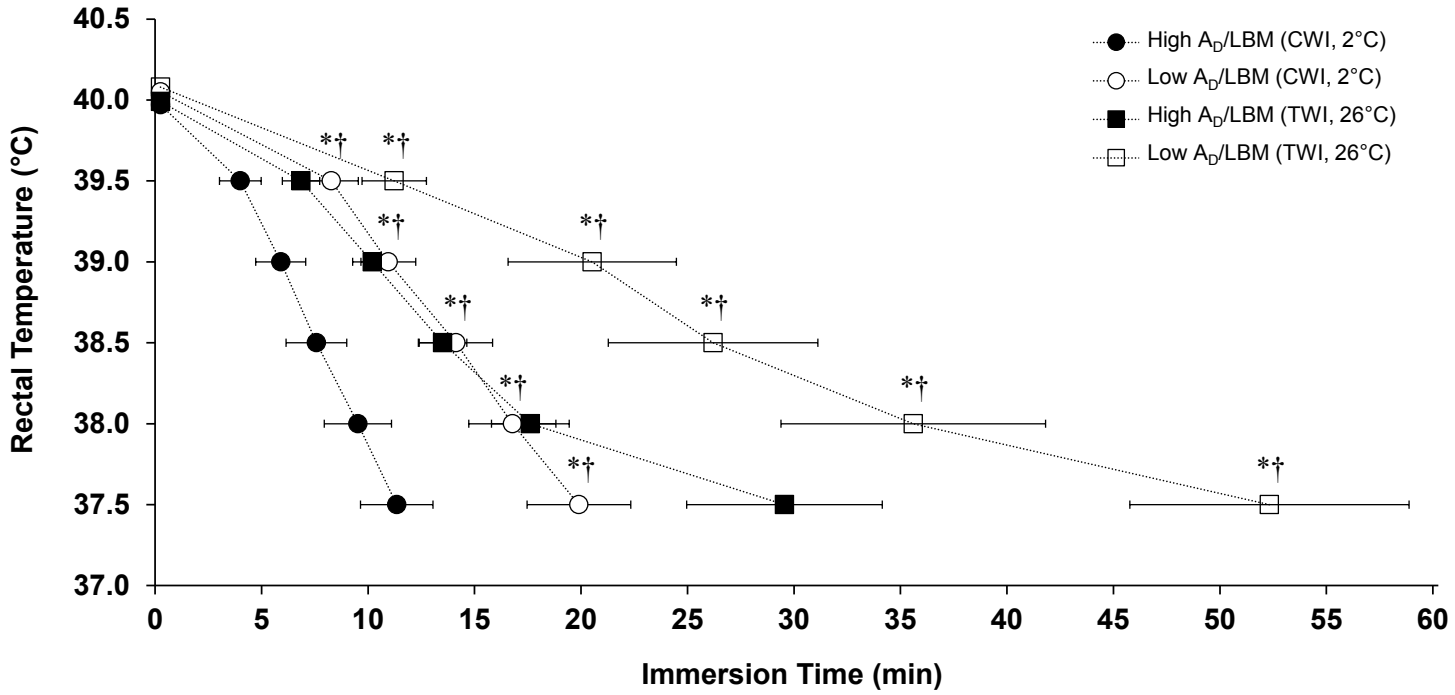

Figure 1. Mean ± standard error (SE) rectal temperature response during cold water immersion (CWI, 2°C) and temperate water immersion (TWI, 26°C) for the High and Low A_D/LBM groups. *, indicates values significantly different between groups (High vs. Low A_D/LBM; $p < 0.05$). †, indicates values significantly different between conditions (2 vs. 26°C; $p < 0.05$).

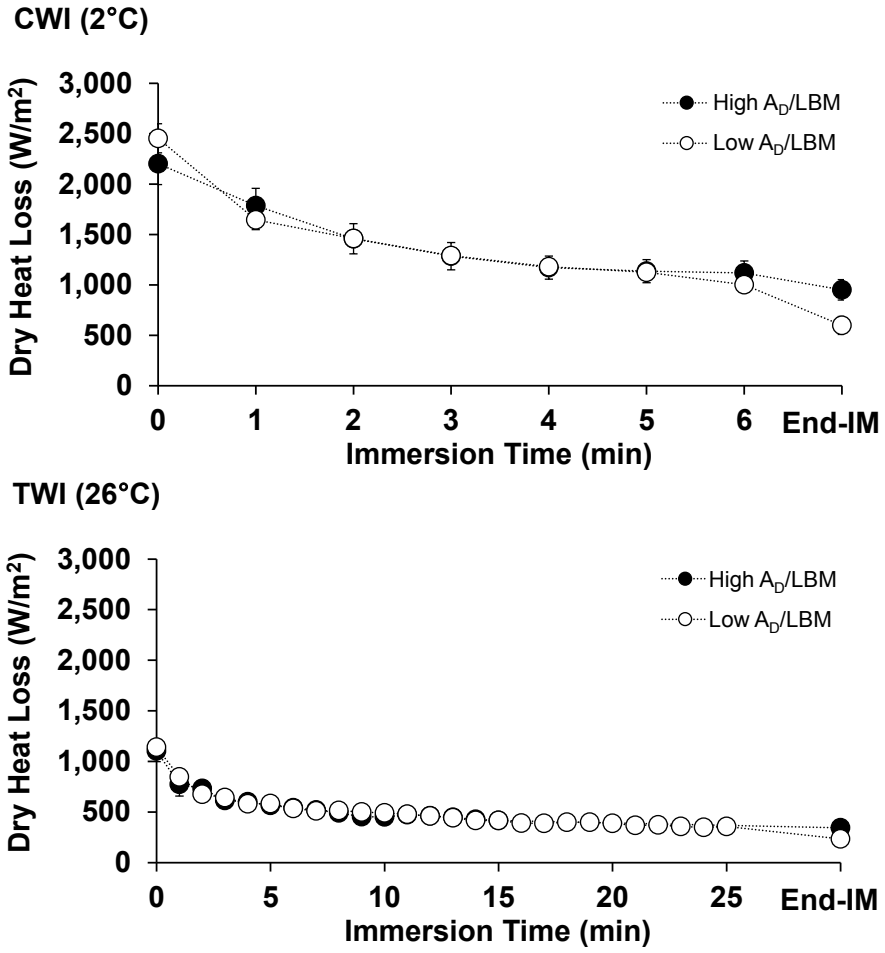

Figure 2. Mean ± standard deviation (SD) dry heat loss (W/m^2) during cold water immersion (CWI, 2°C, top panel) and temperate water immersion (TWI, 26°C, bottom panel) for the High and Low A_D/LBM groups.

PART THREE: GENERAL CONCLUSIONS OF THE THESIS

This thesis work was directed at evaluating the effects of differences in body surface area-to-lean body mass ratio (A_D/LBM) on core temperature cooling rates during cold water immersion (CWI, 2°C) and temperate water immersion (TWI, 26°C) following exercise-induced hyperthermia. In order to evaluate these effects, twenty male participants were divided into 2 groups; High A_D/LBM (315.6 ± 7.9 cm^2/kg, n = 10) and Low A_D/LBM (275.6 ± 8.6 cm^2/kg, n = 10). On two separate occasions, participants ran on a treadmill in the heat (40.0°C, 20% relative humidity) wearing an impermeable rain suit until rectal temperature reached 40.0°C (~45 min). Following exercise and a 5-min transition period where participants sat upright, participants were immersed up to the nipples (arms remained out of the water) in either a cold (2ºC) or temperate (26ºC) circulated water bath until rectal temperature returned to 37.5ºC.

In accordance with our hypothesis, individuals rendered severely hyperthermic during prolonged exercise in the heat with a High A_D/LBM (315 cm^2/kg) had a ~1.7-fold greater overall rectal cooling rate relative to those with Low A_D/LBM (275 cm^2/kg) during both CWI (High: 0.27 ± 0.10 vs. Low: 0.16 ± 0.10°C/min) and TWI (High: 0.10 ± 0.05 vs. Low: 0.06 ± 0.02°C/min). Further, overall rectal cooling rates during CWI were ~2.7-fold greater than during TWI for both the High (CWI: 0.27 ± 0.10 vs. TWI: 0.10 ± 0.05 °C/min) and Low (CWI: 0.16 ± 0.10 vs. TWI: 0.06 ± 0.02°C/min) A_D/LBM groups.

In summary, we demonstrate that A_D/LBM has a profound influence on core cooling rates in hyperthermic individuals during water immersion. Therefore, it is important to consider A_D/LBM when determining the duration of the immersion period. We show that

individuals with a Low A_D/LBM have a reduced core cooling rate relative to those with a High A_D/LBM, and differences in cooling rate are likely attributed to a greater residual heat load stored in muscle tissue. In addition, study findings provide new and important knowledge on the benefits of CWI in the treatment of EHS patients. Results show that CWI provides the most effective cooling treatment irrespective of physical differences (i.e., A_D/LBM) between individuals and that CWI can minimize variations in immersion times attributed to differences in A_D/LBM.

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PART FIVE: APPENDIX

Appendix A: Ethics (REB) Certificate

File Number: H11-09-05 **Date (mm/dd/yyyy):** 01/10/2014

Université d'Ottawa University of Ottawa
Bureau d'éthique et d'intégrité de la recherche Office of Research Ethics and Integrity

Ethics Approval Notice

Health Sciences and Science REB

Principal Investigator / Supervisor / Co-investigator(s) / Student(s)

First Name	Last Name	Affiliation	Role
Glen	Kenny	Health Sciences / Human Kinetics	Principal Investigator
Heather	Wright	Health Sciences / Human Kinetics	Co-investigator
Brian	Friesen	Health Sciences / Human Kinetics	Research Assistant

File Number: H11-09-05

Type of Project: Professor

Title: Whole-body Cooling Following Exercise-induced Hyperthermia: Biophysical Considerations

Renewal Date (mm/dd/yyyy)	Expiry Date (mm/dd/yyyy)	Approval Type
01/04/2014	01/03/2015	Ia

(Ia: Approval, Ib: Approval for initial stage only)

Special Conditions / Comments:
N/A

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File Number: H11-09-05 **Date (mm/dd/yyyy):** 01/10/2014

Université d'Ottawa University of Ottawa
Bureau d'éthique et d'intégrité de la recherche Office of Research Ethics and Integrity

This is to confirm that the University of Ottawa Research Ethics Board identified above, which operates in accordance with the Tri-Council Policy Statement and other applicable laws and regulations in Ontario, has examined and approved the application for ethical approval for the above named research project as of the Ethics Approval Date indicated for the period above and subject to the conditions listed the section above entitled "Special Conditions / Comments".

During the course of the study the protocol may not be modified without prior written approval from the REB except when necessary to remove subjects from immediate endangerment or when the modification(s) pertain to only administrative or logistical components of the study (e.g. change of telephone number). Investigators must also promptly alert the REB of any changes which increase the risk to participant(s), any changes which considerably affect the conduct of the project, all unanticipated and harmful events that occur, and new information that may negatively affect the conduct of the project and safety of the participant(s). Modifications to the project, information/consent documentation, and/or recruitment documentation, should be submitted to this office for approval using the "Modification to research project" form available at:

http://www.research.uottawa.ca/ethics/forms.html

Please submit an annual status report to the Protocol Officer four weeks before the above-referenced expiry date to either close the file or request a renewal of ethics approval. This document can be found at:

http://www.research.uottawa.ca/ethics/forms.html

If you have any questions, please do not hesitate to contact the Ethics Office at extension 5387 or by e-mail at: ethics@uOttawa.ca.

Signature:

Mélanie Rioux
Ethics Coordinator
For Gilles Morier, Acting Director of the Office of Research Ethics and Integrity

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Appendix B: Participant Background Letter and Consent Form

Background information for the participant

Whole-body cooling following exercise-induced hyperthermia: biophysical considerations

Investigators:

Dr. Glen Kenny, Dr. Heather Wright and Brian Friesen

Human and Environmental Physiology Research Unit, School of Human Kinetics,

University of Ottawa, Ottawa, ON, Canada.

Background

The majority of exertional heat stress casualties occur in military operations, industrial work and sporting events where the combination of high ambient air temperatures, elevated relative humidity, and physical exertion can result in core temperature increases to 39.5°C or higher (Hales et al. 1987; Yaqub and Al Deeb 1998). If heat injuries are not recognized and treated immediately, they can potentially result in loss of consciousness, severe tissue damage, organ failure, and even death (Howe and Borden, 2007). The severity of exertional heat strain is especially related to the duration of core temperature elevation (Armstrong et al. 2007; Smith 2005; de Galan and Hoekstra 1995). Therefore, rapid cooling of hyperthermic individuals back to a normal resting core temperature should be the main goal of any treatment strategy (Casa et al. 2005, 2007; Gaffin et al. 2000; Proulx et al. 2003; Smith 2005).

Cold water immersion is currently viewed as the 'gold standard' treatment for hyperthermia (Casa et al. 2007), largely due to heat transfer properties of water. Recently, studies have reported that the interaction between physical characteristics and core temperature in response to cold water immersion differs in individuals rendered hyperthermic. Lemire et al. (2008) showed that core temperature cooling rates were similar between individuals with high (~23%) and low (~13%) percent body fat levels when immersed in 2°C water following exercise-induced hyperthermia. By matching males and females for body surface area to mass ratio,

Lemire et al. (2009) demonstrated that lean body mass was the most important factor in determining core temperature cooling rates following exercise-induced hyperthermia. Lemire et al. (2009) also showed that that core temperature cooling rates in previously hyperthermic females were ~1.7 times faster compared to males while immersed in 2°C water, despite being matched for body surface area to mass ratio and having a greater percent body fatness. As such, Lemire et al. (2009) proposed that the body surface area-to-lean body mass ratio may better explain core cooling variations in hyperthermic individuals.

Purpose

The purpose of the proposed study is to examine the influence of different biophysical determinants, such as lean body mass, body surface area, and body surface area to lean body mass ratio on whole-body cooling rate in hyperthermic individuals.

This study has practical implications for the development and advancement of health and safety guidelines as they relate to heat stress and/or injuries in the military and sporting industries, via the identification of individuals who are more at risk of heat related injuries.

Funding for this research is provided by the Natural Sciences and Engineering Research Council of Canada (NSERC). This research study is part of Dr. Kenny's NSERC funded research program. Portions of the data collected will be used by Mr. Brian Friesen as part of his Master's thesis.

Subject profile

Only healthy (no history of respiratory, metabolic, cardiovascular, blood pressure disease, or of diabetes, and currently not on medication for any of these conditions) male subjects, aged between 18 and 45 years, will be selected for the study. As a subject, you will be asked to participate in one preliminary session and two experimental sessions, to be conducted on different days and separated by a minimum of 48 hours. A total of 40 subjects will be recruited.

Preliminary session

The preliminary session and the experimental sessions will take place at the Human and Environmental Physiology Research Unit (HEPRU) at the University of Ottawa. The time involvement will be approximately 1 hour for the preliminary session. During this preliminary session, all procedures will be reviewed and the experimental equipment to be used in the experiment (i.e. skin and esophageal probes, blood flow monitors, etc.) will be introduced. You will then be asked to complete a *Physical Activity Readiness Questionnaire (Par-Q)*. In addition, you will be asked to read and sign an Informed consent. Following the orientation, height and weight will be measured as well as blood pressure. Body composition will then be measured by hydrostatic weighing and by skinfolds (7 sites). At the end of this session, you will be asked to perform a maximal exercise test (VO_2 max) on a motorized treadmill while oxygen consumption is measured by an automated system. During this test, you will run at a speed in which you are able to maintain comfortably,

while the treadmill inclination is increased by 1% every minute until you choose to stop or until they can no longer run at the required speed.

Experimental sessions

The experimental sessions will begin with an instrumentation period. Once all the equipment and probes (see description below) are in place and functioning, baseline data will be collected at an ambient temperature (Ta) of 25.0ºC for 20 minutes. You will then be dressed with a whole-body nylon suit after which you will enter a thermal chamber (40ºC). There will be a 20-minute habituation period in order for body temperature to stabilize. You will then be asked to run on a treadmill at 60-65% of your pre-determined VO_{2max} until rectal temperature reaches 40.0°C (this will take approximately 30 to 60 minutes), and/or volitional fatigue. Volitional fatigue will be defined as an inability to maintain the required exercise intensity and/or a verbal manifestation from the participant to stop. You will need to reach a core temperature of 39.5°C to be included in the data analyses. The test will, however, be terminated should you experience any distress or if the research coordinator feels that you are in distress.

Following the exercise, the nylon suit will be removed. You will then be immersed to the shoulders in a recumbent position, in a circulating water bath (Jacuzzi, J-315, Advanced Spas, OH, USA) controlled at either 2°C or 26°C, (based on pre-trial randomization). You will remain in the circulating water bath until your core temperature is reduced to 37.5°C. Although we cannot provide a precise indication of the immersion time, you should be aware that the immersion time should be on average no greater than 45 min (for the 26°C water

temperature). You can also expect that water immersion may be as short as 5 minutes (for the 2°C water temperature). Therefore, it is important for you to understand that these times vary with lean body mass, percentage of body fat, shivering capacity, etc. However, the colder water temperature will result in significantly shorter immersion periods. Given that these are novel experiments using a revised protocol, we cannot provide precise information. You should be reminded that you may exit the water bath at any time should you feel unable to complete the trial. Once you have achieved the designate exit core temperature of 37.5°C, you will then exit the water, during which time your core temperature will be monitored for a minimum of 30 minutes. Measurements will continue until the researchers feel that you have fully recovered to pre-trial conditions. You will be informed at the beginning of each trial what water temperature will be used during the cooling period.

Please note that you will be asked to abstain from alcohol and severe or prolonged physical activities for at least 12 hours prior to all sessions. It is highly recommended that you avoid eating for at least two hours before the trial. You are asked to ensure that you be properly hydrated by drinking at least 100 mL every hour awake prior to the experimental trials.

Esophageal probe: In order to monitor central body temperature, a flexible esophageal temperature probe (2 mm in diameter) will be inserted through one of your nostril, while you swallow sips of water. The tip of the probe, once fully inserted in your esophagus

(swallowing tube), will rest at the level of the heart. There can be mild discomfort and mild gagging reflex from swallowing the probe. However, this sensation soon passes.

Rectal probe: A flexible probe will be inserted through the anus into the rectum (10 cm). This probe provides us with an indication of the accumulated heat storage in the core. You should be aware that there is some risk associated with the insertion of a rectal probe. With the insertion, there is a risk of perforation of the rectum, and this may cause some discomfort and minor irritation. However, proper instruction will be given to you on the placement of the rectal probe to ensure your safety and comfort. You will be responsible for the insertion of this probe.

Skin probes: Twelve skin probes will be taped to the skin surface with hypoallergenic tape. These probes give an indication of skin temperature and heat loss from the skin surface. Some hair may need to be shaved (by the use of a disposable razor) in order to secure the probes adequately to the skin surface. Some discomfort may be experienced upon removing the tape.

Blood pressure: Blood pressure will only be monitored before and after the exercise period. Blood pressure will be monitored at the brachial artery manually with a sphygmomanometer and a stethoscope, as well as with an automated blood pressure cuff (Welch Allyn ABPM 6100) at pre-selected intervals.

Blood flow: A flexible laser probe will measure skin blood flow non-invasively at the mid-forearm. This measuring device does not result in any discomfort or residual medical effects.

Oxygen consumption: An automated metabolic cart (MOXUS) will be used to assess oxygen consumption during the graded exercise testing during the preliminary session and during resting and recovery periods of the experimental sessions. The participants will be required to wear a breathing valve connected to the metabolic cart and a nose plug for the majority of the study.

Heart rate: Heart rate will be monitored by a strap placed around the chest (Polar Vantage heart rate monitor).

Risks and discomforts

All research staff are trained and CPR, and in the event of a health related emergency, we have emergency phones located in the laboratory for immediate contact with University emergency response (University Protection Office).

You should be aware that there are inherent physical risks associated with any form of exercise. There is essentially no major risk for young, healthy, active people while performing the submaximal exercises. Some effects of maximal exercise testing are nausea, dizziness, fainting, abnormal blood pressure, chest pain and leg cramps. The 'Guidelines for Graded Exercise Testing and Exercise Prescription' (by the American College of Sports Medicine) indicate that for men under 40 years of age and women under 50 years of age, with no symptoms or risk factors for cardiovascular disease, the presence of a physician during the test is not required.

The incidence of cardiac arrest during maximal exercise tests is 1 in 10 000 tests. You may stop at any time during these tests. All tests will be conducted under standardized conditions for human exercise experiments as laid out by the Canadian Society for Exercise Physiology and the American College of Sports Medicine.

Perforation of the esophagus or oral or nasal cavities, as well as the rectum can occur during insertion of the esophageal and rectal probes (potentially causing inflammation and infection). However, such an incident is very rare and no such incident has ever occurred in this laboratory. The risk of transmission of infectious disease is negligible as each subject has his own sterile probes that will be disposed of once all tests have been completed. There is also some risk of skin irritation and rash associated with the taping of the skin probes.

There are also certain risks that accompany a marked elevation in core temperature. These include: headache, extreme weakness, dizziness, nausea, hyperventilation, hypotension, confusion, diarrhoea, vomiting and loss of consciousness. During all experimental protocols, you will be monitored closely by the research assistant. These risks will, however, be minimized by terminating the exercise at the first sign of distress and cooling the individual immediately. Further, core body temperatures will be recorded and examined continuously during the experimental trials, and exercise will be terminated if you reach 40.0°C rectal temperature. Additionally, during the experimental protocols, a circulating cold water bath will be available if needed to rapidly cool you. If you become light headed or dizzy, exercise will be terminated and a mat will be readily available, in an adjacent room maintained at a comfortable ambient temperature, where you will be laid in

the supine position, cooled with cold towels, and given a commercially available sports drink (Gatorade®) in order to rehydrate and maintain blood sugar.

Sudden whole-body cold water immersion can evoke an increase heart rate, a reflex inspiratory gasp, and uncontrollable hyperventilation (increase of depth and frequency of breathing). These responses will be experienced, to some degree, during the immersions at 2°C. However, these cold shock responses will be attenuated by a simple two-stage immersion procedure involving immersion to the waist for 30 seconds before full immersion to the shoulders. Although there is a risk of hypothermia following the immersion, this is rather unlikely since you will be removed from the water when your core temperature reaches 37.5°C. The sudden drop in body temperature may cause shivering, induce numbness to the extremities, and may induce some temporary loss of motor control. You may experience some discomfort or pain as the fingers and toes cool. In order to minimize the initial shock of immersion and the residual pain and numbness felt at the extremities (non-freezing cold injuries) during the early stages of immersion, you will be wearing neoprene gloves and boots during each immersion. You shouldn't feel cold or numbness until several minutes after exposure to the water.

Anonymity and Confidentiality

Anonymity is ensured throughout all aspects of this research study. All data will be presented in pooled form and all raw data will be stored under alphanumeric codes in computer memory. All data will be kept in the Human and Environmental Physiology Research Unit (HEPRU) which is protected by controlled access which is restricted to the investigators. The data will be kept for a period of 10 years post-publication. No records bearing your name will leave the institution. You will not be identified in any reports or publications. You are encouraged to request and discuss the results of the experimental trials at any time. The results of the preliminary session (Body composition and VO_{2max} test) will be available to the participant upon completion of the study.

For the entire duration of the study, it is fully understood that you may refuse to participate or withdraw from the study at any time, without question or prejudice.

INFORMED CONSENT OF PARTICIPANT

Research involving human subjects requires written consent of the participants.

I, _____, hereby volunteer to participate as a subject in the study entitled "Whole-body cooling following exercise-induced hyperthermia: biophysical considerations." I have read the information presented in the above background information and I have had the opportunity to ask questions to the investigators. I understand that my participation in this study, or indeed any research, may involve risks that are currently unforeseen.

I recognize that there will be no direct benefit to me from my participation in this study (besides receiving an aerobic fitness and body composition evaluation).

I have been given a copy of this Background Letter and Consent Form for me to keep.

Study A:

Signature of Participant: _____ Date: _____

Signature of Researcher: _____ Date: _____