Proceeding of the LAVC
Latin American Veterinary Conference
Apr. 23-26, 2012 – Lima, Peru

Next LAVC Conference:

Apr. 22-25, 2013 – Lima, Peru

HEAT STROKE AND HYPOTHERMIA

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Homeothermic animals need to keep their core temperature within a set range to allow all body systems and reactions to work appropriately and prevent severe damage or even death. Several interlinked mechanisms, ultimately regulated by the thermoregulatory center in the hypothalamus, ensure that a constant temperature is maintained in the face of changing environmental and internal conditions. When these compensatory mechanisms are overwhelmed, body temperature goes over or under the set limits, and a series of deleterious effects can occur.

Both heat stroke and hypothermia are common emergency presentations, or can develop whilst the animal is in hospital (particularly hypothermia). A thorough understanding of the temperature preservation mechanisms and the pathophysiologic changes associated with overheating and hypothermia, as well as with rewarming and cooling, are necessary to understand the different therapeutic options, monitoring required and complications.

Heat stroke

Heat stroke is a condition of extreme hyperthermia resulting from the body's inability to dissipate heat generated by metabolism, exercise, environmental conditions or a combination various or all of these. Core temperature has to be (or has been) above 41ºC (106ºF), and signs of neurological and other organ dysfunction are usually present. Heat stroke can be classified as classical (resulting from exposure to a hot and humid environment) or exertional (associated with intense physical exercise). A combination of both can frequently be encountered, particularly if there has been a lack of acclimatization (such as in working dogs at the beginning of the warm season, or if they move to a warmer area, or in a dog that has been frantically trying to escape from a locked car in the sun).

There does not appear to be a direct correlation between core temperature and severity of clinical signs or outcome, nor has a cut-off value for temperature at which prognosis clearly changes been identified. However, time to cooling does seem to have an effect on outcome, suggesting that longer times at a certain temperature might have more detrimental effects than shorter periods at a higher temperature.

Due to the paucity of information about heat stroke in small animals, most information is derived from human medicine, and also from experimental models. This information, however, should be interpreted with caution. The canine brain, for instance, has a much higher thermal resistance than the human brain. This may account for neurological signs often being the first to be present in people, and for the higher incidence of neurological damage that people seem to suffer when compared to our patients.

In homeothermic animals, heat is produced from metabolism or gained from the environment, and is dissipated by conduction, convection, radiation and evaporation. Conduction occurs when the body is in contact with a cooler surface, and in our patients has a very limited role due to the insulating abilities of the coat. Convection is transference to the air as it passes over the body, such as happens with the wind (or a fan). Radiation is the natural release of heat from the body into the environment. Finally, evaporation is fluid changing to vapor, an endothermic process. Evaporation is the most important process for dissipating heat with environmental temperatures above 32ºC (89.6ºF). In people, it occurs mostly through perspiration. In dogs and cats, perspiration occurs via the footpads, rendering this a largely inefficient heat dissipation method, and evaporation happens through panting instead. With increases in blood temperature of less than 1ºC (1.8ºF), the thermoregulatory center in the hypothalamus is activated, and there is increased delivery of blood to the body surface, as well as increases in cardiac output and minute ventilation, and panting. If the animal becomes dehydrated, evaporation, radiation and convection heat losses are reduced, and thermoregulation is impaired.

Although it is easy to assume that heat stroke is more common in areas with high temperatures and humidity, the body can adapt to these environmental conditions through the process called acclimatization, which is partially completed over 10 to 20 days, but might require up to 60 days to be completed. Adaptative mechanisms aim at conservation of water, enhanced cardiovascular performance, salt conservation, increased plasma volume and GFR, and an increase in the resistance to rhabdomyolysis. During heat stroke there is also activation of the Acute Phase Response (APR), which protects against tissue injury and promotes repair. Depending on all the mediators involved, APR can have a combination of protective and destructive effects, as well as inflammatory and/or anti-inflammatory effects. APR has to be exaggerated and inflammatory to be involved in the development of heat stroke.

A recently discoverered set of players in the pathophysiology of this condition are the Heat Shock Proteins (HSPs), synthetized by virtually all cell types in response to increased temperatures, that act to help maintain cellular function and structural integrity. Aging, lack of acclimatization and genetic polymorphisms are associated with fewer levels of HSPs, and therefore with increased risk of heat stroke. Genetic predisposition could be one of the reasons for the overrepresentation of certain breeds such as Golden and Labrador Retrievers or Belgian Malinois, although it is unlikely to be the only one. Identifying genetically predisposed patients could allow for

prophylactic treatment and ensure that all other risk factors are minimized. NSAIDs, as HSPs up-regulating agents, may play a role in preventing heatstroke, but clinical evidence supporting its use is lacking.

The pathophysiology of heat stroke, regardless of the type, has many similarities to sepsis, as the high temperature triggers a systemic inflammatory response which ultimately leads to multiple organ dysfunction syndrome (MODS). In heat stroke, circulatory collapse (including myocardial disfunction), renal failure, ARDS, DIC, rhabdomyolysis, hepatic failure, pancreatitis, and intestinal ischemia are all manifestations of MODS.

On presentation, it is important to remember that patients can be hyper, normo or hypothermic, particularly if cooling measures have been started by the owners before presentation. Therefore, heat stroke should not be disregarded in a patient with normal or low core temperature if the history reveals recent exercise or confinment in a hot and humid environment and other clinical and/or clinicopathological findings are compatible. Clinical signs of shock (either in the hyperdynamic or hypodinamic phases), panting and neurological signs including ataxia, blindness, seizures and/or coma, petechiations or echymoses and hemorrhagic diarroea may be obvious on presentation or develop during the initial phases of treatment. Of all the clinical signs, seizures have been associated with increased risk of death. Obesity is not only a predisposing factor but also also a bad prognostic indicator.

Clinical pathology usually reveals changes associated with severe hemoconcentration and/or dehydration, as well as azotemia and also commonly hypoglucemia. Hypoglucemia on presentation, particularly if refractory to initial treatment, and increased creatinine after 24 hours (suggesting renal failure) are also risk factors for death. Thrombocytopenia, prolongation of PT and aPTT have all also been identified as risk factors for death. Nucleated red blood cells are a common finding, and its presence and number have been recently associated with outcome. More than 18 nRBC /100 WBC have got 91% sensitivity and 88% specificity for death.

Therapy must include respiratory and/or ventilatory support (oxygen therapy including intubation and ventilation when required), rapid cooling and fluid therapy to replace volume losses and optimize perfusion. Secondary complications, either present or potential, must be addressed then (hypoglycemia, coagulopathies, ARDS, renal failure). It is important to remember that hypoglucemia is not always present in an animal presenting with seizures, and conversely some animals might be hypothermic and show other neurological signs than seizures (such as depression or coma). Therefore, empirical supplementation with intravenous dextrose should not be attempted and any glucose administration should be guided by the blood glucose concentration. Ideally, cooling should be accomplished by evaporative mechanisms. Wetting the animal with cool water and placing it by a fan is very efficient, as it uses evaporation, conduction and convection. Very cold or ice water baths should be avoided as they cause severe peripheral vasoconstriction and core temperature can therefore increase. It can also cause shivering, which would work towards increasing the temperature. Procedures such as cool gastric lavage, peritoneal lavage or cool water enemas are labor consuming and, although effective at achieving core cooling, they are usually not practical, can interfere with monitoring and make rebound hypothermia more likely. Active cooling should stop between 39.5ºC and 40ºC (103ºF-104ºF) to prevent both shivering and rebound hypothermia.

As there is usually a severe water deficit, crystalloids should be the initial fluid of choice. In cases where hypoalbuminemia is severe, colloids can be used once the initial loading with crystalloids has been achieved and volemia is not being maintained. Experimental studies in rats favour small volume resuscitation using hypertonic saline and hydroxyethyl starch.

Physical and laboratorial parameters related to perfusion and volume (e.g. PCV and TS, lactate) should be assessed at baseline and frequently thereafter to monitor progression and response to therapy. A urinary catheter should be placed to monitor urine output and allow urine collection for analysis.

Cardiac arrhythmias rarely need to be pharmacologically addressed, but if they do, lidocaine is usually effective at controlling them, either as boluses or constant rate infusion. Post-heat stroke arrhythmias are likely to be associated with myocardial damage, and in some studies have been associated with mortality, but this finding has not been consistent across different studies.

NSAIDs, as discussed earlier, have HSPs up-regulating effects that could prove beneficial in the management of heatstroke, despite having been traditionally not recommended due to the belief thathypoerthermia is not mediated by the hypothalamus. Although there could be a potential indication as a prophylactic treatment during heat waves or prior to extrenuous exercise, the well-known adverse effects associated with these compounds, both at renal, gastrointestinal and platelet level, would strongly advise against their use in clinical cases.

Hyperbaric oxygen therapy has been shown experimentally and in some studies in people to improve outcome by limiting brain and pulmonary damage. These are target organs in human heat stroke, but in dogs they appear to be more resistant and suffer less damage as shown by pathology studies.

Mortality in heatstroke ranges from 10-80% in people, and in small animals has been reported to be around 50%, although in the author's experience the mortality rates seem to be lower. Several risk factors, as discussed earlier, have been identified, but as no clear cut-off points for mortality have been found, aggressive therapy should be instituted as soon as possible for any patient presenting with heat stroke. More than half of the fatalities seem to occur during the first 24 hours, and according to one study death is unlikely if the animal survives the first 48 hours, suggesting most lesions can recover if the animal survives the initial period.

Hypothermia

Hypothermia is a subnormal body temperature in a homeothermic animal. It can be primary (in an animal with normal heat production and resulting form extremely cold environmental conditions), or secondary (in which heat producing mechanisms are impaired, and can exist with even warm environmental conditions).

In clinical practice, most of us have to deal with many more patients suffering from secondary hypothermia than from primary hypothermia. Interestingly, adverse effects are seen at much higher temperatures in patients suffering from secondary hypothermia than in patients suffering from primary hypothermia. Indeed, animals suffering from primary hypothermia as low as 32ºC will only display mild clinical signs such as shivering, piloerection and heat seeking, whilst patients with secondary hypothermia and temperatures below 36.7 can start showing abnorally low MAP and mental depression. Hence the expression "it is not dead until it is warm and dead" that our human counterparts use as an axiom for accidental hypothermia victims.

Therefore, and due to its higher incidence and more severe adverse effects, this presentation will focus mostly on secondary hypothermia. Nevertheless, most of the recommendations and warming procedures can be equally used for cases of primary hypothermia. Primary hypothermia has been classified as Mild (32ºC-37ºC / 90ºF – 99ºF), Moderate (28ºC – 32ºC / 82ºF – 90ºF), Severe (20ºC – 28ºC / 68ºF – 82ºF) and Profound or Critical (<20ºC / <68ºF). Secondary hypothermia has been classified as Mild (36.7ºC-37.7ºC / 98ºF-99.9ºF), Moderate (35.5ºC-36.7ºC / 96ºF - 98ºF), Severe (33ºC – 35.5ºC / 92ºF – 96ºF), and Profound or Critical (< 33ºC / < 92ºF). Under primary hypothermia, asystole rarely occurs above 20ºC / 68ºF.

Whilst heat production is a result of cellular metabolism and is ultimately regulated by the hypothalamus, the four basic mechanisms of heat loss have been described above. Hypothermia will occur from increased heat loss, decreased heat production or a combination of both. Whilst in primary hypothermia the body is not able to maintain the critical temperature level or hypothalamic set point, it is not uncommon for mild to moderate secondary hypothermia to be endogenously triggered as a protective mechanism, aiming at decreasing the energetic requirements from vital body systems (such as brain and heart). However this is not the only cause for secondary hypothermia, and even when "intentional", secondary hypothermia can carry deleterious effects that far outweigh the beneficial ones. It is also common for secondary hypothermia to be iatrogenic, as associated with procedures under anesthesia.

Regardless of the original cause, thermoregulation itself becomes impaired when core temperature falls below 34ºC (94ºF), and a spiral of events (cesation of shivering, peripheral vasodilation, decreased metabolic rate, CNS depression leading to hypothalamic hyporesponsiveness) leads to further heat loss and increased hypothermia. Below 31ºC (88ºF), thermoregulation ceases completely, and without prompt intervention death will be inevitable, particularly in the event of secondary hypothermia.

From a metabolic and acid-base point of view, hyperglucemia is common in the initial stages, and frequently progresses to hypoglucemia as the temperature falls further. Initial hypokalemia due to increased urinary losses will lead to hyperkalemia at later stages, and can account for cardiac arrhythmias. Respiratory acidosis (secondary to respiratory and CNS depression) and metabolic acidosis (lactic acidosis secondary to hypoperfusion) commonly coexist.

It is difficult to evaluate hemostasis as all tests measure at normal body temperature and therefore do not reflect what is happening in the hypothermic individual. Research reveals that thrombocytopathia is present even with mild to moderate hypothermia, but as with any potential changes in secondary hemostasis, they do not seem to be clinically significant.

After an initial response consisting of increasing cardiac output and periperal vasoconstriction, with decreasing temperatures there is a decrease in cardiac contractile response and arteriolar responsiveness which eventually results in hypoperfusion and increased heat loss due to peripheral vasodilatation. Different arrhythmias have been described, including atrial fibrillation, ventricular fibrillation and asystole. In cats, fibrillation seems to be far less common than in dogs and bradycardia usually leads directly to asystole, possibly due to the smaller heart size.

Respiratory changes may come not only from hypoventilation but also from concurrent pulmonary edema and pneumonia, which occur commonly and occasionally progress to ARDS.

Although there is consistent evidence suggesting that mild hypothermia is neuroprotective and beneficial in the face of several neurological problems (such as head trauma or stroke), caution must be used when examining the data. Most of these come from very well-controlled experimental studies, and in clinical studies in people only mild hypothermia was allowed. Considering that cerebral blood flow has been shown to drop by more than 6% for each degree centigrade (2ºF) below normal core temperature, aggressively cooling brain injured patients or allowing moderate to severe hypothermia in these patients is probably not appropriate and not supported by the existing evidence. Mild hypothermia, however, could be beneficial and might not be addressed immediately if not showing signs of further compromising the patient.

Immune function is also impaired with hypothermia, and there is increased risk of infections. In light of abnormal perfusion and drug distribution, however, broad spectrum antibiotic therapy should not be started until

temperature has normalised or clinical signs of infection are present. Whenever possible, samples for isolation and culture should be obtained from any wounds, tracheal washes, or other potential infectious foci.

The main purpose of treatment is to warm up the patient to the normal clinical range (or at least to mild hypothermia with absence of clinical or laboratorial abnormalities) as soon as possible. However, given the changes in cardiovascular status and body fluids associated with hypothermia, ensuring appropriate fluid ressuscitation is mandatory prior to and during rewarming efforts. Close monitoring is mandatory, as aggressive fluid therapy can increase the risk for complications such as pulmonary edema. Crystalloids are usually the fluid of choice, a replacement fluid should be used, supplemented accordingly with glucose and/or potassium if required. Antiarrhythmics and catecholamines should not be used with moderate to severe hypothermia, as the response to them can be, if any, unpredictable at best. Moreover, most abnormalities will resolve as temperature increases providing volume status is maintained and major electrolyte and acid-base abnormalities are corrected.

There are different group methods to warm a patient, which can be chosen based on the severity of the hypothermia and clinical signs, cost and clinician preferences. Regardless of the method used, temperature should be increased at least 1-2 ºC (2ºF-4ºF) per hour, and active rewarming should stop when core temperature reaches 37ºC (98ºF) to prevent rebound pyrexia.

Passive surface methods: external covers (blankets, foil, bubble wrap), will prevent further heat loss but not actively warm. These rely on the animal's ability to generate heat (such as when recovering from anaesthesia), and are iindicated in mild hypothermia with appropriate perfusion status.

Active surface warming: heating pads/bottles, circulating air/water, heat lamps, etc. These apply heat to the surface, and can therefore be used for moderate to severe hypothermia, requiring volume support to be provided during rewarming. Close monitoring and caution are to be used to prevent thermal burns and to avoid further heat loss from peripheral vasodilatation.

Active core warming: faster and more effective, but also more invasive. Inhaled heated air (which should be humidified), peritoneal or pleural lavage, warm bladder lavages, warm enemas and warm intravenous fluids. These methods will provide central heat, aiming at more rapidly warming the core. They are reserved for severe or critical hypothermia, and although they will prevent dilatation of peripheral arterioles, local changes in vascular tone can result in circulatory compromise. Of all these, warm intravenous fluids (to temperatures up to 42ºC-43ºC / 107ºF- 109ºF) seems to be the least effective.

During rewarming and in the immediate post-rewarming period, a series of complications can occur, and prompt recognition and treatment is mandatory to reduce the chances of an adverse outcome. Amongst these complications, the most commonly encountered are cerebral edema, pneumonia, pulmonary edema, pancreatitis, "shock gut", hypotension and core temperature afterdrop (although the latter two seem to be clinicallly insignificant in people). Other complications that are more difficult to treat include reperfusion injury and ARDS.

There is paucity of data regarding prognosis for primary hypothermia in dogs and cats, but with appropriate therapy many human patients recover with normal full neurological function. As for secondary hypothermia, prognosis is likely to be linked to the underlying cause as well as to both the duration and severity of the hypothermia. No studies have shown an ideal or minimal re-warming rate, and although a rewarming rate of 1-2ºC (2-4ºF) has been deemed safe and effective, considerably faster rates are often advocated and easily reached when using active core warming methods.

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Key words: Heat stroke, Hyperthermia, Cooling, Heat Shock Proteins, Hypothermia, Thermoregulation, Rewarming, Temperature.