Integrative Human Cardiovascular Responses to Hyperthermia

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3.1 Introduction

When ambient temperature exceeds that of the skin, heat is transferred from the surrounding environment to the cooler body tissues, and internal body temperature begins to rise. With an increase in core temperature of as little as 3–4 °C potentially proving fatal [1], the presence of raised tissue temperatures results in profound changes in vascular tone and cardiac output, alongside a redistribution of blood flow from core to peripheral sites in order to promote heat loss to the environment [2]. Even at rest, the magnitude of increase in cardiac output is striking, with elevations of 5–8 l/min reported during prolonged severe passive heating, an increase second only to that witnessed during aerobic exercise [3, 4]. This increase in blood flow is directed predominantly to the cutaneous (skin) circulation, aided by hyperthermia-induced vasoconstriction in splanchnic, renal, and cerebral vascular beds. Recent evidence suggests that skeletal muscle, fat, and bone blood flow may also contribute

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to the observed hyperemic response, although the magnitude of this effect appears relatively modest.

The superimposition of exercise onto a hyperthermic individual results in one of the greatest challenges faced by the human cardiovascular system. Even when normothermic, the profound ability of skeletal muscle to vasodilate during intense whole-body exercise [5] exceeds the capacity of the heart to maintain the level of blood flow required for metabolic demand [6, 7]. When exercise is performed in a hyperthermic state, the combined demand of both skeletal muscle and skin vascular beds for O_2 delivery and heat dissipation—alongside a host of other vascular, hormonal, and neural alterations—can rapidly push the cardiovascular system to its limits [8, 9]. Despite this, however, mean arterial pressure is only slightly reduced, and cardiac output and active skeletal muscle blood flow are maintained or may even be increased at all but the very highest intensities of whole-body exercise. This chapter aims to document the integrative cardiovascular response to heat stress, firstly during progressive increases in body temperature at rest (i.e. passive heat stress, induced through thermal interventions such as wearing a suit that circulates hot water, exposure to sauna, or hot water baths), followed by cardiovascular adjustments across a spectrum of exercise intensities (i.e. exercise heat stress, primarily via the use of water-perfused suit while cycling or exposure to very hot environmental temperatures). As the majority of human research studies in this field have been carried out in young healthy adults, it is important to note that the absolute cardiovascular responses described in this chapter likely apply to this population alone, and should not be considered representative of other groups such as clinical patients or the elderly. Likewise, conditions such as orthostatic stress, dehydration, or haemorrhage—which may act to further compromise cardiovascular function in the heat—are outside the scope of this chapter, and so will not be addressed.

3.2 Respiratory and Cardiovascular Responses to Passive Heat Stress

The overall respiratory and cardiovascular adjustments observed during passive heat stress are at first glance similar to that observed during exercise, comprising an increase in respiratory rate, an increase in cardiac output, a decrease in peripheral resistance, and a selective elevation and redistribution of blood flow from the core to the extremities (Fig. 3.1). In contrast to exercise, however, these changes are largely driven by thermoregulatory as opposed to metabolic requirements, and are therefore underpinned by distinct respiratory, cardiac, and vascular adjustments. These act to maximise convective heat transfer within the body and evaporative heat dissipation to the surrounding environment while preserving mean arterial and perfusion pressure and increasing O_2 delivery in many tissues above the metabolic demand.

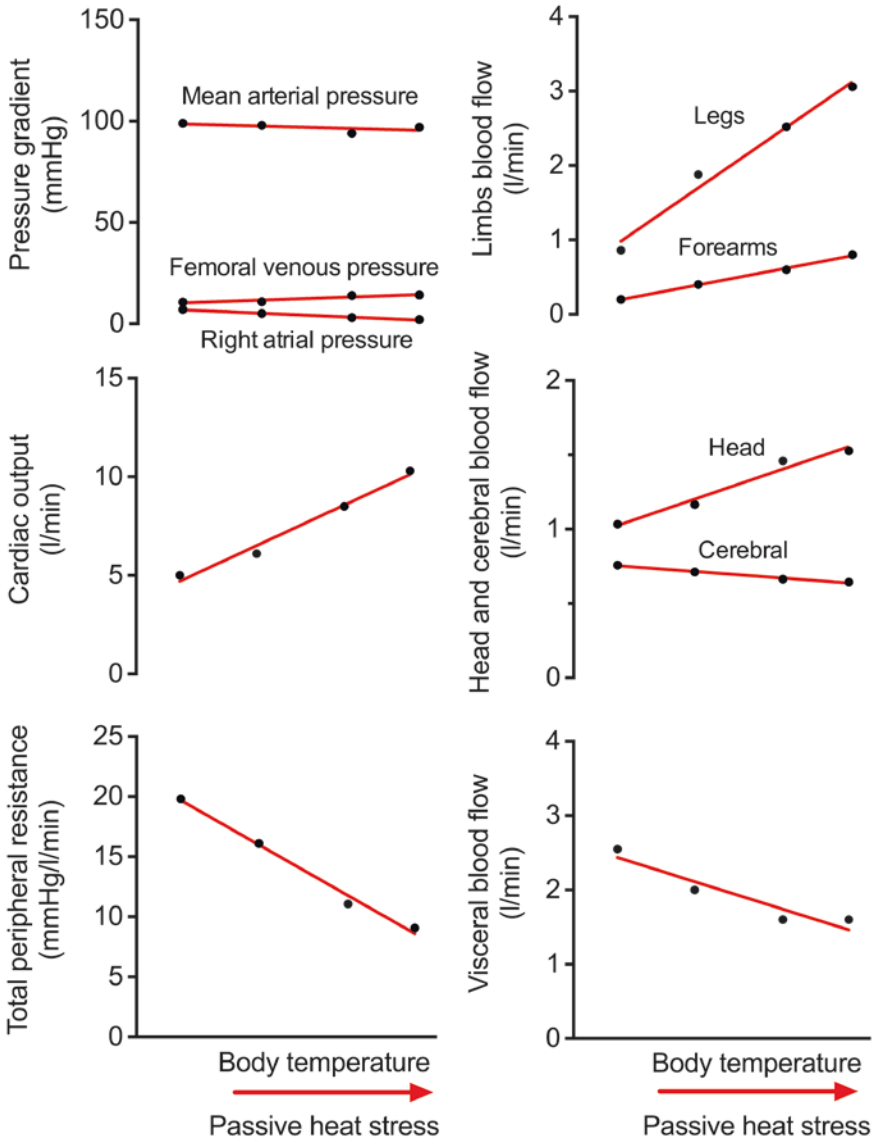

Fig. 3.1 Systemic and regional haemodynamic responses to progressive passive heat stress-induced hyperthermia. Data for mean arterial pressure, femoral venous pressure, cardiac output, and total peripheral resistance graphs are redrawn from [10] and [22]. The limbs blood flow graph is based on data reported by Pearson et al. [10] (legs) and Kalsi et al. [45] (forearms), whereas the head and cerebral blood flow graph is from [12]. Lastly, the visceral blood flow and right atrial pressure graphs are based on data from [4]. The increase in blood flow in the legs, arms, and head accounts for the majority (>80%) of the increase in cardiac output

3.2.1 Respiratory Responses to Passive Heat Stress

Elevations in core temperature >1 °C induce a hyperventilatory response in humans, despite a small absolute increase in metabolic requirements and O_2 consumption ($\Delta\dot{V}O_2$ ~0.15 l/min or 70% increase in resting metabolic rate) [10]. The potential mechanisms controlling the hyperventilatory response to hyperthermia are outside the scope of this chapter, but are discussed in detail in a recent review [11]. In hyperthermic but euhydrated individuals, arterial O_2 content is unchanged or increased, and mixed venous O_2 is significantly increased due to the significant increase in blood flow to the cutaneous and deep tissue circulations for thermoregulatory purposes [10]. As a result, even at the very highest levels of heat stress, O_2 delivery to both thermoregulatory and metabolically active tissues is elevated well in excess of that required to maintain the modest increases in $\dot{V}O_2$, and systemic and limb O_2 extraction is therefore markedly blunted (see Fick principle in Fig. 3.2). In contrast to its negligible effect on arterial O_2 content, however, the effect of hyperventilation on intravascular CO_2 levels is pronounced [12]. This has potential implications for brain blood flow and cerebral O_2 delivery, as will be discussed later in the chapter.

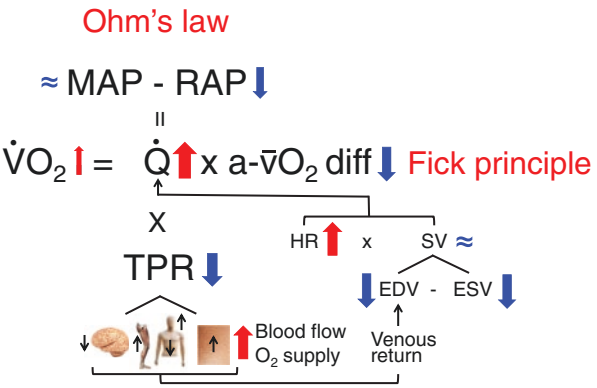

Fig. 3.2 Schematic illustration of the impact of severe whole-body heat stress on physiological function according to Ohm's law and the Fick principle. Ohm's law states that perfusion pressure equals flow x resistance, with pressure being the force that drives flow and resistance the force that opposes flow. The Fick principle, in turn, determines the rate of oxygen consumption by the human body, an organ, limb, or tissue. This is equal to the product of blood flow and the arterial-venous oxygen content differences. Note that blood flow is the common denominator in both equations. $\dot{Q}$ cardiac output, *TPR* total peripheral resistance, *MAP* mean arterial pressure, *RAP* right atrial pressure, $\dot{V}O_2$ systemic oxygen consumption, *a-vO_2 diff* arterio-mixed venous oxygen content differences, *HR* heart rate, *SV* stroke volume, *EDV* end-diastolic volume, *ESV* end-systolic volume

3.2.2 Cardiac Responses to Passive Heat Stress

At the most fundamental physical level, the cardiovascular system can be thought of as a variation of Ohm's law, where pressure (in this case the pressure gradient between the arterial circulation and the right side of the heart) is the product of flow x resistance. Therefore, if blood pressure is to be maintained in the face of substantial reductions in peripheral resistance (due to profound vasodilation within the peripheral tissues), blood flow must also increase in a proportionate manner (Fig. 3.1). During passive heat stress, this is achieved through elevations in cardiac output, which increases by ~3 l/min for every 1 °C increase in core body temperature [4, 10, 12–19], and can result in elevations in cardiac output of >5 l/min during severe whole-body hyperthermia. In basic terms, these profound increases in cardiac output can be mediated by one of the three mechanisms: an increase in heart rate, an increase in stroke volume, or a combination of the two.

Heart rate: Heart rate increases at a rate of ~35 beats/min/°C core temperature [3, 4, 12, 14–16, 20] and is indisputably the primary determinant of cardiac output during prolonged passive heat stress. The mechanisms underlying this increase are multifactorial, with roughly equal contributions from both neural pathways (60%) and a direct effect of temperature on the pacemaker of the heart itself (40%) [21]. Around 75% of neural-mediated increases result from the combined effects of increased sympathetic nerve activity and elevated levels of circulating catecholamines, altering the sino-atrial node pacemaker current and causing an increase in heart rate of ~7 beats/min for every 1 °C increase in mixed venous blood temperature.

Stroke volume: In contrast to heart rate, stroke volume has been found to remain unchanged or to even slightly increase during passive heat stress [4, 13, 22]. This finding is remarkable given that whole-body hyperthermia results in a profound reduction in central blood volume [23], cardiac filling time, cardiac filling pressure, and end-diastolic volume [3, 4, 22, 24–26], thereby decreasing the amount of blood available for ejection during each ventricular contraction. In spite of this, the preservation of stroke volume observed in the majority of studies to date suggests that compensatory adjustments to cardiac function are able to effectively counteract this challenge, either through improvements in diastolic function, systolic function, or both. Multiple studies have indicated that, despite decreases in end-diastolic volume, diastolic function may in fact be enhanced during hyperthermia [27, 28], thereby protecting stroke volume in the face of the decreased filling pressures previously described [22, 29]. Systolic function is also enhanced, as decreases in end-systolic volume mirror the drop in end-diastolic volume [22]. Although the cellular and molecular mechanisms underlying these regulatory adjustments are still not fully characterised and understood, potential explanations may involve the interaction of numerous functionally intertwined factors, including an enhanced intrinsic

myocardial contractility [22], an increased rate of myocyte relaxation [29], and improved cardiac 'suction' during ventricular filling as a result of an increased left ventricular untwisting velocity [22, 28].

3.2.3 Vascular Responses to Passive Heat Stress

Skin blood flow: The skin—with its large surface area (1.5–2.0 m^2) and abundant sweat glands (~2 million)—provides a 30 μm thick interface between the human body and external environment, and is therefore the most important tissue for thermoregulatory control during heat exposure. As a result, the majority of the increase in cardiac output and blood flow 'redistribution' from the splanchnic, renal, and cerebral organs observed during prolonged passive heating is likely directed towards this vascular bed (Fig. 3.1). Although the exact magnitude is unknown because direct measures at whole-body level has never been obtained, whole-body skin blood flow (estimated from the increase in cardiac output and decline in visceral blood flow) is routinely reported to be in the region of 7–8 l/min at the most extreme levels of resting heat stress. Early findings which led to the adoption of this figure [3, 13, 30], however, have rarely—if ever—been replicated, with levels closer to 4–5 l/min more commonly reported [4, 10, 12, 14–19] (Fig. 3.1). The control of skin blood flow during heat stress is a complex process involving both central and local thermoregulatory networks, and can be additionally modified by numerous non-thermoregulatory feedback mechanisms such as exercise [31], circadian rhythms [32], metaboreceptors [33], and baroreceptors [34]. Core temperature is often considered the major driving stimulus behind changes in skin blood flow at rest, as a 1 °C increase in core temperature has been demonstrated to have a ninefold greater effect on skin blood flow than the same increase in skin temperature. It should be noted, however, that the capacity to alter skin temperature during prolonged or severe heating is substantially greater than that possible for core temperature (~15 °C compared to ~3 °C), resulting in the potential for a much greater contribution from local temperature-sensitive mechanisms than is often appreciated. In addition, with these peripheral mechanisms able to induce a maximal cutaneous vasodilation even when core temperature remains unchanged [35–39], passive heat stress via exposure to high skin temperatures therefore has the capacity to elevate skin blood flow through predominantly local mechanisms prior to the development of increased core temperatures [17, 40]. Although increases in cardiac output are sufficient to offset this profound cutaneous vasodilatory response at rest, the superimposition of additional stresses such as dehydration, orthostatic stress, or—as will be discussed subsequently—exercise, may have implications for the maintenance of perfusion pressure.

Muscle blood flow: The question of whether increases in skin blood flow account for the full hyperaemic response during passive heating has remained highly controversial for many years, mainly due to the difficulty in separating skin (average depth

~30 μm) and underlying skeletal muscle tissue perfusion in vivo and the variety of experimental techniques employed among studies. With early research concluding that peripheral vasodilation was confined to the skin alone [41–43], the widely held view has been that skeletal muscle tissue is unresponsive to increases in deep tissue and blood temperature, which themselves can increase up to 5 °C during local and whole-body heating [10, 17, 42, 44, 45]. However, a number of later studies have since cast doubt on these findings. Firstly, substantial elevations in thigh skeletal muscle perfusion have been observed in studies using high frequency microwave diathermy to achieve intense local deep muscle heating [46–50]. While it could be argued that the extreme stimulus (muscle temperature 40–45 °C) employed during this technique is outside normal physiological limits, later studies involving techniques such as contrast-enhanced ultrasound [51], near infra-red spectroscopy [52], Xe^{133} clearance [53], laser Doppler flowmetry [54], and duplex Doppler ultrasound [10, 17, 55] have since supported these findings using more traditional and physiologically relevant methods of passive heating. Collectively, these data—together with the observation that resting metabolic rate in heat-stressed humans is modestly elevated—indicate that skeletal muscle blood flow may make a modest yet meaningful contribution to heat-stress hyperemia, particularly when considering its large contribution to body mass. The mechanisms underlying this response remain unclear, but appear to be solely mediated at the local level and—much like in the skin—are the net result of the augmented vasodilator activity overriding the parallel increase in vasoconstrictor activity [45, 53, 55–59]. Multiple vascular, interstitial, and intracellular signalling mechanisms sensitive to increases in temperature are likely involved in this response [56, 58–62]. One potential intravascular mechanism for control of tissue blood flow with alterations in local temperature could be the recently proposed temperature-dependent release of ATP from the circulating erythrocytes [45, 58]. This is an attractive possibility because of ATP's strong vasodilator and sympatholytic properties [45, 63–66] and the direct relationship between blood temperature and plasma ATP during passive and active hyperaemic conditions [10, 45, 58, 67].

Visceral blood flow: In direct contrast to the peripheral circulation, splanchnic (i.e. stomach, liver, spleen, pancreas, intestine) and renal (kidney) blood flow is substantially reduced in the hyperthermic state (Fig. 3.1). This phenomenon most likely occurs due to temperature-driven reflex vasoconstriction within the abdominal vascular beds, thereby contributing to the redistribution of blood flow and volume to the peripheral vasculature and aiding in the maintenance of mean arterial pressure [68]. The presence of this response was first suggested in classic studies in the 1960s, where central blood volume and hepatic blood flow were estimated to decrease in some [30, 68], but not all studies [3]. Revisiting this question in more recent times, estimates of visceral blood flow have demonstrated decreases in the region of 30% during severe heat stress [4], while estimates of blood volume in different regions of the human torso have suggested reductions of between 14% and 23% in the heart, central vasculature, thorax, inferior vena cava, and liver [23].

These findings, combined with the well-documented decrease in central venous (right atrial) pressure during heat stress, highlight the ability of hyperthermia to elicit selective vasoconstriction within the central vasculature, thereby aiding the redistribution of up to ~1 l/min blood flow to the periphery independently of the much larger increase in tissue blood flow and cardiac output (~5 l/min).

Cerebral blood flow: Passive elevations in core body temperature are associated with progressive reductions in cerebral (CBF) blood flow (~0.1 l/min or 15% fall in CBF; Fig. 3.1) [12, 69], with these effects occurring largely as a function of a hyperventilation-induced reduction in the potent cerebral vasodilator CO_2 [70]. Increases in body core temperature by as little as 1 °C can result in changes in minute ventilation and CO_2 of +40% and −10%, respectively [12], while further increases >1.5 °C result in marked hyperventilation and a decrease in CBF to levels ~20% below that seen in thermoneutral conditions. In contrast to blood perfusion in the brain-supplying internal carotid and vertebral arteries, blood flow in the external carotid artery, which perfuses the face and neck [12, 69], increases in a linear fashion with body temperature—leading to an overall elevation in blood flow to the head of ~0.5 l/min or 48% [12] (Fig. 3.1). This response appears to act independently of CBF [71], and is likely driven by thermoregulatory (thermosensitive) rather than blood gas or pH-related mechanisms [12, 69].

3.2.4 Summary

Passive heat stress results in a decrease in peripheral resistance, an increase in cardiac output, and a selective elevation and redistribution of blood flow from the core to the extremities, head, and superficial tissues of the torso. Despite modest increases in aerobic metabolism, this response is predominantly driven by thermosensitive mechanisms, resulting in significant cardiovascular strain even at rest, alongside tissue blood flows well in excess of that required to meet additional metabolic requirements.

3.3 Respiratory and Cardiovascular Responses to Exercise Heat Stress

The combination of exercise and heat stress places additional functional and regulatory demands on the cardiovascular system as both the metabolic and thermoregulatory demands of the body must be met. A long-standing question is whether the human circulation can appropriately meet the demands for blood flow of both the active skeletal muscles and skin when exercise heat stress engaging a large muscle mass is performed (e.g. cycling, running, rowing, swimming). The answer to this question is a complex one, with evidence suggesting different circulatory responses depending on both the magnitude of hyperthermia experienced and the

type of exercise performed (i.e. small vs. large muscle-mass exercise, prolonged submaximal exercise vs. incremental maximal exercise, etc.). While circulatory adjustments may be sufficient to support blood perfusion during small muscle-mass exercise and during early whole-body exercise at low-to-moderate intensities, the superimposition of heat stress during exhaustive whole-body exercise can rapidly push the cardiovascular system to its regulatory limits, where both peripheral blood flow and cardiac output become impaired [72, 73]. Under these circumstances, aerobic power and endurance capacity may be hindered due to the development of severe hyperthermia alongside an attenuated O_2 delivery to the active skeletal muscles, heart, and brain. In this section, we will explore how global cardiovascular function, O_2 delivery to regional tissues and organs, and removal of heat from exercising limbs are altered by exercise heat stress at different exercise intensities. Building upon our previous findings in resting conditions, we will begin with small muscle-mass exercise in the heat (when overall metabolic demands are low), before progressing to whole-body exercise at both submaximal and maximal levels. As the focus of this chapter is on whether the cardiovascular system is capable of sustaining dual metabolic and thermoregulatory requirements of exercise in the heat, we will address these questions using data from uncompensable heat-stress conditions, where skin temperature is held at very high levels (39–41 °C) while core temperature increases to different degrees (38.5–40 °C). As such, we will not address data pertaining to compensable heat-stress conditions, where core temperature can increase to 39–40 °C while becoming significantly dehydrated, but skin temperature is stable around 32–35 °C. Decrements in endurance capacity in these conditions are associated with the physiological and perceptual strain caused by dehydration and core hyperthermia, which are discussed elsewhere [74].

3.3.1 Respiratory Responses to Exercise Heat Stress

Oxygen transport from the atmospheric air to the skeletal muscle mitochondria (where the majority of ATP and heat are produced during exercise [75]) is a major determinant of aerobic power and endurance capacity, regardless of environmental conditions. As the lungs are the first potential site limiting oxygen transport through their impact on alveolar O_2 diffusion and—according to the Fick principle—arterial O_2 content, we will briefly discuss below whether or not respiratory responses may limit aerobic exercise capacity in the heat.

Submaximal exercise:Similar to observations during passive heat stress, prolonged submaximal exercise in the heat is accompanied by a ventilatory response higher than that required to meet metabolic demand [76–78]. This hyperventilation is characterised by an increase in breath frequency rather than tidal volume, and appears dependent solely on the rate of rise in core temperature, as skin temperature plays a negligible role [78].

Maximal exercise: Minute ventilation is also elevated during the submaximal stages of incremental exercise in the heat [76], before peaking at similar values to exercise in control conditions at maximum exercise intensities [76, 79]. In contrast to prolonged exercise, however, the ventilatory response during graded exercise is not solely dependent on thermal stimuli, as neural, metabolic, and reflex mechanisms may all play a role [80]. Regardless of the intensity of the exercise performed or the mechanisms involved, however, O_2 content is either unaffected or elevated even at the very highest levels of hyperthermia and/or exercise intensity, suggesting that decrements in O_2 transport and aerobic capacity during strenuous exercise in the heat do not arise from direct respiratory limitations negatively impacting blood O_2 content. In contrast, reductions in arterial CO_2 due to a hyperthermia-induced hyperventilatory response may have implications for the control of CBF, as will be discussed later in the chapter.

3.3.2 Cardiac and Peripheral Skeletal Muscle, Skin, and Visceral Responses to Exercise Heat Stress

Oxygen transport via the systemic circulation (i.e. convective O_2 delivery = blood flow x arterial O_2 content) is the next potential limiting step in oxygen utilisation by tissues and organs. In the following sections, we will review the systemic, muscle, skin, visceral, and cerebral vascular responses and their consequences on systemic and regional O_2 utilisation with emphasis on the influence of exercise type and intensity.

Submaximal exercise: Studies utilising small muscle-mass exercise (e.g. single-leg knee-extensor exercise) demonstrate an elevation in both leg blood flow and cardiac output during exercise heat stress—suggesting an additive effect of metabolic and thermoregulatory blood flow requirements when whole-body physiological demand is very low (power output 10–50 W; Figs. 3.3 and 3.4). Even at these low absolute exercise intensities, however, this effect is lower than would be expected given the magnitude of hyperemia observed when heat stress and exercise are studied in isolation. As an example, while severe passive hyperthermia results in elevations in leg blood flow and cardiac output of ~1 l/min and ~5 l/min, respectively, the superimposition of the same thermal stimulus onto single-leg knee-extensor exercise in the same individuals results in increases of only ~0.5 l/min and ~3 l/min—an attenuation of 40–50% of the response seen at rest [10, 55, 81]. When a larger muscle mass is engaged (e.g. cycling), the hyperthermia-induced augmentation in exercising limb blood flow disappears altogether (Fig. 3.4) [82–85], suggesting that the much greater metabolic and thermoregulatory effects of whole-body exercise on exercising leg blood flow (~16 to 19 l/min at peak exercise) cancel out the independent influence of hyperthermia observed during passive heating or small muscle-mass exercise (Figs. 3.1 and 3.4). This response is likely due in part to an attenuation in the skin circulation, as reduced cutaneous vasodilator activity during exercise has been shown to sharply curtail skin blood flow (compared to resting

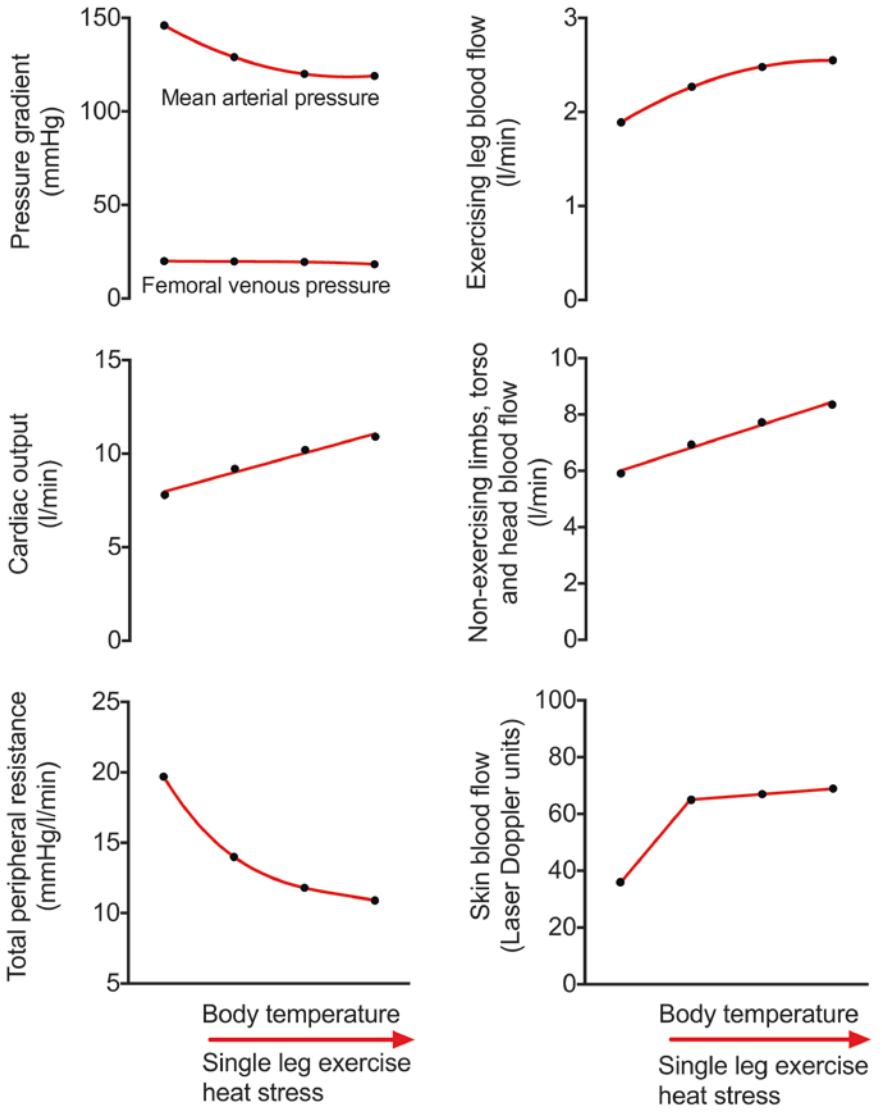

Fig. 3.3 Systemic and regional haemodynamic responses to combined constant-load single-leg knee-extensor exercise and graded heat stress. Redrawn from [10]

values) when core temperature increases >38 °C [86]. Although restrictions in skin blood flow may be expected to compromise thermoregulation, a number of factors likely help to offset this apparent insufficient vasodilatory response. Firstly, exercise reduces the core temperature at which sweating is initiated, thereby facilitating heat loss at an earlier stage [87]. Secondly, active muscle blood flow plays a key role in

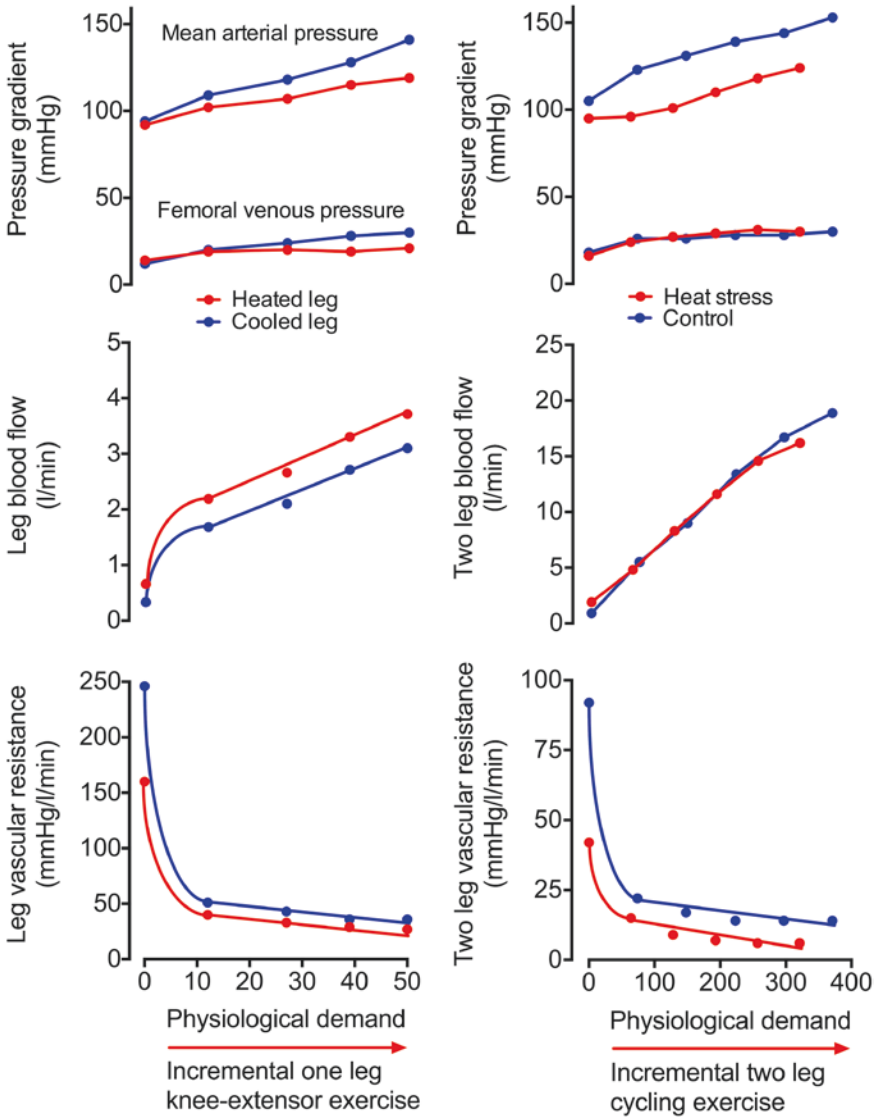

Fig. 3.4 Leg haemodynamic responses to incremental knee-extensor exercise to volitional exhaustion and incremental cycling to voluntary exhaustion with exposure to heat stress (induced by 1 h of whole-body exposure to heat stress with a water-perfused suit prior to exercise and maintained during exercise) and control conditions. Redrawn from [55, 85], respectively

thermoregulation during exercise, aiding in the convective transfer of heat from the interior of the exercising muscles to the overlying skin. This heat transfer pathway can account for the dissipation of >60% of the leg energy turnover during both prolonged [88] and incremental exercise [67], and thus may explain why exercise heat stress has no additive effects on locomotor limb blood flow during whole-body exercise. It may also help to explain why cardiac output only shows small increases

(1–3 l/min) compared to passive heat stress or exercise in control conditions [10, 82–85], as increases in exercising limb blood flow account for the majority of the increase in cardiac output during constant-load and incremental exercise [6, 7, 64, 72, 89]. Despite these haemodynamic adjustments, progressive increases in core temperature will not be prevented during uncompensable heat-stress conditions, and whole-body hyperthermia therefore becomes an important factor in the development of fatigue during prolonged exercise in hot environments [90].

Maximal exercise: The combination of heat stress and whole-body exercise at near-maximal intensities (e.g. 80–100% $\dot{V}O_{2max}$) poses one of the greatest challenges to cardiovascular control. Severe hyperthermia results in a quicker onset of fatigue due to a more rapid reduction in mean arterial blood pressure, cardiac output, and blood flow to the working skeletal muscles of the locomotor limbs compared to exercise at temperate ambient temperatures [72, 73] (Fig. 3.5). This fall in cardiac output occurs due to a decline in stroke volume, as heart rate is higher over

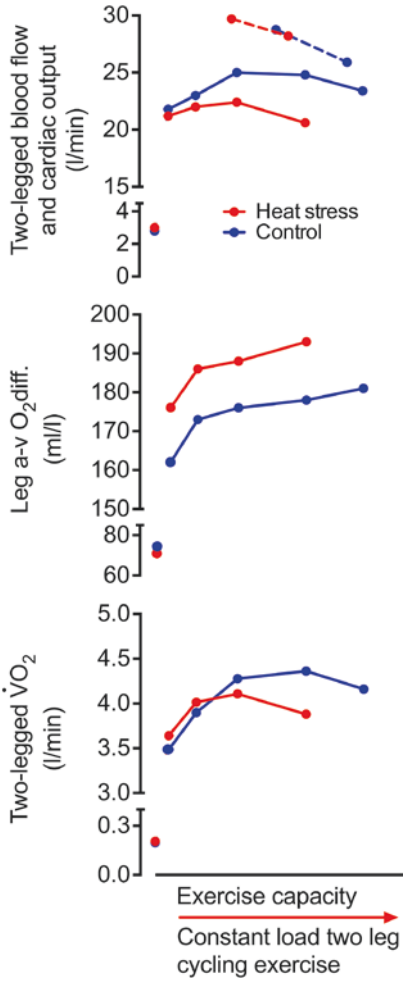

Fig. 3.5 Cardiac output (dashed lines) and leg haemodynamic and metabolic responses (solid lines) to constant-load cycling to voluntary exhaustion with exposure to heat stress (induced by 1 h of whole-body exposure to heat stress with a water-perfused suit prior to exercise and maintained during exercise) and control conditions. Redrawn from [72]

time and attains similar maximal values compared to temperate conditions [72, 73, 85, 91]. Similar to passive heat stress, incremental exercise results in selective reductions in visceral blood flow (up to 20–40% of resting values). The impact of exercise on visceral vasoconstriction appears stronger than that observed during graded passive heat stress [92, 93], and as a result, the addition of heat stress onto exercise does not seem to change the rate of decline in visceral blood flow as exercise intensity increases. It is therefore unlikely that redistribution of blood flow from splanchnic and renal organs contributes significantly to the peripheral blood flow responses during exercise heat stress. Ultimately, the fall in exercising leg blood flow appears to be associated with reductions in perfusion pressure secondary to the fall in cardiac output, rather than an active vasoconstriction process in the exercising limb itself, as limb vascular conductance is largely stable throughout exercise [85]. Although this accelerated decline in flow is often portrayed as an inability of the heart to supply both skin and muscle circulations for metabolic and thermoregulatory purposes [8], two major observations argue against a role of skin hyperperfusion per se as the limiting factor affecting maximal endurance capacity in hot environments. Firstly, stroke volume is reduced to a greater extent during maximal exercise in temperate conditions, compared to the same exercise performed in the heat [72]. Secondly, despite decreases in both stroke volume and cardiac output immediately prior to exhaustion in a hot environment, their absolute values remain elevated compared to those observed in temperature conditions [72]. Instead, a shortened cardiac cycle—perpetuated by hyperthermia-induced increases in heart rate—likely compounds the fall in cardiac filling and end-diastolic volume [22, 72, 94]. In these non-steady state physiological conditions, maximal heart rate is attained at a faster rate than in comparable exercise in a temperate environment and, immediately prior to exhaustion, is accompanied by falls in stroke volume, cardiac output, perfusion pressure, leg blood flow, and eventually, O_2 delivery to the working skeletal muscle [72, 90] (Fig. 3.5). This reduction in convective O_2 delivery reduces limb aerobic metabolism, because maximal functional O_2 extraction of the exercising limb tissues (~90 to 95%) is achieved in the early stages of severe-intensity exercise [45, 72]. Ultimately, these hemodynamic alterations compromise active limb and systemic oxygen uptake and, at least in part, contribute to the reduced aerobic power and endurance capacity when exercising in a hyperthermic state (Fig. 3.6).

3.3.3 Cerebrovascular Responses to Exercise Heat Stress

The cerebral vascular bed is small in comparison to other peripheral tissues, and is strongly regulated by autoregulation and arterial CO_2 levels. As such, its response to both heat stress and exercise is distinct to that observed in other peripheral vascular beds, and may independently contribute to impaired exercise capacity. Dynamic exercise requires the activation of motor and cardiorespiratory neurons, and is generally thought to necessitate increases in CBF and O_2 supply in order to meet the presumed greater ‘brain metabolic activity’ [95, 96]. As a result, any

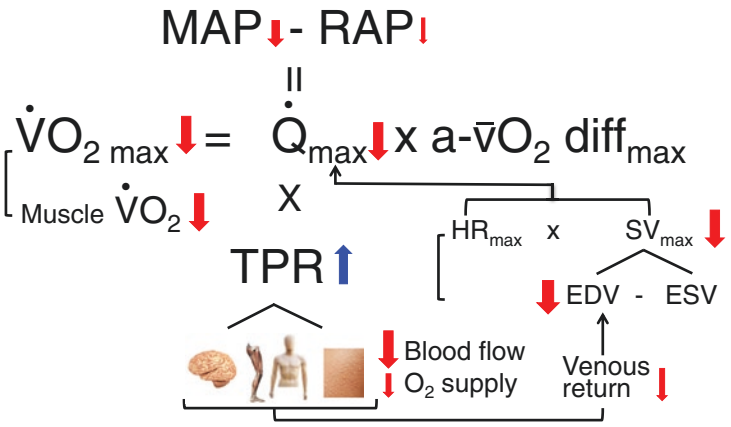

Fig. 3.6 Schematic illustration of the impact of severe whole-body exercise heat stress on physiological function according to Ohm's law and the Fick principle. Note that impaired aerobic capacity is associated with blunted peripheral blood flow and cardiac output and enhanced peripheral vascular resistance, preferentially affecting active skeletal muscle. Diminished venous return and filling of the heart is proposed as a primary factor reducing stroke volume, and thus cardiac output

factors compromising CBF may potentially compromise motor neurone activation and exercise capacity.

Submaximal exercise: At the onset of prolonged submaximal exercise (<60% $\dot{V}O_{2max}$), CBF increases by ~20% above baseline values, irrespective of the ambient conditions [76, 97–100]. If submaximal exercise is continued in a cool environment, CBF remains stable as long as the rise in internal body temperature and associated ventilatory and blood CO_2 responses are prevented [76, 91, 101]. However, the development of hyperthermia during exercise heat stress results in a relative hyperventilation (discussed previously), an accompanying reduction in the potent cerebral vasodilator CO_2—even at submaximal exercise intensities—and ultimately a progressive reduction of CBF back towards resting baseline values [76, 100, 101].

Maximal exercise: When incremental exercise is performed to near-maximal levels in temperate conditions, the augmented minute ventilation observed during the later stages (i.e. above the ventilatory threshold) also results in a fall in CBF towards baseline values [97, 98, 102]. When exercising in a hyperthermic state, this fall in CBF occurs both at a lower absolute work rate during incremental protocols [85, 99] and sooner during severe constant-load exercise [73], suggesting that augmented core temperature plays a role in the differing CBF dynamics. Similar to passive heat stress, blood flow to other tissues across the head remains high, with external carotid artery blood flow shown to more than double from resting values (up to ~700 ml/min) [73, 99, 100, 103]. This substantial increase in blood flow is related to the rise in body temperature, which is perhaps unsurprising as the external carotid arteries in part perfuse the cutaneous circulation of the face and neck. While this association has led some to hypothesise that the rise in external carotid artery blood flow may 'steal' blood destined for the cerebral vasculature [98], this is unlikely as changes in

blood flow in these different tissues appear unrelated [69]. Despite the marked fall in CBF, however, global aerobic metabolism of the brain does not appear to be compromised at any level of exercise intensity due to compensatory elevations in brain O_2 extraction [73, 99]. Thus, reduced brain oxygen consumption is unlikely to contribute to the fall in aerobic power and endurance capacity during exercise heat stress (Fig. 3.6).

3.3.4 Summary

Exercise heat stress can place substantially greater functional and regulatory demands on the cardiovascular system compared to heat stress alone. Although the magnitude of cardiovascular response differs depending on the overall metabolic demand, the independent circulatory effects of heat stress and exercise are not additive. On the contrary, exercising limb blood flow during moderate to heavy intensity whole-body exercise is actually not different from that seen in normal conditions. The superimposition of heat stress onto maximal whole-body exercise, however, more rapidly pushes the cardiovascular system to its regulatory limits, where systemic and regional tissue and organ blood perfusion become restricted. While some organs can cope better with the decline in convective O_2 supply (e.g. the brain), a compromised active skeletal muscle O_2 metabolism is a major factor explaining why aerobic capacity is reduced in the heat-stressed human.

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