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Review

Cardiovascular adaptations supporting human exercise-heat acclimation

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ABSTRACT

This review examines the cardiovascular adaptations along with total body water and plasma volume adjustments that occur in parallel with improved heat loss responses during exercise-heat acclimation. The cardiovascular system is well recognized as an important contributor to exercise-heat acclimation that acts to minimize physiological strain, reduce the risk of serious heat illness and better sustain exercise capacity. The upright posture adopted by humans during most physical activities and the large skin surface area contribute to the circulatory and blood pressure regulation challenge of simultaneously supporting skeletal muscle blood flow and dissipating heat via increased skin blood flow and sweat secretion during exercise-heat stress. Although it was traditionally held that cardiac output increased during exercise-heat stress to primarily support elevated skin blood flow requirements, recent evidence suggests that temperature-sensitive mechanisms may also mediate an elevation in skeletal muscle blood flow. The cardiovascular adaptations supporting this challenge include an increase in total body water, plasma volume expansion, better sustainment and/or elevation of stroke volume, reduction in heart rate, improvement in ventricular filling and myocardial efficiency, and enhanced skin blood flow and sweating responses. The magnitude of these adaptations is variable and dependent on several factors such as exercise intensity, duration of exposure, frequency and total number of exposures, as well as the environmental conditions (i.e. dry or humid heat) in which acclimation occurs.

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1. Introduction

It is well established that cardiovascular strain contributes to impair aerobic exercise performance in the heat (Rowell, 1974; Chevront et al., 2010; Nybo et al., 2014) and that cardiovascular adaptations are

important contributors to the improved exercise capacity and reduced risk of serious heat illness conferred by exercise-heat acclimation (Sawka et al., 2011). Early physiologists recognized that a reduction in the elevated heart rate from heat stress likely was an important marker of adaptation to hot climates (Sundstroem, 1927). Lee and Scott (1916) were among the first to appreciate that the cardiovascular system likely imposed a physiological limitation to exercise performance under heat stress by “drafting blood away from the brain and the muscles to the skin”. Subsequently, Hill and Campbell (1922) demonstrated that

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improved evaporative cooling of the skin reduces cardiovascular strain and “keeps off fatigue” during exercise-heat stress. Perhaps the most important modern contributions regarding cardiovascular control with heat stress were made by Rowell (1974); Rowell et al. (1996) and Johnson (1977); Johnson et al. (2014), and integrated adjustments in such controls are critical to human heat acclimation (Taylor, 2014; Périard et al., 2015a). This review examines the cardiovascular adaptations along with total body water and plasma volume adjustments that occur in parallel with improved heat loss responses during exercise-heat acclimation. These physiological adaptations/adjustments are critical to exercise-heat acclimation as upright posture, increased cutaneous vasodilation and greater sweat secretion provide severe challenges to blood pressure regulation, performance, and health during exercise hot conditions.

2. Adaptation to heat

When humans are repeatedly exposed to conditions that are sufficiently stressful to elicit profuse sweating and elevate skin and core temperature, adaptations develop that reduce the deleterious effects of heat stress: heat acclimation or acclimatization. Heat acclimation refers to repeated periods of heat exposure undertaken in artificial or laboratory settings, whereas heat acclimatization results from exposure to natural environments. Although both natural and artificial hot environments elicit similar physiological adaptations (Armstrong and Pandolf, 1988; Wenger, 1988), heat acclimatization provides more specific responses due to exposure to the exact conditions that will be encountered during work or competition (i.e. exercise task, solar radiation and terrain/geography) (Périard et al., 2015a). The phenotypic adaptations that develop during repeated exposure to hot conditions improve performance during submaximal exercise, increase maximal aerobic capacity (VO_{2max}) (Sawka et al., 1985; Lorenzo et al., 2010) and enhance thermal comfort (Lemaire, 1960; Folk, 1974; Gonzalez and Gagge, 1976) in the heat. These benefits are achieved through plasma volume expansion, better maintenance of fluid balance, enhanced sweating and cutaneous blood flow responses, lowered exercising metabolic rate, and acquired thermal tolerance through the heat shock response, all of which contribute to improved cardiovascular stability and exercise performance during heat stress (Wyndham et al., 1976; Hori, 1995; Sawka et al., 1996; Horowitz, 2014; Périard et al., 2015a).

Physiological adaptations related to repeated heat exposure develop relatively quickly with 75–80% of the acclimation process occurring in the first 4–7 days (Fig. 1) (Pandolf, 1998; Shapiro et al., 1998). These adaptations can be categorized into short-term (<7 days),

medium-term (8–14 days) and long-term acclimation (>15 days) (Garrett et al., 2011). Horowitz et al. (1993, 1996, 1998) argue that heat acclimation develops as a continuum of processes and have proposed a conceptual model characterized by a distinct biphasic pattern. The initial short-term phase is transient and manifested by a decreased effector organ output-to-autonomic signal ratio, such that accelerated efferent activity is required to override the suboptimal peripheral responsiveness and produce adequate effector output. The second long-term phase is stable and characterized by an increased effector organ output-to-autonomic signal ratio, as both central and peripheral adaptations enhance physiological efficiency and reduce the need for accelerated excitation.

Although passive heat exposure induces adaptations commensurate with that magnitude of strain (Takamata et al., 2001; Beaudin et al., 2009; Brazaitis and Skurvydas, 2010) and passive hot water immersion after exercise can improve endurance performance in the heat (Zurawlew et al., 2015), the inclusion of exercise with heat exposure provides additional strain that generally elicits more profound adaptations (Armstrong and Pandolf, 1988; Wenger, 1988). Accordingly, the magnitude of physiological adaptation induced by heat acclimation or acclimatization depends largely on the initial heat exposure status (i.e. recent heat exposure, season, fitness level), as well as the exercise intensity, duration, frequency, and number of heat exposures, along with the induction protocol (Sawka et al., 1996; Taylor, 2000; Taylor, 2014; Périard et al., 2015a).

Repeated exercise-heat exposure at a constant work rate (i.e. traditional occupational and military heat acclimation protocol) is not likely as effective in eliciting adaptation as maintaining hyperthermia at a given core temperature (e.g. 38.5 °C; controlled hyperthermia or isothermic heat acclimation) (Taylor, 2000, 2014). Indeed, the traditional heat acclimation model offers a constant forcing function (i.e. fixed endogenous and exogenous thermal loads), which as adaptations progressively develop, results in decreased physiological strain and reduced further adaptations (Eichna et al., 1950; Fox et al., 1963a; Rowell et al., 1967). In contrast, with controlled hyperthermia protocols the forcing function is increased in proportion to the adaptations by manipulating the endogenous and/or exogenous thermal loads (Garrett et al., 2011; Taylor, 2014). Therefore, it is suggested that greater physiological adaptations occur during a given period with controlled hyperthermia than traditional approaches. Interestingly, recent studies have not found greater adaptations with controlled hyperthermia and the explanation for those findings are unclear (Gibson et al., 2015a,b).

The similar adaptations between some traditional and controlled hyperthermia approaches may stem in part from different acclimation protocols inducing distinctive autonomic responses that result in

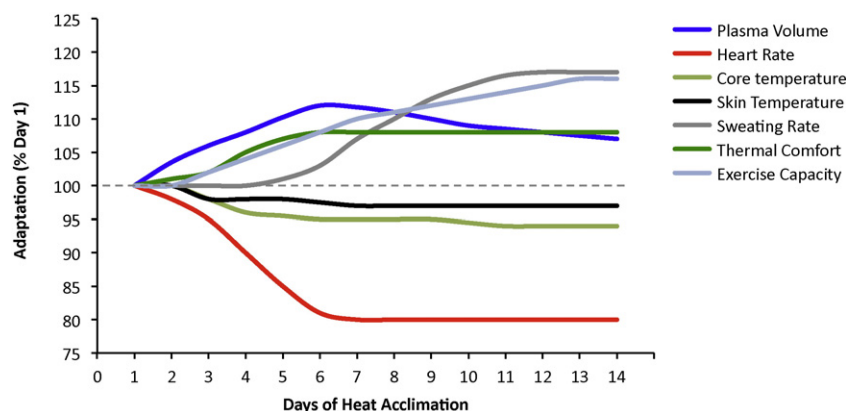


Fig. 1. The time course of adaptations to exercise-heat acclimation. Within a week of acclimation plasma volume expansion occurs and heart rate is reduced during exercise at a given work rate. Core and skin temperatures are also reduced when exercising at a given work rate, whereas sweat rate increases. Perceptually, the rating of thermal comfort is improved. As a result, aerobic exercise capacity is increased. Of note, the magnitude of these adaptations is dependent on the initial state of acclimation and the acclimation protocol (e.g. environmental conditions and exercise intensity). Adapted with permission from Périard et al. (2015a).

comparable physiological adjustments. For example, Moran et al. (1996) demonstrated in rats that both heat acclimation and exercise training improve cardiac efficiency (i.e. decreased rate pressure product: heart rate \times systolic blood pressure) during exercise in the heat; however this was achieved via different pathways. Heat acclimation attenuated the increase in blood pressure, whereas exercise training had a more pronounced effect on heart rate during exercise in the heat (Moran et al., 1996). In humans, a controlled exercise intensity heat acclimation protocol has recently been suggested whereby maintaining a given level of cardiovascular strain during daily exercise-heat exposure may optimize adaptations (Périard et al., 2015a). The level of strain achieved and sustained in this protocol would correspond to the heart rate associated with a specific relative exercise intensity (e.g. percent $\dot{V}O_{2\max}$, ventilatory or lactate threshold) in cool conditions. This heart rate would be sustained during exercise in the heat by increasing the power output accordingly as the individual adapted. Consequently, absolute work rate would increase as acclimation developed, thus providing a constant cardiovascular stimulus, based on the level of strain targeted.

The physiological adaptations associated with heat acclimation are transient and gradually disappear if consistent heat exposure is not maintained. The adaptations that develop most rapidly (e.g. improvements in heart rate) during acclimation are also those that are lost most quickly (Williams et al., 1967; Pandolf et al., 1977). Currently, there is no agreement concerning the rate of decay for heat acclimation. For example, it has been suggested that one day of exercise in the heat is required for every 5 days spent without heat exposure to maintain adaptation (Pandolf et al., 1977; Taylor, 2000), while others have proposed that one day of acclimation is lost for every 2 days spent without heat exposure (Givoni and Goldman, 1972). Notwithstanding, there is support for the notion that aerobic fitness and regular exercise are critical during the decay period in providing stimulus for maintaining the achieved adaptations (Pandolf et al., 1977; Weller et al., 2007).

3. Total body water and blood (plasma) volume

The fraction of mass represented by water in the human body is ~60%. This fraction varies in relation to body composition however, such that total body water estimations are generally calculated as a constant fraction of fat-free mass with a factor of ~0.737 (Wang et al., 1999). During the first week of heat acclimation, total body water generally increases by 2–3 L (~5–7%) (Bass et al., 1955; Wyndham et al., 1968; Patterson et al., 2004a, 2014). This increase is divided between

extracellular (plasma and interstitial fluid) and intracellular fluid compartments. The division of the total body water increase between compartments is variable, with studies reporting that extracellular fluid accounts for greater, equal and smaller than its percentage increase in total body water after heat acclimation (Sawka and Coyle, 1999). Fig. 2 provides body fluid compartment values before, during (day 8) and after (day 22) exercise-heat acclimation (Patterson et al., 2004a). Total body water, extracellular and intracellular fluid volumes and plasma volume were expanded either during or after exercise heat acclimation. The increase in total body water during heat acclimation was likely due to the large aldosterone and arginine vasopressin secretion occurring during exercise-heat stress (Francesconi, 1988), with blood and plasma concentrations increasing by 200–300% after exercise in both hot-dry and hot-wet environments, relative to resting values (Francesconi et al., 1983; Nielsen et al., 1993; Nielsen et al., 1997). A further pathway modulating the increase in total body water lies with the conservation of sodium that occurs with heat acclimation, which also helps maintain the number of osmoles in the extracellular fluid, and thus to conserve or increase extracellular fluid volume during adaptation (Nose et al., 1988).

Acutely, plasma volume expansion occurs after 3–4 days of heat exposure (Senay et al., 1976; Sawka and Coyle, 1999). The expansion typically varies between 4 and 15%, but can range from 3 to 27% (Bass et al., 1955; Senay et al., 1976; Nielsen et al., 1993; Patterson et al., 2004a, 2014; Karlsen et al., 2015a), with erythrocyte volume remaining unaltered (Sawka and Young, 2000). Typically, the greatest expansion of plasma volume is observed on about the fifth day of exercise-heat acclimation in fully hydrated individuals. Previous studies have described the rapid increase in plasma volume as being a transient phenomenon, with a small contraction occurring from this expanded state after one week of acclimation (Fig. 1) (Wyndham et al., 1968; Senay, 1979; Shapiro et al., 1981). More recently however, it has been suggested that this phenomenon may have been an experimental artifact stemming from the traditional constant work rate model of heat acclimation. It would appear that by using the controlled hyperthermia approach, which maintains a constant adaptation stimulus by clamping core temperature (e.g. 38.5 °C) throughout acclimation, plasma volume remains expanded (~14%) for a sustained period (8–22 days) of heat exposure (Fig. 2) (Patterson et al., 2004a, 2014).

The pathways via which the increase in plasma volume may be maintained include the oncotic effect of a net increase in total intravascular protein content during heat acclimation, which causes a movement of fluid from the interstitial to the intravascular space (Senay et al., 1976; Senay, 1979; Harrison et al., 1981). The increase in

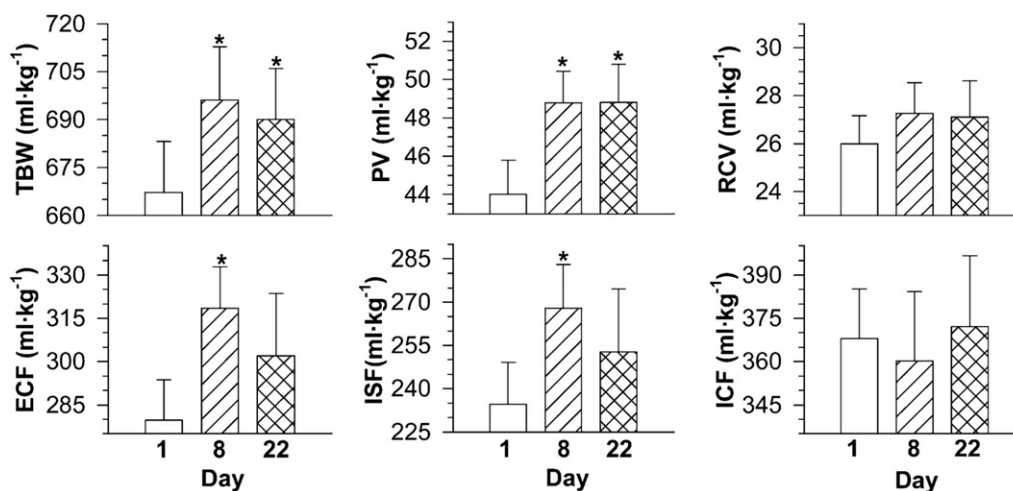


Fig. 2. Resting total body water (TBW), plasma volume (PV), red cell volume (RCV), extracellular fluid (ECF), interstitial fluid (ISF) and intracellular fluid (ICF) prior to and during a three-week heat acclimation regimen. Upper panels $n = 12$, lower panels $n = 8$ (mean \pm SEM). *Significantly different from Day 1 ($P < 0.05$). Reprinted with permission from Patterson et al. (2004a).

intravascular protein content is purported to stem in part from increased de novo albumin synthesis (Horowitz and Adler, 1983; Yang et al., 1998), a reduction in protein loss through the cutaneous capillaries in response to an acclimation-induced decrease in skin blood flow (Harrison, 1985), as well as a reduction in the permeability of cutaneous capillaries to large molecules, wherein protein remain within the intravascular space (Senay, 1970, 1972); adaptations which in turn support plasma volume expansion. The maintenance of plasma volume expansion is also associated with an increase in extracellular fluid, mediated by the retention of crystalloids, primarily sodium chloride (Mack and Nadel, 1996; Patterson et al., 2004a, 2014).

The retention of plasma volume expansion during chronic heat acclimation is in contrast to the acute effect of plasma volume expansion. Using a hyperoncotic 25% albumin solution or 0.9% saline, Hubbard et al. (1984) demonstrated that plasma volume was acutely expanded for 9–12 h in both hot and temperate conditions, but by a greater magnitude under heat stress. The authors further demonstrated a return in plasma volume to near baseline values by 24 h post-infusion, which is suggestive of a circadian pattern of plasma volume expansion and contraction. Interestingly, it was noted that after albumin infusion, heat exposure significantly increased plasma volume compared with saline and appeared to extend the retention time of the infused albumin, resulting in a more prolonged increase in oncotic pressure (Hubbard et al., 1984). Although debate remains as to what level plasma volume can be expanded and whether or not this expansion is sustained during heat acclimation, an increase in plasma volume does provide two major physiological advantages: i) increasing vascular filling pressure to support cardiovascular stability (i.e. increased stroke volume and arterial blood pressure) (Senay et al., 1976), and ii) increasing the specific heat of blood (Blake et al., 2000), thus improving heat transfer from the core to the skin and theoretically allowing slightly lower cutaneous blood flow responses (Sawka et al., 2011). Fig. 3 provides the relation between the percent changes in heart rate at the end of exercise (4 h) to the percent change in plasma volume after 10 days of humid heat acclimation, relative to the first day of heat exposure (Senay et al., 1976). These data suggest that plasma volume expansion, and thus perhaps improved cardiac filling, contribute to the reduced heart rate response during heat acclimation. This is similar to the expansion of blood volume (i.e. plasma and erythrocyte) that occurs during aerobic training and which is considered an important contributor to improvements in endurance performance by allowing for greater

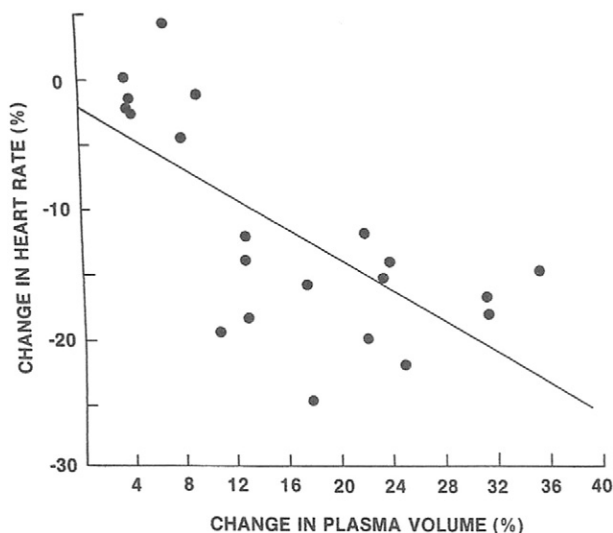


Fig. 3. Percent changes in heart rate relative to percent changes in plasma volume at the end of 4 h of exercise following 10 days of heat acclimation. Values from the first day of heat exposure were taken as control values. Redrawn with permission from Senay et al. (1976).

ventricular filling and a consequent larger stroke volume (Hellsten and Nyberg, 2016).

4. Fluid balance and dehydration

Thirst during exercise-heat stress has historically not been considered a good indicator of body water needs since ad libitum water consumption often resulted in incomplete fluid replacement, or voluntary dehydration (Adolph and Dill, 1938; Bean and Eichna, 1943; Eichna et al., 1945; Adolph, 1947; Greenleaf and Sargeant, 1965; Greenleaf et al., 1983; Armstrong et al., 1985; Greenleaf, 1992). Drinking behavior and fluid replacement are processes influenced by physiological, psychological and environmental factors, as well as issues related to fluid palatability, food intake, and gastric distension/discomfort (Ormerod et al., 2003). The mechanisms via which drinking and fluid replacement are regulated during and following exercise include a sodium ion-osmotic-vasopressin pathway (Andersson et al., 1980) and a renin-angiotensin II-aldosterone pathway (Fitzsimons, 1979). It is suggested that thirst sensations occur in response to changes in plasma osmolality, plasma volume, and angiotensin II (Fitzsimons, 1979; Epstein, 1982; Rolls and Rolls, 1982). Heat acclimation improves the relationship of thirst to body water needs by a reducing the time to first drink, increasing the number of drinks consumed per heat exposure, and increasing mean volume per drink (Greenleaf et al., 1983; Hubbard et al., 1990), such that voluntary dehydration is markedly reduced (~30%) (Bean and Eichna, 1943; Eichna et al., 1945; Eichna et al., 1950). Fig. 4 plots the difference between ad libitum water intake and water loss during 6 days of humid heat acclimation (Eichna et al., 1945). Note that after three days water deficits were reduced by 50%. Thus, heat acclimated individuals are better able to maintain hydration status during exercise-heat stress and minimize body water losses, provided access to fluids is not restricted.

Another important adaptation from heat acclimation to defend extracellular volume, and thus plasma volume, is improved sodium reabsorption in the eccrine sweat gland (Quinton, 2007). Indeed, an unacclimated person may secrete sweat with a sodium concentration of 60 mEq/L or higher, and therefore if sweating profusely can lose large amounts of sodium (Allan and Wilson, 1971). With heat acclimation, eccrine sweat glands increase sodium reabsorption along the duct, which can reduce sweat sodium concentrations to as low as 10 mEq/L. Fig. 5 demonstrates the relationship of sweat sodium concentration and sweating rate before and after heat acclimation (Allan and Wilson, 1971). As indicated, sweat sodium concentration is significantly reduced for a given sweat rate following acclimation.

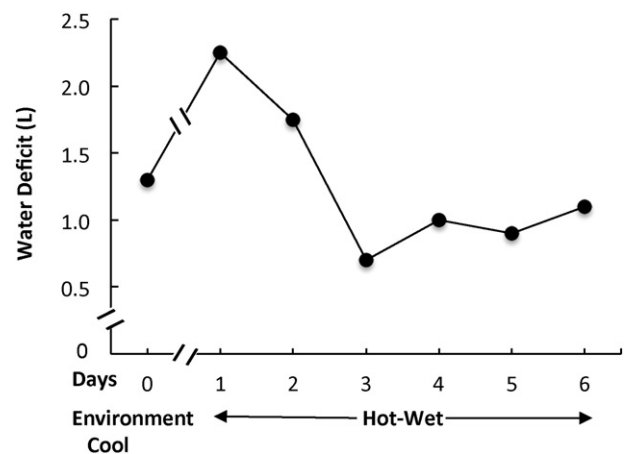


Fig. 4. Difference between ad libitum water intake and water loss in 15 men during work in humid heat over a 6-day period, compared with work in a cool environment (Eichna et al., 1945). Redrawn with permission from Sawka et al. (1984).

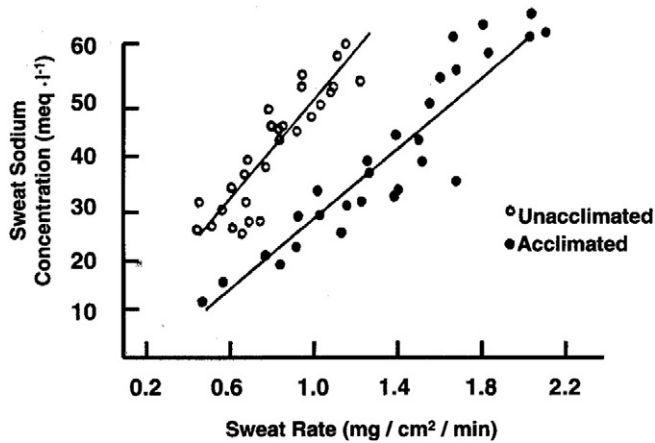


Fig. 5. Sweat sodium concentration in relation to sweat rate in the unacclimated and acclimated state. Adapted with permission from Allan and Wilson (1971).

Dehydration, or a reduction in total body water and plasma volume, is known to adversely increase cardiovascular strain and impair aerobic performance during exercise-heat stress (Adolph, 1947; Morimoto, 1990; Sawka and Coyle, 1999; Sawka et al., 2015). The deleterious cardiovascular effects of dehydration are characterized by difficulty to sustain blood pressure and cardiac output, and a potential reduction in skeletal muscle blood flow during exercise-heat stress (Sawka and Coyle, 1999; Sawka et al., 2011; Nybo et al., 2014; Sawka et al., 2015). As shown in Fig. 6, combining dehydration with exercise-heat stress results in reduced cardiac output and skeletal muscle blood flow, compared to when euhydrated (Gonzalez-Alonso et al., 1998). Drinking sufficient fluids to minimize dehydration during heat acclimation should therefore help to sustain cardiac output and perhaps skeletal muscle blood flow, and thus optimize exercise capacity under heat stress.

Adaptations in sweat rate were among the first described in response to heat acclimatization. Indeed, by the end of the 1940's it was widely accepted that heat acclimatization increases sweating capacity (Dill et al., 1933; Adolph and Dill, 1938; Dill et al., 1938; Robinson et al., 1943; Horvath and Shelley, 1946). Along with a shift in the onset threshold for sweating, which occurs earlier and at a lower core temperature, almost exact parallel improvements are noted in skin blood flow (Nadel et al., 1974; Roberts et al., 1977). These sweat and skin blood flow responses are indicative of central and peripheral adaptations (Nadel et al., 1971), which are depicted in Fig. 7. At the central level, heat acclimation decreases the body temperature at which thermoregulatory sweating and skin vasodilation are initiated. This adjustment in onset threshold is proposed to correspond to an absolute change in mean body temperature, rather than to the attainment of a predetermined mean body temperature (Patterson et al., 2004b). Peripheral adaptations, manifested by changes in sweat rate and sensitivity, occur at the level of the sweat glands (Fox et al., 1964; Chen and Elizondo, 1974; Inoue et al., 1999; Buono et al., 2009a; Buono et al., 2009b), which become resistant to fatigue so that higher sweat rates can be sustained, particularly in humid climates (Fig. 8) (Gonzalez et al., 1974). These adaptations include improved cholinergic sensitivity, and increased size and efficiency of eccrine glands in producing sweat per unit length of secretory coil (Sato and Sato, 1983; Sato et al., 1990). Peripheral factors contributing to improved sweating and skin blood flow responses likely include an increase in the number and sensitivity of muscarinic receptors, a decrease in cholinesterase activity that potentiates and prolongs acetylcholine concentration in the cholinergic neural junction, which improves the vascular response to a given acetylcholine level, or alterations to the pathway of vasodilation within smooth muscles or the endothelial cells (Lorenzo and Minson, 2010).

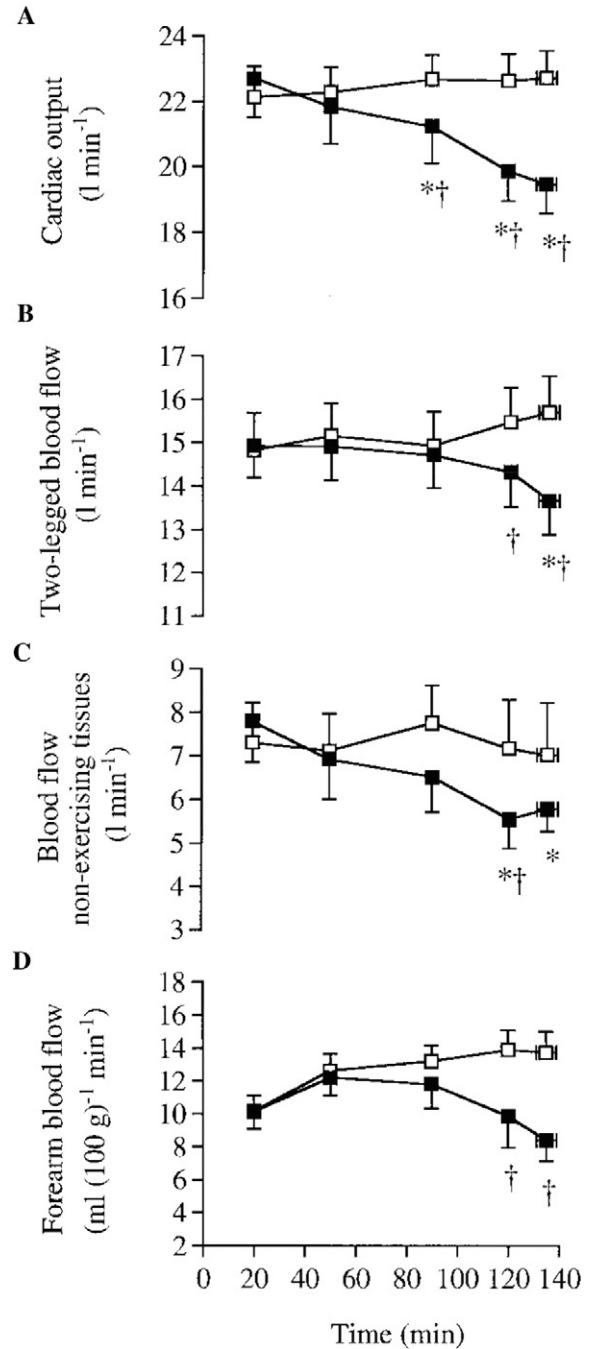


Fig. 6. Cardiac output and blood flows during dehydration and control trials. A: cardiac output, B: 2-legged blood flow, C: non-exercising tissue blood flow, D: forearm blood flow. Filled squares represent dehydration and open squares represent control. *Significantly lower than 20 min value ($P < 0.05$). †Significantly lower than control ($P < 0.05$). Reprinted with permission from Gonzalez-Alonso et al. (1998).

5. Cardiovascular adaptations to heat acclimation

The primary cardiovascular challenge during exercise in the heat is to provide sufficient cardiac output to adequately perfuse skeletal muscle to support metabolism, while simultaneously perfusing skin to support heat loss. The traditional belief was that skeletal muscle blood flow is not altered by heat stress and that increases in cardiac output support elevated skin blood flow requirements (Rowell, 1974; Johnson, 1977). Recent studies however, show that elevated tissue/blood temperatures induce an increase in skeletal muscle

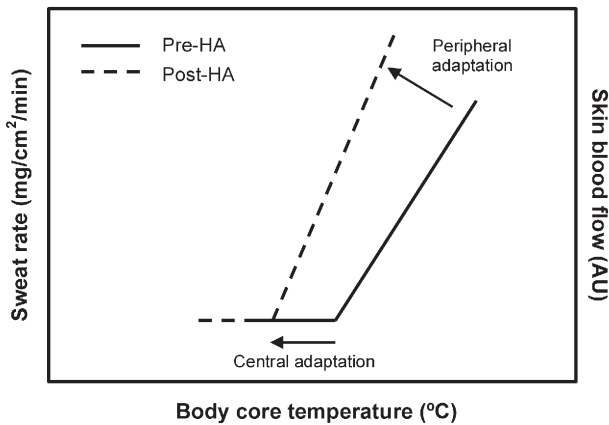


Fig. 7. Schematic representation of the central and peripheral adaptations that occur in response (Pre vs. Post) to heat acclimation (HA). The body core temperature threshold for the onset of sweating is reduced, while the rate and sensitivity (i.e. slope) are increased (Nadel et al., 1974; Roberts et al., 1977). Concomitantly, the body core temperature threshold for the onset of cutaneous vasodilation is reduced, whereas skin blood flow sensitivity is increased (Fox et al., 1963b; Roberts et al., 1977; Yamazaki and Hamasaki, 2003; Lorenzo and Minson, 2010). Adapted from Nadel et al. (1974) and Werner (1994) and reprinted with permission from Périard et al. (2015a).

blood flow during rest and exercise (Pearson et al., 2011; Chiesa et al., 2015; Gonzalez-Alonso et al., 2015). The mechanisms mediating this increase may include an interaction of metabolic and thermal stimuli inducing the release of erythrocyte-derived ATP, a potent vasodilator (Gonzalez-Alonso et al., 2015). Thus, it may be postulated that in unacclimatized individuals higher body/tissue temperatures would induce greater skeletal muscle blood flow requirements, and that with heat acclimation these requirements might decline with lower body/tissue temperatures during exercise-heat stress.

These metabolic and thermoregulatory demands are generally viewed as competing, whereby cardiac function is altered, the distribution of cardiac output is modified, and/or the ability to sustain adequate blood pressure is compromised (Rowell, 1986; Sawka et al., 2011). Alternatively, the conflict between regulatory systems may be viewed as commensalism: an integrated balance of regulatory control where

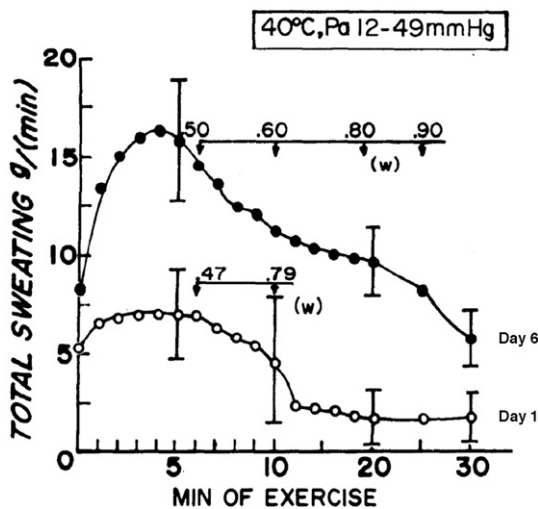


Fig. 8. Improvements in sweating capacity on Days 1 and 6 of cycle ergometer exercise (25–30% $\dot{V}O_{2max}$) in 40 °C air temperature and increasing humidity from a vapor pressure of 12 mmHg to 49 mmHg each day. Skin wettedness (w) is equal to skin evaporation (E_{sk})/maximum evaporative capacity (E_{max}). Adapted with permission from Gonzalez et al. (1974).

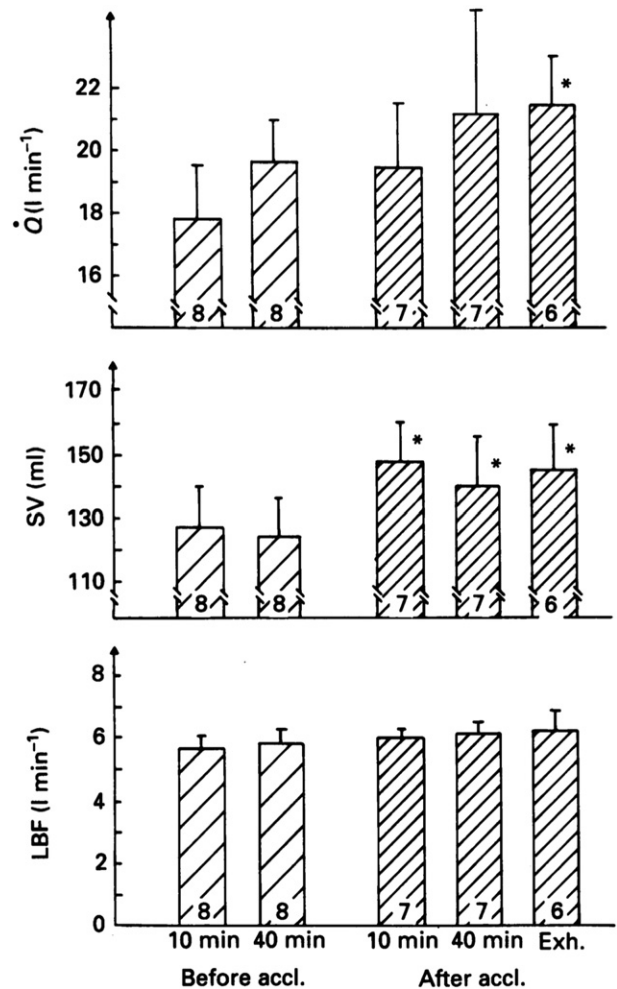


Fig. 9. Cardiac output (Q), stroke volume (SV) and leg blood flow (LBF) during exercise (10 and 40 min) and just before volitional exhaustion (Exh). Open hatching: before acclimation. Close hatching: after 9–12 days of acclimation. Before acclimation the 40 min values were those taken just before exhaustion (mean \pm SEM). Number of measurements indicated. *Significantly different from final measurements before acclimation ($P < 0.05$). Reprinted with permission from Nielsen et al. (1993).

one circulation benefits without substantially affecting the other (Kenney et al., 2014). Notwithstanding, heat acclimation improves the ability to sustain cardiac output during exercise-heat stress. Fig. 9 provides an example of this improvement with cardiac output, stroke volume and leg blood flow responses during exercise to exhaustion in a hot-dry environment before and after heat acclimation (Nielsen et al., 1993). Notably, heat acclimation improved the ability to perform endurance exercise in the heat. This was accompanied by lowered heart rate, increased stroke volume and sustained leg blood flow, and sustained or improved cardiac output responses.

The effects of heat acclimation on stroke volume and cardiac output during exercise-heat stress depend largely on exercise intensity, as well as the type and severity of the heat stress. For example, two studies in which low to moderate work was conducted in the heat reported increases in stroke volume with little change in cardiac output as heart rate decreased with acclimation (Rowell et al., 1967; Wyndham et al., 1968). Another study reported a decrease in cardiac output in association with a reduction in cutaneous blood flow, but little change in stroke volume as heart rate decreased, again during work performed in hot conditions (Wyndham, 1951). A separate study reported a mixed pattern, with two subjects showing a steady increase in stroke volume, one a transient increase reversing after the sixth day, and one showing no increase with heat acclimation (Wyndham et al., 1976). The reason

for these differences is unclear, although differences in the methodology to assess these parameters may account for some variation, while another possibility might relate to exercise being performed in dry heat (Rowell et al., 1967) versus humid heat (Wyndham, 1951; Wyndham et al., 1968, 1976).

Nielsen et al. (1993, 1997) examined stroke volume responses during exercise (45–50% $\dot{V}O_2$ max) before and after dry (40 °C, 10% relative humidity; RH) and humid (35 °C, 87% RH) heat acclimation. The authors reported that during exercise, dry heat acclimation increased stroke volume (~21 mL/beat) and cardiac output (~1.8 L/min) (Nielsen et al., 1993), whereas humid heat acclimation did not influence either response (Nielsen et al., 1997), despite both studies reporting a plasma volume expansion of 9–13%. Others have also shown that 10 days of dry heat acclimation improves maximal stroke volume and cardiac output during a $\dot{V}O_2$ max test in cool (13 °C), but not hot (38 °C) conditions, without influencing maximum heart rate (Lorenzo et al., 2010). Moreover, short-term moderate intensity (70% $\dot{V}O_2$ max, 30 min/day) exercise-heat acclimation in 30 °C and 50% RH has been shown to increase plasma volume and stroke volume, and decrease heart rate (Goto et al., 2010). Taken together, these observations indicate that heat acclimation improves central hemodynamics, but that the magnitude of improvement may depend on the environmental condition (i.e. dry vs. humid heat), acclimation protocol (i.e. stimulus impulse), exercise intensity, and subject population. Hence, additional research is required to fully elucidate the impact of heat acclimation on central hemodynamic responses.

The hallmark cardiovascular adaptations induced during heat acclimation include a lowering of heart rate and an increase in stroke volume, which support the maintenance of cardiac output and the regulation of blood pressure during submaximal exercise (Table 1). The lowering of heart rate and increased stroke volume are likely supported by changes in myocardial autonomic tone. Autonomic adjustments during exercise are mediated by central command, cardiopulmonary and arterial baroreflexes, and carotid chemoreflexes (Fisher et al., 2015), all of which are further modified during exercise-heat stress (Nybo et al., 2014). Therefore, the net affect on parasympathetic/sympathetic efferent activity and thus myocardial chronotropic, inotropic and lusitropic properties is likely specific to the exercise intensity, hydration status, fitness level, as well as heat acclimation status. With heat acclimation, it is anticipated that better tissue perfusion, reducing metaboreceptor stimulation; reduced metabolic lactate production, reducing carotid chemoreflex stimulation for respiratory compensation; improved cardiac filling and blood pressure regulation, reducing low and high pressure baroreceptor stimulation; and tissue (i.e. muscle and brain) temperatures, modifying central command; all contribute to alter cardiac autonomic regulation.

A direct effect of temperature on cardiac pacemaker cells may also contribute to the lowering in heart rate during exercise at a given workload (Berlyne et al., 1974; Horowitz and Meiri, 1993). This heat acclimation-induced bradycardia may further relate to a decrease in overall thermal (i.e. lower core and skin temperatures) and concomitantly cardiovascular strain, and to alterations in total blood volume

Table 1

Adaptations in cardiovascular function associated with heat acclimation that lead to improved cardiovascular stability.

Cardiovascular parameter	Adaptation
Heart rate	Lowered
Stroke volume	Increased
Cardiac output	Better sustained
Blood pressure	Better sustained
Myocardial compliance	Increased
Myocardial efficiency	Increased
Cardioprotection	Improved

Adapted with permission from Sawka et al. (2011).

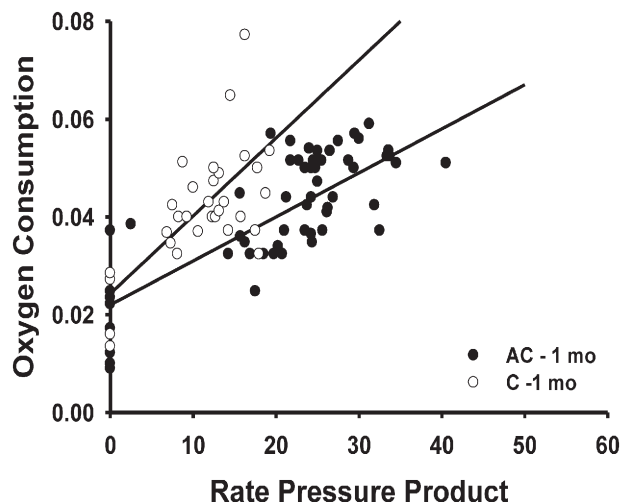


Fig. 10. Relationship between oxygen consumption and cardiac work (expressed as the rate-pressure product) in hearts of sedentary unacclimated (C) and heat acclimated (AC) rats for 1 month. Marked shift to the right of the regression line of heat-acclimated hearts compared with that of unacclimated hearts implies significantly increased work efficiency of heat-acclimated hearts ($P < 0.0007$) (Levy et al., 1997). Reprinted with permission from Horowitz (1998).

(Shapiro et al., 1998), which as discussed earlier may reduce both skin and skeletal muscle blood flow requirements. The increase in plasma volume may serve to support greater venous return and cardiac preloading, leading to improved ventricular filling and increased stroke volume (Senay, 1986). A rightward shift in the diastolic pressure-volume curve thus occurs, which allows for greater ventricular filling and augmented stroke volume without a change in pressure (Horowitz, 2003). Additionally, exercise-heat acclimated rats demonstrate increased left ventricular compliance and systolic pressure generation while myocardial $\dot{V}O_2$ (i.e. the energetic cost of pumping) is lowered (Fig. 10) (Horowitz et al., 1986a,b; Levy et al., 1997). The reduced myocardial $\dot{V}O_2$ is believed to be associated with myosin ATPase activity changes (Horowitz et al., 1986a). Globally, the adaptations are suggested to stem from concerted adjustments induced by exercise-heat acclimation that alter the mechanisms associated with the excitation-contraction coupling cascade, Ca^{2+} regulation, contractile and metabolic responses (Horowitz et al., 1993; Horowitz, 2003; Kodesh et al., 2011). Although it remains to be determined whether such functional adaptations occur in humans, heat stress is known to reduce left ventricular pressure and increase left ventricular systolic function (Crandall et al., 2008; Brothers et al., 2009), such that following heat acclimation greater ventricular filling may occur at a lower ventricular pressure.

Molecular adaptations at the level of the cardiac muscle also occur in response to the induction of heat shock proteins (Hsp), which were originally described for their role as molecular chaperones in maintaining cellular conformation and homeostasis (Locke, 1997; Kregel, 2002). The heat shock response induced during exposure to heat stress confers transient thermotolerance and protection against subsequent exposure, as well as cardioprotection (Horowitz and Assadi, 2010). Interestingly, exercise-heat acclimation appears to increase basal intracellular Hsp72 and Hsp90 levels, and blunt the acute response (i.e. inducibility) to exercise in the heat as adaptations develop (Amorim et al., 2015; Périard et al., 2015a). McClung et al. (2008) demonstrated in peripheral blood mononuclear cells that individuals demonstrating the greatest physiological adaptations exhibit the greatest blunting in ex vivo Hsp72 and Hsp90 inducibility. At the extracellular level, increases in the basal expression of Hsp72 following exercise are less consistent. Indeed, whilst similar increases in intracellular (i.e. monocyte) and extracellular Hsp72 expression occur immediately following exhaustive exercise in the heat, the extracellular expression

decreases below basal (i.e. pre-exercise) levels 24 h after exercise (Périard et al., 2012), whereas intracellular levels increase (Périard et al., 2015b).

6. Aerobic exercise performance

Heat acclimation can have profound benefits on cardiovascular function and concomitantly aerobic performance in the heat. For example, Racinais et al. (2015) demonstrated that three cycling time trials (43 km) undertaken in hot outdoor conditions (~37 °C) were initiated at a similar power output to that of time trials conducted in cool conditions (~8 °C) (Fig. 11). However, a marked decrease in power output occurred in the heat following the onset of exercise, which was partly recovered after one week of training in the heat and almost fully restored after two weeks of training in the heat. As expected, heart rate was similar during all trials in the heat and slightly higher than in the cool, which supports the contention that a similar relative exercise intensity (i.e. % $\dot{V}O_2\text{max}$) was maintained (Périard et al., 2011; Wingo et al., 2012; Périard and Racinais, 2015) and that with heat acclimation absolute intensity (i.e. power output) increased.

Heat acclimation has been shown to improve the $\dot{V}O_2\text{max}$ of trained individuals in hot conditions with Sawka et al. (1985) reporting a 4% (49 °C) improvement and Lorenzo et al. (2010) and Keiser et al. (2015) noting increases of 8–10% (38 °C). Despite these improvements, acute heat stress mediates a reduction in $\dot{V}O_2\text{max}$ relative to values recorded in temperate conditions that cannot be compensated for by heat acclimation (i.e. $\dot{V}O_2\text{max}$ in the heat remains lower than in cool conditions). Notwithstanding, heat acclimation has been shown to increase cycle exercise time trial performance in the heat in conjunction with an increase in cardiac output and lactate threshold, plasma volume expansion, lower skin temperatures, and a larger core-to-skin gradient after heat acclimation (Lorenzo et al., 2010). Moreover, the increase in performance was proportional to the increase in $\dot{V}O_2\text{max}$ in the heat (Lorenzo et al., 2010), which further reinforces the notion that relative exercise intensity significantly influences self-paced exercise performance in the heat (Périard et al., 2011; Périard and Racinais, 2015).

Observations of enhanced self-paced exercise performance have also been noted in cool conditions in proportion to improvements in $\dot{V}O_2\text{max}$ under the same conditions (Lorenzo et al., 2010). This supports previous observations of heat acclimation increasing $\dot{V}O_2\text{max}$ in trained (3–5%) (Sawka et al., 1985; Lorenzo et al., 2010), untrained (13%) and unfit (23%) individuals in cool conditions (Shvartz et al., 1977), and reinforces the 32% increase in run time to exhaustion noted in fit individuals after heat acclimation via post-exercise sauna bathing (Scoon et al., 2007).

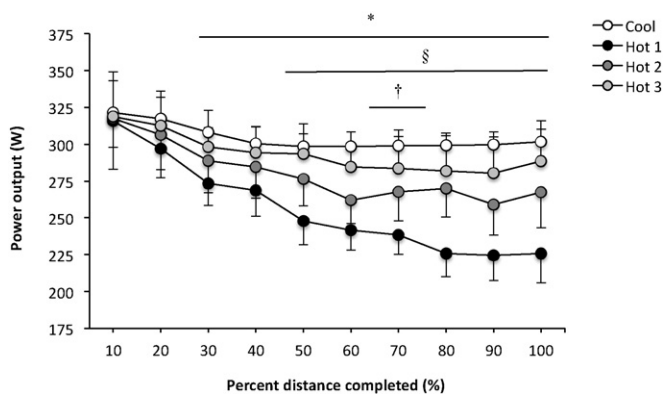


Fig. 11. Power output during 43.4 km cycling time trials performed in Cool (~8 °C; average of trials performed before and after heat acclimatization) and Hot (~37 °C) conditions after one (Hot 1), six (Hot 2) and fourteen (Hot 3) days of training in the heat. *†‡Cool time trial significantly higher than TTH-1, TTH-2, and TTH-3, respectively ($P < 0.05$). Redrawn with permission from Racinais et al. (2015).

It also supports findings of team-sport athletes improving endurance performance (i.e. Yo-Yo Intermittent Recovery test) in temperate conditions (~22 °C) following training camps in the heat (~34 °C) (Buchheit et al., 2011, 2013; Racinais et al., 2014). The pathways via which a transfer of adaptation between hot and cool conditions would increase performance might be linked to a variety of ergogenic responses, including cardiovascular, thermoregulatory and cellular adaptations (Lorenzo et al., 2010; Bruchim et al., 2014; Corbett et al., 2014). In contrast, other investigations in which 5 days of isothermic (~38.6 °C) heat acclimation with permissive dehydration (Neal et al., 2015), 10 days of constant intensity (50% $\dot{V}O_2\text{max}$ heart rate) heat acclimation (Keiser et al., 2015), and 14 days of natural heat acclimatization (Karlsen et al., 2015b) were utilized, did not demonstrate an improvement in $\dot{V}O_2\text{max}$ or time trial performance in cool conditions in trained cyclists. Clearly, this will become a controversial area and merit additional research with well-designed protocols to elucidate the mechanisms and possible transfer of ergogenic benefits from heat acclimation towards improving aerobic performance in cooler conditions.

There are several additional potential benefits that may be conferred by heat acclimation that could contribute to improved exercise capabilities. Heat acclimation can decrease the oxygen uptake response to submaximal exercise (Sawka et al., 1983, 1996). The greater reliance on carbohydrate as a fuel source during exercise in the heat is also influenced by heat acclimation (Young et al., 1985; Febbraio et al., 1994), with muscle glycogen utilization decreasing by 40–50% (King et al., 1985; Kirwan et al., 1987). This glycogen-sparing effect of heat acclimation has also been shown to be quite small however, and apparent only during exercise in cool conditions (Young et al., 1985). A further effect of heat acclimation is the reduction of blood and muscle lactate accumulation during submaximal exercise (Febbraio et al., 1994) and the increase in power output at lactate threshold (Lorenzo et al., 2010; Neal et al., 2015). The mechanisms mediating these adaptations remain unclear, but could stem from the increase in total body water enhancing lactate removal through increased splanchnic circulation (Rowell et al., 1968), or through increased cardiac output and decreased metabolic rate delaying lactate accumulation (Sawka et al., 1983; Young et al., 1985).

7. Summary

Acute heat stress impairs aerobic exercise capacity and elevated cardiovascular strain has long been considered an important contributor. Repeated heat exposure however, induces adaptations that abate cardiovascular strain and likely contribute to attenuate the exercise performance impairment, and reduce the risk of serious heat illness. The cardiovascular adaptations supporting this include an increase in total body water, plasma volume expansion, better sustenance and/or elevation of stroke volume, reduction in heart rate, improvement in ventricular filling and myocardial efficiency, and enhanced skin blood flow and sweating responses. The magnitude of these adaptations is dependent on several factors such as exercise intensity, duration, frequency and number of exposures to the heat, as well as to the environmental conditions (e.g. dry vs. humid heat) and protocol in which acclimation occurs.

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