Exertional heat stroke

Exertional heat stroke is a potentially lethal condition that can occur in otherwise healthy individuals participating in endurance exercise. Its recognition in the field and effective, prompt treatment by active cooling is essential if mortality and permanent neurological morbidity is to be avoided.

The increasing popularity of mass participation endurance events necessitates that on-site medical teams be well versed in the management of both common and life-threatening conditions. Exertional heat stroke is one such condition, which if left untreated can be fatal.

Heat stroke represents the severe end of a spectrum of heat-related illnesses and results from an inability to balance metabolic heat loss with heat production. Classical heat stroke is commonly seen during hot weather conditions and found in sedentary individuals, usually with comorbid conditions or in the elderly. Exertional heat stroke is seen in exercising individuals and may present even in cooler weather conditions. Both conditions can be fatal, with exertional heat stroke the third highest cause of death for athletes.

The ABCDE resuscitation algorithm is essential for any resuscitation, not least in a collapsed athlete. However, at sporting events it is the authors' opinion that if the core body temperature is not considered immediately as part of the management rubric, the ABCDE algorithm will be a fruitless exercise. Hence, at endurance sporting events, we propose that TABC should be considered as an essential modification to the usual algorithm, with T representing immediate consideration being given to the core body temperature. This suggestion is not out of keeping with current knowledge concerning the use of therapeutic hypothermia in the management of out of hospital cardiac arrests as well the European Resuscitation Councils and American Heart Association guidance on management of hyperthermia (Field et al, 2010; Koster et al, 2010; Soar et al, 2010).

Definition

Exertional heat stroke is defined as a core temperature over 40°C accompanied by CNS dysfunction such as confusion, ataxia, reduced level of consciousness, seizures or coma. Heat exhaustion is a less severe presentation of heat-related illness but may rapidly progress to exertional heat stroke; in heat exhaustion the core temperature is 37–40°C and there are no neurological symptoms.

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Thermoregulation

Humans are homeotherms that maintain a core body temperature close to 37°C through complex feedback mechanisms coordinated centrally by the hypothalamus, where an average body temperature is compared against a 'set point', and efferent responses are modulated accordingly. At rest heat is generated by metabolism and comes mainly from the major organs, which constitute the body's 'core'. During exercise a significant amount of extra heat is released from active skeletal muscles. Excessive heat is transferred to the body's surrounding 'shell' (skin and subcutaneous tissues) via the circulation and then to the environment, in order to maintain normothermia. Heat dissipation can only occur if a temperature gradient exists from the core through to the shell and then to the environment. If the temperature of the environment increases, the gradient is diminished. Also, if barriers exist to the transfer of heat from the core to the periphery, such as a low cardiac output or profound vasoconstriction, heat will accumulate in the core. This situation may be found during endurance swims or triathlon swims where a wetsuit is worn and where water temperatures may be elevated, or as a result of intrinsic athlete-dependent factors which prevent adequate heat loss from the core.

Heat is dispersed to the environment through four exchange mechanisms: radiation, conduction, convection and evaporation. Radiation accounts for the majority of heat lost from the naked body at rest while evaporation, by far the most effective cooling mechanism, becomes increasingly important as core body temperature rises. As with heat transfer, there must be a water vapour gradient to facilitate evaporation, hence humid conditions hinder heat dissipation to the environment.

Exercising in hot conditions

The metabolic rate can increase up to 20 times above the basal rate during exercise (Weibel et al, 1992), and in order to maintain normothermia the additional heat burden must be removed from the body.

Providing the extra heat load from exercise does not exceed heat loss capacities, a homeothermic equilibrium can be reached at a higher core temperature by increasing cardiac output, cutaneous blood flow and sweat production. Compensatory vasoconstriction in the renal and splanchnic circulation occurs to allow a greater blood volume to perfuse the skin. Sweating increases as core body temperature rises until 39°C, when maximal sweat rates are achieved. Above this temperature threshold heat loss becomes increasingly ineffective, and core body temperature can begin to rise dramatically if exercise continues. Also if atmospheric relative humidity rises above 60% the risk of exertional heat stroke greatly increases because sweating becomes less effective. Environmental heat stress can be best assessed using a wet bulb globe temperature. This heat stress index will take radiant heat and humidity into consideration and can be used to assess the likelihood of exertional heat stroke occurring at athletic events (Armstrong et al, 2007; Roberts, 2010).

The pathophysiology of heat stroke

The pathophysiology of exertional heat stroke involves many complex organ interactions, including the hypothalamus, heart and gut. In the trained maximally adapted athlete, the systems work synergistically to enable an optimum performance. However, in the decompensated hyperthermic state, a number of factors contribute to the eventual decline of the athlete (*Table 1*).

Direct cellular heat stress

In the adapted state, heat shock proteins – small proteins produced within the cell in response to cellular stress (De Maio, 1999) – are able to repair the damage caused by non-lethal hyperthermia; their production permits a greater tolerance to heat at a cellular level (Feige and Mollenhauer, 1992). However, in exertional heat stroke, hyperthermia in the overwhelmed system causes direct cellular damage, including damage to ion channels and lipid membranes resulting in increased cell permeability with attendant disruption to cell proteins and eventual apoptosis.

Thermoregulatory failure

The preoptic area and anterior hypothalamus play an important role in thermoregulation. A study suggests that metabolic acidosis may inhibit warm-sensitive neurons in the preoptic area and anterior hypothalamus, thereby disrupting normal heat loss mechanisms (Wright and Boulant, 2007). This suggests that metabolic acidosis in exertional heat stroke may have a direct causal effect in athletes and may explain the occurrence of exertional heat stroke in less extreme environmental conditions.

Table 1. Factors contributing to decompensation in exertional heat stroke

Direct cellular heat stress
Cardiac conduction abnormalities
Proinflammatory cytokines
Circulatory dysfunction

Cardiovascular instability

It is unclear whether dehydration is a causative or an associated factor in exertional heat stroke. It was previously felt that dehydration representing >2% loss of body weight during competition would significantly affect athletic performance and from this one might surmise that dehydration would have a major role to play in the causation of exertional heat stroke. Indeed, in the authors' experience it is not uncommon for the athlete suffering with exertional heat stroke to require upwards of 2 litres of fluid during resuscitation. However, Zouhal et al (2011) showed that athletes with a greater percentage body weight loss during the race produced faster race times. The authors' observation that athletes suffering with exertional heat stroke tend to present with hyperdynamic circulations would also be in keeping with the thinking that dehydration or rather the need for extensive fluid resuscitation is an associated rather than causative factor in exertional heat stroke.

Cardiac conduction abnormalities

The adverse effects of environmental heat stress on the myocardium are diverse and multifactorial. Studies conducted in heat stroke victims report that a hyperdynamic circulation with sinus tachycardia is a common finding, with atrial fibrillation and sinus bradycardia also being possibilities (al-Harthi et al, 1992). Electrocardiogram tracings demonstrating ST segment depression, and non-specific T wave changes may also be found (al-Harthi et al, 1992). It is likely that the effects on the myocardium are both locally and centrally controlled (Samonina and Abushinova, 1988). It has also been suggested that proinflammatory cytokines have a role in cardiac contraction abnormalities and are further evidence of the multifactorial nature of the decline seen in exertional heat stroke (Ren and Wu, 2006).

Systemic inflammatory response

A systemic inflammatory response is a recognized final common pathway in many conditions, including heat stroke, sepsis, burns and trauma, and typically leads to multiorgan damage and death (Purvis and Kirby, 1994; Leon and Helwig, 2010). In exertional heat stroke, several factors contribute to this systemic inflammatory state. Redistribution of blood flow away from splanchnic vessels, following increased exercise intensity and heat stress, result in the translocation of

endotoxins across the gut wall which in turn stimulate the release of proinflammatory cytokines (Gonzalez-Alonso et al, 2008). This has been termed 'heat sepsis' by a number of authors (Lim and Mackinnon, 2006; Selkirk et al, 2009). Exercising muscles also release proinflammatory cytokines (Nieman et al, 2001) and systemic inflammatory response has been associated with hyperthermia after endurance activity (Fehrenbach and Schneider, 2006). Indeed, severity of illness in heatstroke is associated with interleukins 1 and 6, and interferon-gamma (Bouchama et al, 1993). In addition, an imbalance in cellular respiration resulting in excessive production of reactive oxygen species – a situation known as 'oxidative stress' – will further stimulate production of proinflammatory cytokines. Proinflammatory cytokines in turn will cause further oxidative stress resulting in cell injury and apoptosis (Block and Hong, 2005).

Proinflammatory cytokines have an effect on cognitive function and may explain the soft neurological signs associated with exertional heat stroke. One study has shown a correlation between cooling time and interleukin-1 levels (Chang, 1993). However, ongoing raised levels of proinflammatory cytokines may explain intermediate and long-term neurological sequelae associated with exertional heat stroke (Bouchama et al, 1993).

Factors predisposing to exertional heat stroke

There are a number of individual and environmental risk factors that are thought to increase the likelihood of exertional heat stroke (*Table 2*). Conditions that are unusually hot for a region increase the risk of exertional heat stroke as individuals are unlikely to be acclimatized to the higher temperature, even if the absolute temperature is relatively low (Roberts, 2010) and it may take up to 14 days to become adequately acclimatized to the heat (Wendt et al, 2007).

Table 2. Predisposing factors in the development of exertional heat stroke

Intrinsic (individual) risk factors	History of exertional heat illness
	Inadequate heat acclimatization
	Lower level of fitness
	Dehydration
	Higher proportion of body fat
	Presence or recent history of febrile illness
	Sun burn
	Recent or chronic alcohol consumption
Extrinsic (environmental) factors	High wet-bulb globe temperature
	High humidity
	Excessive clothing (including wetsuits)

Malignant hyperpyrexia

It is unclear whether malignant hyperpyrexia, induced by certain anaesthetic agents, and exertional heat stroke are related conditions. While there have been a number of case reports of the two disorders having been diagnosed in the same individual (at different times), a clear association between them has yet to be demonstrated (Hopkins et al, 1991; Tobin et al, 2001; Rae et al, 2008; Capacchione and Muldoon, 2009). Much interest surrounds exertional heat stroke victims in whom only minimal exercise activity was reported. The ineffectiveness of dantrolene (the standard treatment for malignant hyperpyrexia) in the treatment of exertional heat stroke suggests that the two are not related (Hausfater, 2005).

Management of exertional heat stroke

Diagnosis of exertional heat stroke

In the assessment and immediate management of the collapsed athlete, most medics would accept the importance of the 'ABC' (airway, breathing, circulation) resuscitation algorithm, but exertional heat stroke will be missed if a raised core body temperature is not suspected. Although the timely measurement of the core temperature may not be possible, cooling can begin immediately and at the same time as the airway is being assessed. It is the authors' experience that some collapsed athletes will immediately restart spontaneous breathing after iced water is applied to the head and this response may represent immediate bradycardia or return to sinus rhythm by the mammalian diving reflex (Paulev et al, 1990). In addition, the patient may present with profound unconsciousness (Glasgow coma score 3) but it is the observation of the authors that tracheal intubation is rarely required, with rapid cooling improving the Glasgow coma scale and negating the need for this intervention.

A core (rectal) temperature above 40°C and the presence of neurological dysfunction such as confusion, ataxia, reduced level of consciousness, seizures or coma is diagnostic of exertional heat stroke. A high index of suspicion must be maintained in those who have neurological changes and a temperature between 37 and 40°C; treating as for exertional heat stroke is advised in this scenario. A rectal temperature should be performed in any competitor who has collapsed or lost consciousness at an endurance sporting event, in order to confirm or rule out exertional heat stroke. Other forms of temperature measurement are likely to give falsely low readings as a result of the reduced peripheral circulation.

Rapid field diagnosis of exertional heat stroke requires no specific laboratory investigations, however, near-patient testing devices are routinely used at large mass participation endurance sporting events. New rehydration guidelines for athletes, recommending 'ad libitum' drinking during events, rather than the previous advice

Table 3. Systemic manifestations of exertional heat stroke

System	Dysfunction in exertional heat stroke
Cardiopulmonary	Tachycardia, hyperventilation, pale skin and profuse sweating
	Acute circulatory failure
	Electrocardiogram abnormalities including long QT
	Progression to myocardial depression, stunning and infarction
Neurological	Confusion, agitation, combativeness, slurring of words, visual disturbance, ataxia, collapse, seizures and coma
Gastrointestinal	Nausea, vomiting and diarrhoea
	Derangement of liver function and hepatic failure
Musculature	Painful, sore and cramped muscles
	Raised creatinine kinase and rhabdomyolysis
Metabolic	A combined respiratory alkalosis and concomitant metabolic acidosis
	Elevation of serum creatinine kinase, aspartate transaminase and lactate dehydrogenase
	Hyperphosphataemia
	Hypocalcaemia
Haemotological	Thrombocytopaenia
	Leucocytocis
	Disseminated intravascular coagulation
	Haemorrhagic complications including the skin, lungs, conjunctivae and myocardium
Renal	Acute kidney injury
	Rhabdomyolysis

which stated athletes should drink as much as tolerable (Convertino et al, 1996; Sawka et al, 2007) should reduce the number of cases of hyponatraemia secondary to water intoxication. However, blood sodium measurements are nevertheless checked, as are blood glucose and acid-base status.

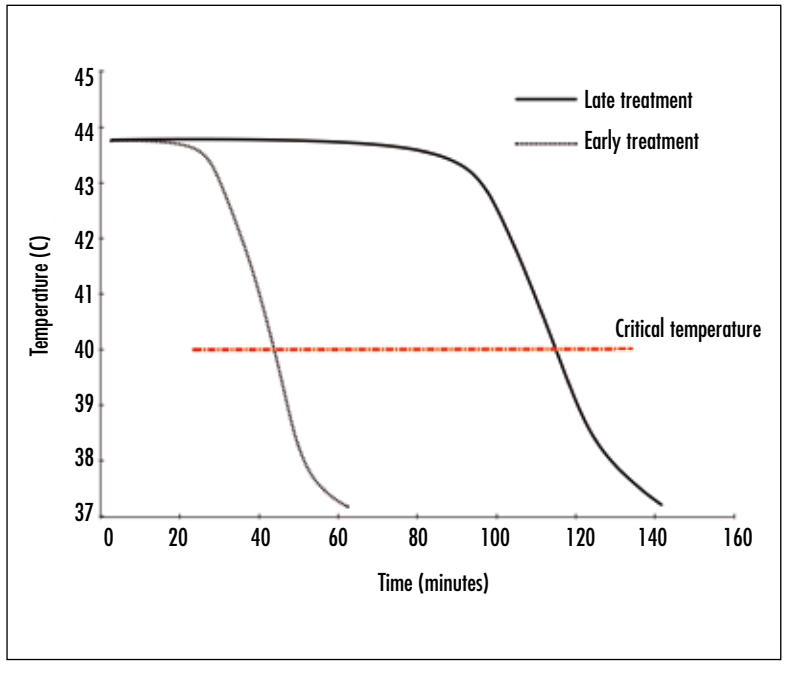
Non-specific symptoms of exertional heat stroke can include weakness, flushing, profuse sweating and subtle changes in personality. *Table 3* lists the full range of potential clinical findings.

Treatment of exertional heat stroke

Exertional heat stroke is a medical emergency. The delivery of immediate on-site aggressive cooling therapy together with appropriate cardiovascular support is therefore paramount for a complication-free survival. The product of temperature and exposure time (degree-minutes) accurately predicts the likelihood of long-term successful outcome (*Figure 1*) (Henderson et al, 1986; Bouchama and Knochel, 2002). Rebound hypothermia can occur with any cooling method and cessation of active cooling should occur at 38.5°C to avoid this (Harker and Gibson, 1995; Proulx et al, 2006). It is therefore important to monitor rectal temperatures until discharge or admission to hospital.

Although neurological dysfunction is usually transient, several case studies suggest that neurological insult may persist beyond resolution of hyperthermia with one study in classical heat stroke reporting 76% of patients as having some degree of neurological dysfunction upon discharge (Dematte et al, 1998).

Figure 1. The cooling curves for early and late treatment intervention in exertional heat stroke. In this series of athletes, those in the early treatment group all survived where as those who were inadvertently treated late all died. Adapted from Roberts (2005).



External cooling methods

A systematic review of clinical studies was unable to identify reliable clinical evidence of the optimum cooling technique (Bouchama et al, 2007). In practice, the selection of a particular method is as much governed by expedience as by clinical evidence. Water immersion is said to produce cooling rates of 0.2°C/minute with low mortality and morbidity and is considered by some to be the 'gold standard' (Costrini, 1990; Armstrong et al, 2007). However there are several limitations to this technique including the induction of shivering and subsequent vasoconstriction, as well as the practical difficulties of monitoring rectal temperature and cardiovascular status while the patient is immersed. Dousing in cool water (at 10–12°C) combined with massage of major muscle groups with ice packs has been shown to be at least 70% as effective as cold water immersion (McDermott et al, 2009).

Various evaporative techniques have been described which involve dousing the skin with water and directing dry air over the surface of the skin. Another variation now widely used at mass participation events involves using towels soaked in iced water being applied over the torso and around the head and neck, with ice packs being applied in the axilla and groin areas. In the authors' experience this typically sees cooling rates of around 0.2°C/minute. 'Body cooling units' have been used with some success but are expensive and may not be practical for large events (Grogan and Hopkins, 2002).

Intra-body cooling methods

Other methods of rapidly reducing core temperature include intravascular cooling, gastric, colonic, bladder and peritoneal lavage with cold fluids, and cold haemofiltration. The use of ice cold intravenous fluids is now well documented in the management of out of hospital cardiac arrests and may provide a useful additional method of cooling, particularly as fluids are required for cardiovascular resuscitation (Lyon et al, 2010; Arulkumaran et al, 2011). However, there are concerns regarding the potential risk of cardiac arrhythmias, myocardial infarction, electrolyte disturbances and seizures (Sinclair et al, 2009; Nielsen et al, 2011).

Pharmacological treatments

Dantrolene is a skeletal muscle relaxant that reduces muscle rigidity and heat production in the sustained muscular contraction seen in malignant hyperthermia and neuroleptic malignant hyperthermia. Current evidence, including a randomized double-blinded trial, suggests that dantrolene is ineffective in the treatment of exertional heat stroke (Bouchama et al, 1991). The justification for use of dantrolene is often the possibility of ingestion of recreational drugs which, although not impossible, is much less likely among serious athletes taking part in long distance events. Empiric use may be considered in athletes who do not respond to the appropriate active cooling techniques. The sheer volume of dantrolene needed to reverse malignant hyperthermia also precludes its routine use in the field.

Fluid resuscitation

It is unclear how much and what type of rehydration fluid should ideally be given following exertional heat stroke. The European Resuscitation Council's guidelines state: 'Use haemodynamic monitoring to guide fluid therapy. Large volumes of fluid may be required', with no references accompanying the statement (Soar et al, 2010).

There is no right answer when it comes to correct fluid management in the critical care situation and the same is true for exertional heat stroke. While much debate surrounds the effects of dehydration on performance in sport, its effect on outcomes after exertional heat stroke are not known. It is the authors' practice, in the unconscious athlete, to start with intravenous compound sodium lactate (Hartmann's solution) given as quickly as the intravenous access allows. In general 2–3 litres of fluid are required intravenously. The athlete will then drink a further average of around 500–1000 ml of fluid before he/she passes urine. It is also the authors' practice to add 10–20 ml of 50% dextrose to the Hartmann's solution. Pure dextrose solutions (e.g. 5%, 10% dextrose) are not used because of their potential to lower serum sodium levels if infused in large quantities.

Again, the interpretation of the literature with regards to blood glucose and glucose administration is not straightforward. In the context of collapse at an endurance event, giving glucose is safer than not giving glucose, when blood glucose measurement may be inaccurate. In the context of cardiac arrest, raised blood glucose levels have been associated with poor outcome. Some have suggested that this poor outcome may be explained by the nature of the resuscitation (Longstreth et al, 1986; Calle et al, 1989). However, other studies have shown that glucose administration may be an important adjunct during resuscitation (Wu et al, 2008; Beiser et al, 2009).

Discharge and 'return to play' after exertional heat stroke

It is the authors' experience that successfully treated athletes go home within 2 hours of first presentation after exertional heat stroke. Stable normothermia must be established and patients must be able to take fluids orally and must have passed urine. Athletes should also be able to demonstrate a return to normal cognition. It is often the case that although the core temperature rapidly returns to normal (usually within 15 minutes of presentation) after aggressive cooling, at this stage, the patient remains disorientated. A pen and paper digit-symbol-substitution-test is used by the authors to chart return towards normal cognition before discharge from the field hospital.

If any of these criteria are not satisfactorily attained or normothermia is not achieved then hospital transfer is mandatory, ideally in the company of an experienced clinician. Patients must also be warned of the late onset of complications, particularly hepatic and renal injury, and advised to seek medical attention if symptoms occur.

Athletes will often wish to know when they can safely return to training and competition. The American College of Sports Medicine have set out general guidance regarding 'return to play' (Armstrong et al, 2007) (*Table 4*), but more specific measures may be required to avoid ongoing morbidity.

Anecdotal evidence suggests that while athletes return to training within a few weeks of exertional heat stroke, they do not feel that they are back to optimum function for some months. Indeed, although digit-symbol-substitution-test scores return towards normal before discharge, when these figures are compared with digit-symbol-substitution-test scores for non-exertional heat stroke athletes (unpublished data), the scores suggest ongoing neurological morbidity. This is in line with studies showing ongoing elevation of proinflammatory cytokines (Bouchama et al, 1993). Chronic exposure of cells to circulating proinflammatory cytokines as well as elevated production of reactive oxygen species may lead to increased oxidative stress and concomitant mitochondrial dysfunction with injury to mitochondrial structures and mitochondrial DNA (Tatsumi et al, 2004; Ruchko et al, 2005). Ongoing failure of proper mitochondrial functioning in aerobic respiration may result in the earlier onset of metabolic acidosis with subsequent bouts of exercise (Robergs et al, 2004) and hence be an explanation for ongoing underperformance. Measurement of proinflammatory cytokines and markers of oxidative stress as well as electroencephalography measurements may offer more specific tools to guide return to optimum function and may avoid repeat episodes of exertional heat stroke in the susceptible athlete.

Conclusions

Exertional heat stroke is a life-threatening condition that can easily be overlooked as a diagnosis unless a patient's core temperature is actively sought. The ever-growing popularity of mass public sporting events encourages under-trained individuals to participate above their capability, sometimes in environmental conditions that heighten the risk of developing exertional heat stroke. Medical personnel at these sporting events need to be educated about exertional heat stroke and have the facilities to cool and treat casualties immediately on scene. Should transfer to hospital be required, an understanding of this condition by the receiving medical team is also essential. **BJHM**

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Table 4. Guidelines for 'return to play' following an episode of exertional heat stroke

To refrain from exercise for at least 7 days after discharge from medical care
Follow up visit after 1 week to assess for the presence of organ dysfunction
Exercise must begin lightly in a cool environment, gradually increasing in duration and intensity over time
A 2-week period of heat acclimatization should be undertaken if intending to compete in a hot environment
If return to normal physical activity is troublesome, a laboratory exercise-heat tolerance test 1 month post exertional heat stroke can be considered

From Armstrong et al (2007)

KEY POINTS

- Exertional heat stoke is a common diagnosis at mass sporting events in temperate climates.
- Rapid diagnosis is an essential component of management and a low threshold of suspicion must be maintained in the collapsed athlete with neurological signs.
- Survival after exertional heat stroke depends on rapid active cooling.
- 'ABC' resuscitation is fruitless without recognition that a raised core temperature is the main driver in the pathology of exertional heat stroke.

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