EXERTIONAL HEAT ILLNESS IN THOROUGHBRED RACEHORSES: OBSERVATIONS AND TREATMENT IN THE FIELD

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The author would like to acknowledge the influence of Professor David Hutchins in learning to appreciate the value of simple clinical observations.

Data on the incidence of exertional heat illness (EHI) in thoroughbred racehorses is unavailable but during the summer months in eastern Australia when the ambient temperature and humidity are high, horses suffering from EHI manifesting as a heat stress/heat stroke syndrome are not uncommon. Appropriate management of these horses is critical as EHI represents a medical emergency. This article attempts to define and describe the spectrum of EHI syndromes and to provide a rationale for treatment protocols in the field.

Introduction

The thoroughbred racehorse is an exceptional athlete, galloping at very high work intensity at speeds of about 70 kilometres per hour over relatively short distances, with some races completed in less than a minute. To achieve this, the heart rate peaks at 250 beats per minute, cardiac output may rise to 450 litres a minute and oxygen consumption is from 160 to 200 millilitres of oxygen per kilogram per minute (Sharp, 2012; Young, 2003; Hodgson and Forman, 2014). It has been calculated (Hodgson, 2014) that heat production under such circumstances can reach 450 kcal/minute, and possibly elevate core body temperature by about 1°C/minute. Unless the heat stored during exercise is dissipated the body temperature will continue to rise to a hypothetical 42°C, which has dire consequences for the animal concerned because heat is toxic to cells and initiates a complex, progressive array of pathophysiology (Bouchama and Knochel, 2002).

In moderate environmental conditions (for example, temperature 20 to 25°C and humidity below 30%) metabolic heat from strenuous exercise is dissipated by radiation and convection to the atmosphere and through evaporative cooling by sweating. However, when the skin temperature and ambient temperature are equal, evaporative cooling is the only avenue for heat loss. In conditions where there is high ambient humidity, the water vapor pressure gradient from skin to air is decreased, thus limiting the ability of the body to lose heat by sweating and posing a serious threat to thermoregulation (McCutcheon and Geor, 2004).

While the physiology of thermoregulation in the horse is comprehensively described in the literature (for example, Guthrie and Lund, 1998; Hodgson, 2014; Hinchcliff et al., 2004; Hodgson et al., 1994), there is scant information on the clinical syndromes of thermodynamics observed in thoroughbred racehorses, whose performances are characterized by short bursts of strenuous, largely anaerobic activity at high intensities (Gerard et al., 2014). This is in sharp contrast to the endurance horse, whose heat exhaustion syndromes have been extremely well documented but are essentially quite different, endurance activity being by nature aerobic, protracted and submaximal in nature, with dehydration a key feature (Lucke and Hall 1980; Landon Fielding et al., 2009).

In the capacity of a race day official veterinarian for Racing New South Wales, the regulatory racing body in New South Wales (NSW), Australia, the author has over a period of twenty years observed and treated horses presenting with EHI syndromes. Unquestionably, such cases constitute a real medical emergency and are extremely challenging because of the narrow time “window” (Yuval et al., 2004) of opportunity for recognition and effective treatment. The highest priority therapeutic objective is to reduce core body temperature to a safe level within thirty minutes if possible, but certainly in no longer than sixty minutes, as recommended by Casa et al., 2007 in humans.
This paper defines the syndrome of EHI in the thoroughbred horse, describes the spectrum of clinical signs, and presents the rationale for treatment in the field.

**Description of Exertional Heat Illness (EHI) in the Thoroughbred Race Horse**

EHI is represented by a continuum of clinical signs along a common pathway from the milder forms of EHI through to heat stroke and death (see Table 1). EHI is seen most commonly in thoroughbred racehorses competing under hot and humid weather conditions, when the mechanism of evaporative heat loss through sweating becomes relatively inefficient at controlling body temperature.

The wet-bulb globe temperature (WBGT°C) is by far the most widely accepted index of heat stress used throughout the world. It takes into account air temperature, humidity and wind velocity to provide a single reading and thus predict the risk of thermal injury (Yaglou and Minard, 1957; Casa and Roberts, 2003; Budd, 2008). The concept of WBGT was introduced in the early 1950s in an attempt to control heat illness in training camps of the United States Armed Services and since that time has been adopted by sporting regulatory bodies world-wide, the US Occupational Health authorities and the American College of Sports Medicine.

For humans, WBGT levels of 21 to 25°C are considered to represent moderate risk of thermal injury (Yaglou and Minard, 1957; Casa and Roberts, 2003; Budd, 2008). Schroter and colleagues (1966) used the WBGT to quantify environmental heat loads during the three-day event competitions at the Atlanta Olympics.

Racing NSW, the regulatory body for horse racing in New South Wales, Australia, has adopted policy recommendations concerning racing in hot weather based on WBGT levels (Racing NSW, 2009). Above a certain level, WBGT 26°C is 28°C there are changes to race-day programming and procedures, the provision of strategically placed hoses, quantities of ice made available and an extra veterinarian assigned to monitor post race recovery and to treat

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<tr>
<th>Heat Stress Level</th>
<th>Clinical Signs</th>
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<tr>
<td><strong>Level 1</strong></td>
<td>'HOT' distressed; skin hot to the touch. Heart rate &gt; 130, respiratory &gt; 60/ min Normal mentation</td>
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<tr>
<td><strong>Level 2</strong></td>
<td>‘HOT’ distressed; elevated HR + RR Irritability – uncooperative; unusual behaviors – head shaking, kicking out – may be confused with colic.</td>
</tr>
<tr>
<td><strong>Level 3</strong></td>
<td>‘HOT’ distressed; elevated HR + RR Abnormal mentation – toward depression, disorientation. Increasingly difficult and dangerous behaviors, unwillingness to move or sudden plunging and stopping haphazardly, wobbly, becoming unmanageable.</td>
</tr>
<tr>
<td><strong>Level 4</strong></td>
<td>‘HOT’ distressed; elevated HR + RR Substantial levels of central nervous system dysfunction. Horse extremely dangerous to itself and handlers, ataxic and uncoordinated – may fall over repeatedly, plunging to its feet, colliding with objects or people in its way. Clinical signs of endotoxaemia are apparent: membranes hyperaemic or &quot;lolly&quot; pink with slow capillary refill times.</td>
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| Table 1. Exertional Heat Illness Syndromes in Thoroughbred Race Horses |
|--------------------------|--------------------------|
| **CONTINUUM**            | HEAT STRESS              |
|                          | **CENTRAL NERVOUS SYSTEM DYSFUNCTION** |
|                          | **HEAT STROKE**          |
|                          | **DEATH**                |
|                          | **Note**: Horses may enter at any point along this continuum |

<table>
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<tr>
<th>Treatment Protocols for Various Levels of Exertional Heat Illness</th>
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<tr>
<td><strong>Level 1: ‘HOT’ horses</strong></td>
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<tr>
<td>• Need to be effectively cooled with copious amounts of cold (iced) water by hosing or bucketing and scraping the heated water off the skin.</td>
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<td>• Important to monitor heart and respiration rates and skin surface temperature.</td>
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<td><strong>Level 2: ‘HOT’ horses + irritability</strong></td>
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<td>• Provide sedation and inhibit serotoninergic activity. Detomidine (10mg/mL) – recommended dose rates for this level are 5µg/kg or 0.25mLs OR Xylazine (100mg/mL) at 0.5 to 1.1mg/kg (2.5 to 5.0mLs) intravenously.</td>
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<td>• If clinical condition not improving as judged by still elevated heart and respiratory rates, give NSAID to control SIRS. Flunixin meglumine – (50mg/mL) as bolus at a dose of 1.1 mg/kg or 10 mLs.</td>
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<tr>
<td><strong>Level 3: ‘HOT’ horses + altered mentation + incoordination ‘wobbly’</strong></td>
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<tr>
<td>• Need to be effectively cooled as above.</td>
</tr>
<tr>
<td>• Provide sedation and inhibit serotoninergic activity. Detomidine (10mg/mL) – increase dose to 30µg/kg or 1.0 to 1.5mLs IV incremental doses to effect.</td>
</tr>
<tr>
<td>• Provide flunixin meglumine to control SIRS. Xylazine (100mg/mL) at 0.5 to 1.1mg/kg (2.5 to 5.0mLs) intravenously.</td>
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<tr>
<td>• Provide neuroprotection and stabilize cell membranes.</td>
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<td>• Address hydration status – may need to give fluids intravenously once central nervous system signs are under control. Dexamethasone (5mg/mL) as bolus at a dose of 0.1 to 0.2 mg/kg or 10-20mLs intravenously.</td>
</tr>
<tr>
<td><strong>Level 4: ‘HOT’ horses + gross signs of central nervous system dysfunction – falling over – dangerous</strong></td>
</tr>
<tr>
<td>• Need to be effectively cooled as above.</td>
</tr>
<tr>
<td>• Provide sedation and inhibit serotoninergic activity. Detomidine at highest dose rate to control nervous system dysfunction and provide serotoninergic depression.</td>
</tr>
<tr>
<td>• Provide flunixin meglumine to control SIRS. Dexamethasone at highest dose rate 0.5 to 2mg/KG intravenously</td>
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<tr>
<td>• Provide neuroprotection.</td>
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horses with signs of EHI if necessary. In the author’s experience the WBGT has been useful in predicting the occurrence of EHI; once a level of at least 24 was reached it was highly likely that on that day we would encounter an increased number of horses with thermoregulatory problems after racing. It should be pointed out, however, that it is a misconception to assume that EHI will only occur on hot days. This author has seen cases of EHI on relatively cool days, and Roberts (2006) has reported heat-related illnesses in humans at an air temperature of only 9.4°C but with relatively high humidity.

In my experience, the clinical continuum of EHI, in order of increasing severity, includes horses that present as:-

(a) **Level 1** – Very ‘hot’ and distressed (see Fig. 3). There are increased rates of respiration (>60-100 breaths per minute) with widely dilated nostrils and heaving thoracic excursions. The heart rate is always elevated > 150 beats per minute and the animal is usually sweating profusely. Most importantly the skin is extremely hot to the touch.

(b) **Level 2** – Irritability: these animals demonstrate unusual behaviors such as kicking out in a random fashion (which may be confused with a colic episode) and are becoming uncooperative (see Fig. 2).

(c) **Level 3** – Altered mentation toward depression and incoordination (wobbly) may be evident. Horses in this group can become unmanageable, plunging and stopping haphazardly with disorientation (see Fig. 1 and Fig. 6 on page 20).

(d) **Level 4** – The final stage, ‘heat stroke’, is where the horse demonstrates substantial levels of central nervous system dysfunction (encephalopathy), throws itself down or falls down repeatedly and is a risk to itself and its handlers. This latter group will progress towards death unless treated rapidly and effectively (see Fig. 4).

All horses in the above groups have tachycardia and hyperventilation (see Table 1). It should be pointed out that a particular horse may be first observed at any point along this continuum, depending upon the conditions of the day, its individual risk factors, and its
core body temperature elevation. It is also important to emphasize that a diagnosis of EHI should not rely solely on the clinical finding of an elevated rectal temperature because this may not be observed due to the lag period of heat build-up post race, often a flaccid empty posterior rectum, and the risk involved in actually taking a temperature from an animal with irritability and altered mentation. It is not considered necessary or a priority to establish hyperthermia before instituting treatment.

TREATMENT PROTOCOLS FOR EXERTIONAL HEAT ILLNESS

Effective and rapid cooling

It is considered an absolute priority that horses with EHI are recognized early, and this requires the active involvement of those who are familiar with the variations in clinical signs described above. Alternatively, horses whose heart and respiratory rates remain elevated post-race can be targeted and presented to the treatment group for evaluation. Ideally, the treatment area should contain a wet room where horses can be housed and where iced water is readily available. An air-conditioning unit or large fan is also advisable.

Effective cooling strategies are the cornerstone of treatment. Casa and colleagues (2007; 2010) have investigated a wide variety of cooling modalities, concluding that ice-cold water immersion is the gold standard for treatment of exertional heatstroke in humans. The physical characteristics of water make it vastly superior to air as a cooling medium. Firstly, water’s thermal conductivity of 630.5 mW/m²°K gives it a much greater potential for heat transfer than air (26.2 mW/m²°K). Secondly, the specific heat of water is 4.2 J/g per °K compared with 1.0 J/g per °K for air, and the density of water is 0.9922 g/cm³ against 0.0012 g/cm³ for air. The volume-specific heat capacity of water is therefore nearly 3500 times greater than that of air. These factors, combined with water’s more effective skin contact, mean that a body can cool four times faster in water than in air of the same temperature. Golden and Tipton (2002) have concluded that water provides the same cooling capacity as air that is 11°C colder.

Critics of the iced water cooling modality argue that it may be counterproductive because it initiates peripheral vasoconstriction (PVC), which reduces the transfer of heat from the core to the skin. However, Casa and co-workers (2007) have strongly argued that such a response is typical only with normothermic individuals immersed in cold water who need to defend their body temperature. It has been shown experimentally in humans that individuals who are hyperthermic due to EHI have blunted responses in terms of PVC (Clements et al., 2002; Golden and Tipton, 2002; Proulx et al., 2003; Toner and McArdle, 1996). Even with some degree of initial PVC, the overall transfer of heat from the core to the skin during the critical period is far greater in cold water than in air. From a clinical viewpoint, the fact that a lowering of core body temperature must be achieved in a limited time demands the most efficient cooling modality available.

Cooling in the horse has been well described in the literature (Hodgson, 2014; Jeffcott and Kohn, 1999; McCutcheon and Geor, 2014; Marin et al., 1998; Williamson et al., 1995) and is best achieved by a team of three people using cycles of hosing with water of sufficient volume, pressure, and low enough temperature to establish a gradient for rapid exchange of heat from core to skin to water. The water is then scraped off and the cycle continued. Attention needs to be paid to the great vessels of the head and neck, the area between the front and back legs, and of course the major body mass. Scraping is essential: if the water is allowed to warm up on the skin the temperature gradient will decrease, reducing the transfer of heat.

Throughout this procedure it is important to monitor heart and respiratory rates and to observe and feel the heat from the skin surface. Once cooling has been achieved the horse can be discharged from the treatment area, however there is a tendency for these horses to present with a rebound hyperthermia about 30 minutes later so that they need to be kept under surveillance and the whole process of cooling may need to be repeated.

The pathophysiology of the EHI pathway and implications for other treatment modalities

Research in humans in the last decade (Epstein and Roberts, 2011; Leon and Helwig, 2010; Bouchama and Knochel, 2002) has provided insights into the pathophysiology of heat stroke and suggested an integrated view, depicting a common pathway from heat stress to heat stroke (see Fig. 5). This has important implications for treatment because it explains the progressive nature of the condition and therefore the need for all phases of EHI to be treated as aggressively as possible. There is convincing evidence that the severity of the illness will be determined by the critical thermal maximum, a term which attempts to quantify the level and duration of elevation in cell temperature that will initiate and potentiate progressive tissue injury (Shapiro et al., 1973; Bynum et al., 1978).

Briefly, from the model of heat stroke based on observations in humans (Bouchama and Knochel, 2002; Leon and Helwig, 2010) and experimental models of heat stroke in laboratory animals, it is suggested that during strenuous exercise there is an elevation of core temperature which stimulates physiological changes. Flow of blood to the skin is increased to accelerate heat transfer to the environment and if this is effective the body core will cool without consequence. This redistribution involves a decrease in blood flow to the gut, and if this is prolonged gut ischemia will result, stimulating oxidative and nitrosative stress. The tight junctions of intestinal epithelial cells increase their permeability and allow the leakage of bacterial endotoxin, which then gains access to the systemic circulation (Dokladny et al., 2006; Lambert et al., 2002). In heat stressed primates endotoxin from the gut enters the circulation at a core temperature of 40°C and its concentration increases as the core temperature rises (Gathiram et al., 1987). The immune system responds to endotoxaemia by activation of the systemic inflammatory response syndrome (SIRS) with increased production of cytokines, interleukin-1 and other immune modulators including prostaglandins. This will cause haemodynamic instability, cardiovascular...
collapse and shock. In concert with the above, hyperthermia also causes thermal injury to the vascular endothelium, initiating coagulation pathways that lead to microvascular thrombosis and disseminated intravascular coagulation (DIC) (Sohal et al., 1968). The SIRS and coagulation pathways interact to cause multi-organ system failure and the progression from heat stress to heat stroke and death (Leon and Helwig, 2010).

To extrapolate this heat stroke model to horses, it is well documented that horses are susceptible to the effects of endotoxin (Carroll et al., 1965; Moore, 2001) and suffer from a similar endotoxaemic syndrome to that seen in humans, with high morbidity and mortality rates (Bryant et al., 2007). In a most interesting study Donovan and colleagues (2007), using a high speed treadmill, exercised horses to absolute fatigue and found that the brief but strenuous exercise induced endotoxaemia and a systemic inflammatory response characterized by elevations in cytokines and prostaglandin F$_2$α and that these elevated concentrations persisted for two hours. Other researchers (Baker et al., 1981; Semrad et al., 1987; Bottoms et al., 1986; Barton et al., 1988; Barton et al., 1988) have reported similar findings in race and endurance horses. These studies support the argument that the heat stroke model as described in man, characterized by gut-driven endotoxaemia and consequent inflammatory cascade, almost certainly pertains to the horse.

From the pathophysiological model – 3 critical points

Firstly, the gut is the origin of the SIRS and endotoxin is the key driver. The most common clinical findings in horses presumed to be endotoxaemic are an alteration of the mucous membranes to a hyperaeremic or ‘lolly pink’ appearance with a slow capillary refill time, and a substantial elevation in heart and respiratory rates. Once heat stressed horses reach level 3 (see Table 1), they invariably exhibit these changes.

The second point is that as EHI syndromes become more severe, normalizing the body temperature alone may not be sufficient because the inflammatory cascade and concomitant effects as described have already been initiated and are progressing. Therefore, in addition to cooling it is necessary to provide therapy to modulate SIRS responses. There is good evidence that the use of a non-steroidal anti-inflammatory drug such as flunixin meglumine has a key role in the treatment of horses with EHI, and in the author’s view, the earlier the better. As stated by Moore (2001), the non-steroidal anti-inflammatory drugs (NSAIDs) and specifically flunixin have been the mainstay for the treatment of endotoxaemic horses for at least two decades and the results of comparative studies clearly indicate the value of flunixin in preventing the endotoxin-induced synthesis of cytokines, prostaglandins and thromboxane which produce many of the clinical signs of endotoxaemia in horses (Moore et al., 1986; Semrad et al., 1987; Bottoms et al., 1981). In the author’s experience, horses with EHI administered flunixin at therapeutic dose rates improve clinically within ten to twenty minutes.

The third critical point is an observation and hypothesis that in the thoroughbred racehorse dehydration is not a driver of EHI but rather an independent risk factor. It is acknowledged that horses presented on race day which have travelled long distances in the heat and sweated profusely, or have had water withheld because of particular training practices will be at higher risk, but in the author’s experience dehydration is not always the determining factor for EHI. This is in contradistinction to the endurance horse where dehydration...
is a key driver of the exhausted horse syndrome (McCutcheon and Geor, 2004; Hodgson, 2014). There is considerable individual variation amongst horses in the degree of sweating and consequent fluid loss and there are many other factors, such as genetic predisposition, temperament, acclimatization to hot weather, ambient levels of temperature and humidity, training schedule, fitness, race duration and intensity, and individual motivation of each horse to race, which all play a role in determining thermoregulatory dysfunction. Irrespective however of whether dehydration is a primary or secondary factor, management of dehydration must be included as part of the treatment protocol.

Central Nervous System Dysfunction Rationale for Treatment

The most challenging aspect of EHI syndromes in thoroughbred racehorses from a management aspect is the emerging symptoms of central nervous system dysfunction and the risk this poses to the people trying to treat these horses.

Cerebral pathophysiology and pathology

It is well documented that the human brain, compared with other organs, is especially vulnerable to hyperthermia, and the severity of the injury depends on the level and duration of overheating (Nielsen and Nybo, 2003). In humans, hallmark signs of the progression of heat-related illness include alterations to mental status such as dizziness, confusion, delirium, combativeness, collapse, seizures and coma (Nybo, 2007). The pathophysiological changes (see Fig. 6) responsible for this symptomatology are, firstly, reduction in cerebral blood flow leading to cerebral ischaemia, and changes to blood-brain-barrier permeability allowing leakage of serum proteins, resulting in vasogenic brain oedema (Sharma and Hoopes, 2003). The latter is crucial in determining the extent of cell injury and consequent brain pathology because swelling of the brain within the rigid cranium has potential neurochemical mediators such as serotonin that are present in the brain where the Purkinje cell layer is most affected (Leon and Helwig, 2010; Binkley et al., 2002). It is worthy of note that despite rapid cooling, about 30% of human patients in the heat stroke category experience permanent neurological impairments that may be related to cerebellar atrophy and infarcts (Argaud et al., 2007; Dematte et al., 1998).

Therapies – glucocorticoids

Treatments that address the central nervous system dysfunction include the use of therapeutic doses of glucocorticoids such as dexamethasone which has been shown to be beneficial in the treatment of brain and spinal cord injury in man, experimental cerebral ischaemia in animals and cerebral injury and trauma in horses (Hall, 1992; Behrmann et al., 1994; Feary et al., 2007; Reed, 1994). More recently Liu and colleagues (2000) experimentally investigated whether intravenous dexamethasone could protect against the heatstroke-induced cerebral ischaemia and neuronal damage in the rat heat stroke model. They used dexamethasone either before heat exposure or 80 minutes after the start of heat exposure and found dexamethasone reduced the heatstroke-induced arterial hypotension, the elevated interleukin levels, cerebral ischemia and neuronal degeneration, and resulted in prolonged survival. Administration of the drug before heat exposure rather than later gave superior results. The authors concluded that dexamethasone was an important modulator of the cerebrovascular and cytokine responses and thereby provided neuroprotective effects in the rat heat stroke model that they employed.

Synthetic glucocorticoids such as dexamethasone have potent anti-inflammatory and immunosuppressive effects that are widely used in the treatment of inflammatory disorders. There are general effects such as
stabilization of cellular and lysosomal membranes and decreasing vascular permeability, as well as more specific effects aimed at modulation of the key chemical mediators of the inflammatory cascade (Anntemper et al., 2002; Zuckerman et al., 1999; Simpson, 1990). Beneficial effects have been shown in the treatment of many inflammatory diseases, acute allergic conditions and endotoxic shock in the horse (Frauenfelder et al., 1982; Lane et al., 1990). In view of this dual action of dexamethasone, firstly in suppression of the inflammatory cascade and secondly in its neuroprotective role in the rat heat stroke scenario, there would appear to be good evidence for its use in the EHI syndrome in thoroughbred race horses. The key, however, is to use this drug as early as possible, a guideline supported by many previous findings (Whitehouse, 2011; Liu et al., 2000).

Therapies – detomidine

As the severity of the EHI syndrome increases so do the manifestations of central nervous system dysfunction, to such an extent that horses presenting at Levels 3 to 4 cannot be cooled because they pose such a risk to treatment personnel. To overcome this, the author has over the years used sedatives such as xylazine or detomidine dosed to effect in managing the adverse nervous system signs. Clinically it has been evident that detomidine was far superior to xylazine and there appeared to be no deleterious side effects with its use in EHI horses. The fact is, however, that most horses received combination therapies such as efficient cooling, flunixin, dexamethasone and detomidine, which confounds the ability to determine the success of individual therapies. Critics of the use of detomidine in EHI horses cite the adverse effects on the cardiovascular system: bradycardia, reductions in cardiac output and hypertension due to peripheral vasoconstriction, then later hypotension (Sarazan et al., 1989), all of which would act to limit the heat transfer process. However, horse and personnel welfare is an absolute priority, and in the author’s opinion this drug has been instrumental in saving people and horses from injury.

The alpha-2 adrenoreceptor agonists are represented by xylazine, detomidine, medetomidine and dexmedetomidine. The first two are widely used in the clinical equine arena whilst the latter two are approved for use in dogs and cats. Detomidine provides reliable dose-related sedative and anaesthetic effects in horses with a rapid onset of action but of longer duration than xylazine (Clarke and Taylor, 1986; Vamio, 1983).

It is beyond the scope of this paper to review the physiology of alpha-2 adrenoreceptors but briefly they are located in the central nervous system and virtually every peripheral tissue. The alpha-2 agonists xylazine, detomidine medetomidine and dexmedetomidine stimulate presynaptic and postsynaptic alpha-2 adrenoreceptors in the CNS, resulting in decreased levels of norepinephrine and dopamine and producing the clinical effects of sedation, analgesia and muscle relaxation which is the basis of their therapeutic efficacy. These alpha-2 agonists are selective but can also activate alpha-1 receptors to a small extent which may play a part in clinical effects but only activation of alpha-2 adrenoreceptors produces sedation. At clinical doses the more selective a drug is toward the alpha-2 adrenoreceptor the more potent it is as a sedative. The ratio of alpha-2 to alpha-1 selectivity has been classified as: medetomidine (1620:1), detomidine (260:1), and xylazine (160:1); (Virtanen and MacDonald, 1985; Virtanen et al., 1988; Virtanen and Nyman, 1985.)

An in-depth study (MacDonald et al., 1988) of the neurochemical effects of medetomidine (a methylated derivative of detomidine) found that it depressed the turnover of noradrenaline and dopamine, and also significantly lowered serotonin levels. In view of this, it is suggested that detomidine might also cause some reduction in serotonin level. This is relevant because Sharma and Dey (1986) have implicated elevated serotonin level as a key driver in the cerebral pathophysiology associated with the heat stress/heat stroke progression. It has been well documented that serotonin is one of the most powerful vasoactive amines, capable of inducing vasoconstriction of cerebral vessels, impairing the integrity of the blood-brain barrier, increasing cerebral vessel permeability and leading directly to cerebral oedema and neurological injury (Winkler et al., 1995). These findings were supported by Kao and Lin (1996), who reported that when the cerebral serotonin system was antagonized experimentally in rats, heatstroke-induced ischaemic damage to the brain was reduced and the rats had increased survival times. More recently, Sharman and Hoopes (2003) used several animal models to study the effects of hyperthermia on chemical mediators within the CNS, and their findings also incriminated serotonin as one of the most active and potent neurochemical mediators in the pathophysiological changes to cerebral function. It may therefore be conjectured that detomidine might not only sedate horses with substantial EHI symptomatology but also provide clinical improvement by decreasing serotonin level to some extent and thereby disabling the deleterious progression of cerebral pathophysiology.

1The Australian context for incidents of heat stress in racehorses may be quite different from that prevailing in the United States of America. The pre-race use of the diuretic drug furosemide (Lasix) is banned in Australia because it is classified as a “prohibited substance”. In the USA however competing horses are routinely administered 350 to 500 milligrams of Lasix by intravenous injection four hours before post time in an attempt to control exercise induced pulmonary haemorrhage (EIPH). Although the effects of the drug are short-lived it will initiate a diuresis that may cause varying degrees of dehydration in individual animals. Under these circumstances dehydration may become a primary driver for heat stress and necessitate that treatment protocols include intravenous fluid therapy at all levels rather than just levels 3 and 4 as described in this paper.
Conclusion

The key issue concerning EHI in thoroughbred racehorses is its early recognition and prompt treatment because it is a genuine medical emergency. It is important to understand that the various stages are located on a continuum, with the milder stages of heat stress progressing toward heat stroke and death if that progression is not halted. Veterinary intervention on race day needs to be pro-active and involves rapid cooling techniques as described, the aim being to lower the animal’s core body temperature within 30 minutes. There is overwhelming evidence that external saturation with ice cold water is the superior cooling modality. All stages of EHI require rapid and efficient cooling.

The driver of EHI syndromes is endotoxin released from a gut compromised by underperfusion following redistribution of a finite cardiac output. Endotoxaemia drives the inflammatory cascade, and cooling alone, at the later stages of EHI may not result in reversal or suppression of this pathophysiological progression, so that immune modulating drugs such as flunixin are considered essential. Synthetic glucocorticoids represented by dexamethasone are also indicated because they not only stabilize cell membranes and leaky capillary endothelium which is a direct effect of heat toxicity but also have been shown to possess neuro-protective effects. Finally, it is emphasized that dealing with heat-stressed horses can be extremely dangerous. They are apt to injure themselves and those trying to treat them and for effective restraint and sedation detomidine is preferred. Interestingly, there is some evidence that detomidine may decrease the level of serotonin in the brain, which has been incriminated as a driver of cerebral pathophysiology in the heat stroke model. This is obviously an area for further research.

The equine veterinarian should be ready for the occurrence of heat stress on any race day especially during the summer months, which means having ice always available and ready access to the necessary medications. Emergency medicine is all about being prepared and time is of the utmost importance for heat-affected animals. Staff in charge of horses at race meetings must be educated to recognize the behavior associated with heat stress in horses and be able to present the horse to the on-duty veterinarian as soon as possible. In an era when the welfare of racing animals is increasingly exposed to public scrutiny the racetrack veterinarian needs to be well informed and well prepared.

The author wishes to acknowledge all those people who have worked tirelessly to treat heat-stressed horses on race day and who have all contributed in some way to the observations in this article. They are Craig Suann, Melissa Kay, Sue McMaster, Kylie Smallwood, Carol Griffiths, Pat Cozzi and Natasha Pesce, and I also acknowledge the input from all of the fine racetrack veterinarians that we work with on a regular basis.

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Figure 6. ‘HOT’ horse with altered mentation toward depression and incoordination.
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