Heat Stroke

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Outline

- Pathophysiology of heat stroke
- Organ systems affected
- Predisposing factors
- Clinical presentation
- Treatments
- Prognosis
Definition of Heatstroke

Dogs:
A syndrome, characterized by core body temperatures >41°C (105.8°F) and central nervous system depression or seizures

Humans:
A form of hyperthermia associated with a systemic inflammatory response leading to a syndrome of multiorgan dysfunction in which encephalopathy predominates
Human vs Veterinary Literature

- One large retrospective study in veterinary medicine and one clinical review
- Most information is extrapolated from human medicine
- Some experimental studies in dogs >20-30 years ago used as basis from human treatment
Outline

🌟 Pathophysiology of heat stroke
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🌟 Predisposing factors
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🌟 Treatments
🌟 Prognosis
Pathophysiology of Heat Stroke

Temperatures That Risk Heat Stroke

<table>
<thead>
<tr>
<th>Temperature (°F)</th>
<th>90</th>
<th>80</th>
<th>70</th>
<th>60</th>
<th>50</th>
<th>40</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td>121</td>
<td>113</td>
<td>105</td>
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<td>95</td>
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<td>100</td>
<td>142</td>
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<td>105</td>
<td>148</td>
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<td>121</td>
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<tr>
<td>110</td>
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<td>135</td>
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</tbody>
</table>

**Heat index**

- 105–130°F: Heat disorder seen in humans, heatstroke possible
- >130°F: Heatstroke highly likely with continued exposure
Thermal Area

Cellular adaptive response to heat

Increased temperatures -> Production of Heat Shock Proteins (HSPs):

- Chaperonin activity
- Modulation of inflammatory responses (decreased IL-1, IL-6, TNF-α NF-κB)
- Regulation of the acute physiological alterations
- Antioxidant effect
- Antiapoptotic effect
Cellular Response to Hyperthermia

When heat overcomes HSPs, or there is lack of acclimatization:

- IL-6 and NF-κB is greatly increased
- Temperatures above 106.7°F for as little as a few minutes can induce cellular apoptosis
- Temperatures above 109.4°F uncouples oxidative phosphorylation and enzymes are denatured
Cellular Response to Hyperthermia

- Temperature dependant electrolyte channels are altered
  - Potassium flows extracellularly leading to increased plasma $[K+]$
  - Rarely seen in veterinary patients
  - Severe hyperthermia also results in increased intracellular $[Ca++]$
  - Can cause damage to myocytes
Adaptive Physiologic Response to Heat Stress

- Increases in temperatures as little as 1°C are detected by hypothalamic and peripheral thermoreceptors
- Cutaneous vascular bed dilates
- Splanchnic venous beds constrict to maintain effective circulating blood volume
<table>
<thead>
<tr>
<th>PHYSIOLOGICAL RESPONSE</th>
<th>EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thermoregulatory</strong></td>
<td></td>
</tr>
<tr>
<td>Core temperature (rest and exercise)</td>
<td>Reduced</td>
</tr>
<tr>
<td>Skin flow</td>
<td>Earlier onset; higher rate</td>
</tr>
<tr>
<td>Skin Temperature</td>
<td>Reduced</td>
</tr>
<tr>
<td>Sweating</td>
<td>Earlier onset; higher rate</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
</tr>
<tr>
<td>Heart rate</td>
<td>Reduced</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Better defended</td>
</tr>
<tr>
<td>Stroke volume</td>
<td>Increased</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>Improved sustenance</td>
</tr>
<tr>
<td>Cardiac efficiency</td>
<td>Increased</td>
</tr>
<tr>
<td>Cardiac compliance</td>
<td>Increased</td>
</tr>
<tr>
<td>PHYSIOLOGICAL RESPONSE</td>
<td>EFFECT</td>
</tr>
<tr>
<td>----------------------------</td>
<td>------------</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
<td></td>
</tr>
<tr>
<td>Metabolic rate</td>
<td>Reduced</td>
</tr>
<tr>
<td>Muscle lactate</td>
<td>Reduced</td>
</tr>
<tr>
<td>Muscle lactate threshold</td>
<td>Increased</td>
</tr>
<tr>
<td>Muscle glycogen</td>
<td>Spared</td>
</tr>
<tr>
<td>Muscle force generation</td>
<td>Increased</td>
</tr>
<tr>
<td><strong>Fluid-Electrolyte</strong></td>
<td></td>
</tr>
<tr>
<td>Fluid balance</td>
<td>Improved</td>
</tr>
<tr>
<td>Sweat electrolyte losses</td>
<td>Reduced</td>
</tr>
<tr>
<td>Plasma volume</td>
<td>Increased</td>
</tr>
<tr>
<td>Total body water</td>
<td>Increased</td>
</tr>
<tr>
<td>Thirst</td>
<td>Improved</td>
</tr>
</tbody>
</table>
Maladaptive Physiologic Response to Heat Stress

- As blood continues to get shunted to the peripheral circulation, perfusion to the gut is compromised.
- Direct heat injury to the gut also causes breakdown of tight junctions and bacterial translocation.
- Direct cytotoxic injury to liver limits ability to overcome portal bacteremia.
- Cerebral blood flow decreases.
Maladaptive Physiologic Response to Heat Stress

Dysregulation of the immune/inflammatory system leads to systemic inflammatory response syndrome (SIRS)

Venous dilation of the splanchnic circulation occurs which leads to severe hypotension
Maladaptive Physiologic Response to Heat Stress

- Splanchnic vasodilation results in decreased central venous pressures, cardiac return, and thus cardiac output
- Blood can no longer be shunted to periphery to participate in heat exchange resulting in perpetuation of central hyperthermia
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Brain Effects of Hyperthermia

- Cerebral blood flow decreases due to systemic hypotension
- Circulating cytokines also lead to intracranial hypertension
- Cerebral perfusion pressure = MAP - ICP
- Cerebral metabolic oxygen requirement increases
- Leads to cerebral ischemia and altered mentation state “heatSTROKE”
Coagulopathies associated with Heatstroke

- Primary initiating factor of coagulopathic state is thermal injury to the vascular endothelium
- Leads to platelet aggregation - may be irreversible, despite cooling
- Platelet activation leads to fibrin deposition occluding vessels - microvascular thrombosis
- Major contributor to MODS

Virchow’s Triad and Tissue Factor
Coagulopathies associated with Heatstroke

Within hours to days, hypercoagulable phase of DIC progresses to hypocoagulable state and clinical bleeding
Effects of Hyperthermia on the GI Tract

- Direct heat injury to enterocytes
- Combined with decreased splanchnic blood flow and gastrointestinal hypoperfusion
- Interferes with mucosal barrier and results in bacterial translocation
Effects on the Muscles

- In dogs, heat stroke is often combined with or a result of exertional hyperthermia
- Decreased intracellular ATP
- Increased intracellular calcium
Effects on Kidneys

- Combination of hypovolemia and dehydration causes decreased renal perfusion
- Rhabdomyolysis results in myoglobinuria and direct tubular injury
- DIC and renal thrombi cause ischemic injury
Necropsy Findings

- Necropsy findings confirm pre-mortem findings
- Microthrombosis
- Multi-organ necrosis
- Increased endothelial permeability
- Did not find blood-bone marrow barrier defects
- Not-detectible by light microscopy
- Response to cytokines
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Types of Heat Stroke

- Classic heat stroke - occurs without history of exercise in patients that have compromised health or exposed to very high environmental temperatures
- Exertional heat stroke - Occurs in healthy individuals where external and internal heat production exceed heat dissipation
Heat Stroke in Dogs

Almost always a combination of both exertional and classic

Dogs in hot cars struggle to get free

Dogs with laryngeal paralysis or brachycephalic conformation doing heavy exercise
## Factors that Decrease Heat Dissipation

<table>
<thead>
<tr>
<th>Predisposing factor</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exogenous</strong></td>
<td></td>
</tr>
<tr>
<td>Lack of acclimatization</td>
<td>Decreased neurohormonal responses</td>
</tr>
<tr>
<td>Confinement and/or poor ventilation</td>
<td>Decreased conduction, convection, radiation, and evaporation</td>
</tr>
<tr>
<td>Increased humidity</td>
<td>Decreased evaporative heat loss</td>
</tr>
<tr>
<td>Water deprivation</td>
<td>Decreased blood volume that leads to decreased cutaneous vasodilation and cooling</td>
</tr>
<tr>
<td>Furosemide</td>
<td>Fluid losses that lead to hypovolemia</td>
</tr>
<tr>
<td>Negative inotropic drugs (β-blockers)</td>
<td>Electrolyte losses that lead to altered electrical activity</td>
</tr>
<tr>
<td>Phenothiazines</td>
<td>Impair cardiac contractility</td>
</tr>
<tr>
<td></td>
<td>Hypohidrosis (in humans)</td>
</tr>
<tr>
<td></td>
<td>Altered autonomic function</td>
</tr>
<tr>
<td>Predisposing factor</td>
<td>Mechanism of action</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Endogenous</td>
<td></td>
</tr>
<tr>
<td>Brachycephalic anatomy</td>
<td>Inadequate ventilatory capacity</td>
</tr>
<tr>
<td>Laryngeal paralysis</td>
<td>Inadequate ventilatory capacity</td>
</tr>
<tr>
<td>Obesity</td>
<td>The insulating effect of fat leads to decreased heat dissipation and decreased ventilation</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>Decreased cardiac output</td>
</tr>
<tr>
<td>Neurological/neuromuscular</td>
<td>Altered thermoregulatory function</td>
</tr>
<tr>
<td></td>
<td>Decreased ventilatory capacity</td>
</tr>
<tr>
<td>Age (geriatric)</td>
<td>As extrapolated from humans, poor acclimatization, compromised cardiovascular response, and deficient voluntary control</td>
</tr>
<tr>
<td>Hair coat and color</td>
<td>Darker coats absorb more heat</td>
</tr>
<tr>
<td></td>
<td>Thicker coats decrease radiation and convection</td>
</tr>
</tbody>
</table>
# Factors that Increase Heat Production

<table>
<thead>
<tr>
<th>Exogenous</th>
<th>Endogenous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamines</td>
<td>Exercise</td>
</tr>
<tr>
<td>Metaldehyde</td>
<td>Pyrexia (febrile disease)</td>
</tr>
<tr>
<td>Macadamia nuts</td>
<td>Hormonal hyperthermia (hyperthyroid)</td>
</tr>
<tr>
<td>Organophosphates</td>
<td>Seizures</td>
</tr>
<tr>
<td>Halothane</td>
<td>Eclampsia</td>
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Historical Findings

Most cases occur early in the summer
- Owner lack of vigilance?
- Lack of acclimation?
- June (28%), July (31%), and August (19%)
- Exertional heat stroke - Heavy exercise prior
- Classic heat stroke - left in car, laryngeal paralysis, brachycephalic breeds
- Dogs may or may not have been cooled at home by owners - will affect rectal temperatures at presentation
Physical Examination Findings

- Rectal temperatures range from out of range high to hypothermia (14%) - often depends on if there was cooling performed at home or at referral vet.
- Most dogs are tachycardic +/- pulse abnormalities (25% arrhythmias).
- Almost all dogs have mental abnormalities ranging from disorientation to coma.
Physical Examination Findings

- Diarrhea and/or blood in stool is often present
- Petechiae, ecchymosis
- Vomiting +/- hematemesis
- Tachypnea, severe panting
Point of Care Blood Work

- Blood smear evaluation often shows nucleated red blood cells - presumed due to thermal damage to the blood bone marrow barrier
- Coagulation tests may reveal prolonged PT and aPTT
- Platelet count often decreased
- PCV and TS often reveal hemoconcentration
- Electrolytes may reveal free water deficits such as increased Na+,
## CBC and Biochemistry

<table>
<thead>
<tr>
<th>Increased Value</th>
<th>Decreased Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT</td>
<td>Glucose</td>
</tr>
<tr>
<td>AST</td>
<td>Platelet count</td>
</tr>
<tr>
<td>CK*</td>
<td></td>
</tr>
<tr>
<td>ALP</td>
<td></td>
</tr>
<tr>
<td>BUN</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>Neutrophils</td>
</tr>
</tbody>
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Evaporative cooling

- Applying room temperature or cool water to patient's skin
- Using fans to circulate air and promote evaporation of water
- Each 1.7ml of water that is evaporated consumes 1 kcal of heat
- Less likely to cause peripheral vasoconstriction, shivering, or patient distress
- Slower than ice bath immersion
Ice water immersion - Conductive cooling

Submerging entire body in ice bath and massaging limbs to promote dermal blood flow and heat exchange

Best method for rapid cooling

Recommended for humans for exertional heatstroke

Many downsides, including personnel needed, difficulty to administer other treatments, ‘overshoot’ hypothermia, shivering, extreme patient discomfort
Invasive Cooling Methods

Cold water lavage of:

- Colon
- Bladder
- GI tract
- Peritoneal cavity
Novel Therapies

- Cooling catheters: Closed system catheters that circulate icewater
- Cooling Bodysuits
Cooling

Recommendations are for termination of active cooling when rectal temp reaches 103.5–104.1F

Overshoot cooling can lead to shivering which will increase core temp, as well as complications from hypothermia

Possible link of vasoconstriction to DIC

Hypothermia inactivates clotting factors
Other Therapeutics

- Dantrolene in malignant hyperthermia
- Reduces release of calcium from sarcoplasmic reticulum
- Studies only support in cases of malignant hyperthermia
Cardiovascular support

- Aggressive IV fluid therapy may be needed to correct hypovolemia and electrolyte abnormalities
- Room temperature fluids will also help with systemic cooling
- Hypertonic saline may not be effective, as patients are often severely dehydrated
- Vasopressors may be needed due to severe vasodilation
Respiratory Support

- Intubation may be required for patients with upper airway obstruction and/or pharyngeal swelling
- Most patients will breath on their own once intubated
- Wake up SLOWLY
Neurologic Support

- Administration of anticonvulsants for patients experiencing seizures such as levetiracetam or diazepam
- Correction of hypoglycemia if present with 0.5ml/kg of 50% dextrose +/- additional dextrose supplementation
- Head elevation +/- mannitol or hypertonic saline if depressed mentation persists and cerebral edema is suspected
Renal Support

- Urinary catheterization may be helpful to monitor urine output and for patient cleanliness if they remain obtunded or stuporous.
- Intravenous fluid support to maintain renal perfusion and assist with diuresis of pigment.
Treatment of Coagulopathy

Currently no support for anti-coagulation for hypercoagulable phase of DIC, often present on presentation

Fresh frozen plasma may be required if patient progresses to hypocoagulable phase of DIC including prolonged clotting times and clinical bleeding
Gastrointestinal Support

- Broad spectrum antibiotics to treat bacterial translocation and septicemia
- Antacids and gastroprotectants such as sucralfate if melena or hematemesis are present or GI bleeding suspected
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Prognosis

Prognostication can be made by a number of factors:

- Patients with increased nRBCs are less likely to survive.
- Patients with hypoglycemia refractory to treatment are less likely to survive.
- Patients presenting >90 minutes after onset of signs are less likely to survive.
Nucleated Red Blood Cells

Retrospective study from Israel
- 18 nRBCs per 100 WBC
- Sen 95% Sp 88% for death

Fig 1. Relative nucleated red blood cells (NRBC) (cells per 100 leukocytes) at presentation and absolute NRBC in 17 survivor and 21 nonsurvivor dogs with heatstroke.

Peripheral Nucleated Red Blood Cells as a Prognostic Indicator in Heatstroke in Dogs
I. Aroch, G. Segev, E. Loeb, and Y. Bruchim
Prognosis

- Persistent neurologic abnormalities are less likely to survive
- Seizures are associated with risk of death
- Prolongations in PT or aPTT are negative prognostic indicators
- Overall mortality is approximately 50-60% - based on old literature
- Dogs that died tend to die quickly - within 24 hours
Heat stroke is a complex disease processes that shares many similarities with sepsis.

Heat stroke is life threatening if not threatened quickly and aggressively.

Patients require intensive therapy involving all body systems.

Non-invasive evaporative cooling is the preliminary treatment of choice.

Owners should attempt cooling at home if >90 minutes away.

First 24 hours are the most critical.
References

Questions?