# 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

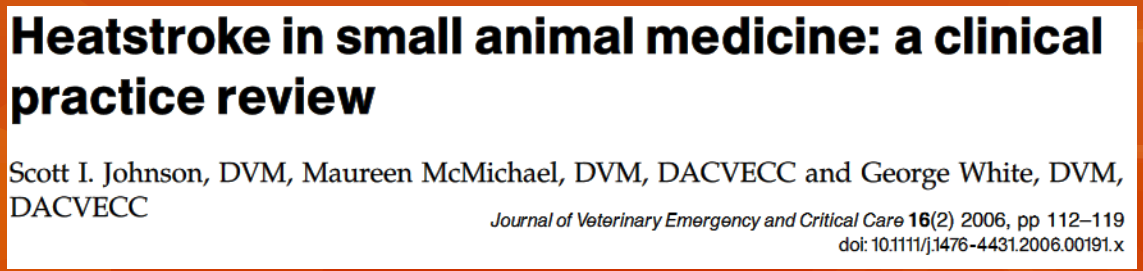
# Human vs Veterinary Literature

- 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

*J Vet Intern Med* 2006;20:38–46

**Heat Stroke in Dogs: A Retrospective Study of 54 Cases (1999–2004) and Analysis of Risk Factors for Death**

Yaron Bruchim, Eyal Klement, Joseph Saragusty, Efrat Finkeilstein, Philip Kass, and Itamar Aroch



**Heatstroke in small animal medicine: a clinical practice review**

Scott I. Johnson, DVM, Maureen McMichael, DVM, DACVECC and George White, DVM, DACVECC

*Journal of Veterinary Emergency and Critical Care* **16**(2) 2006, pp 112–119
doi: 10.1111/j.1476-4431.2006.00191.x

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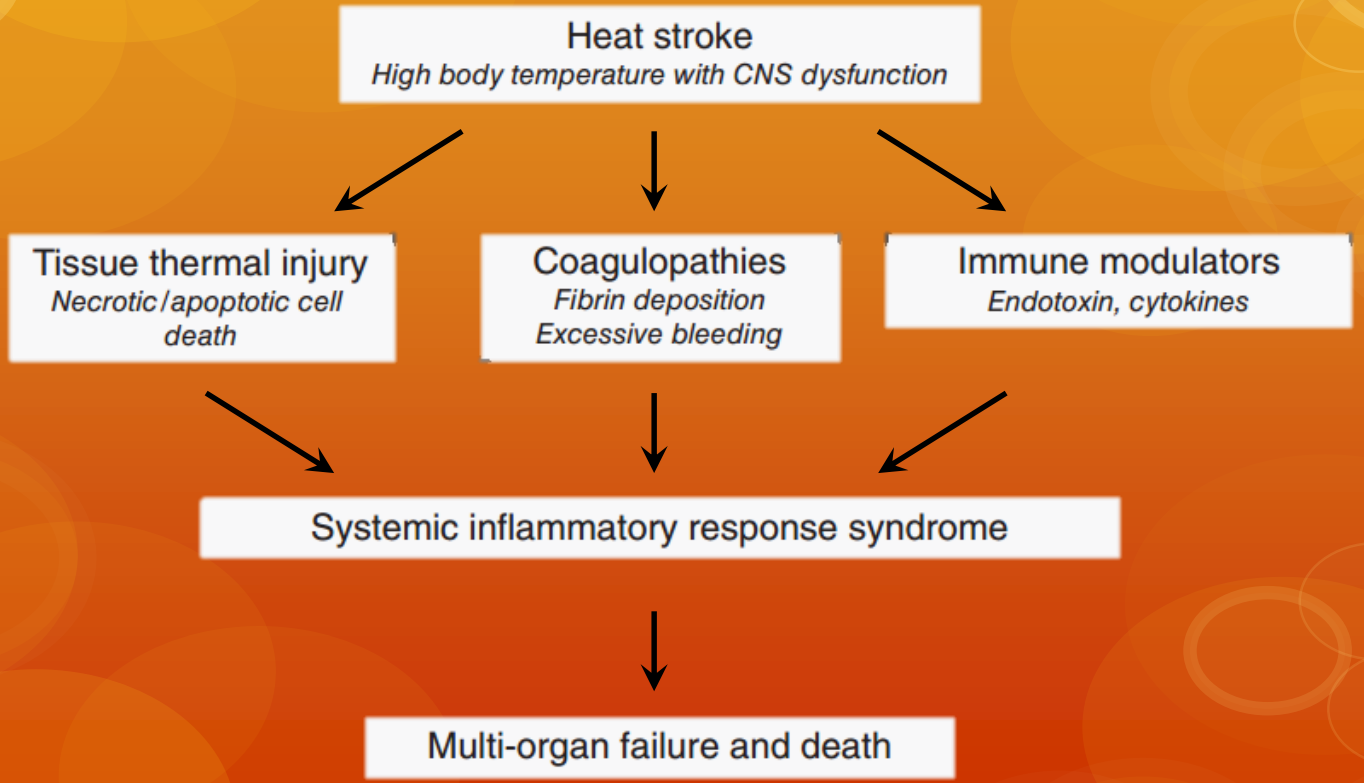
# Pathophysiology of Heat Stroke

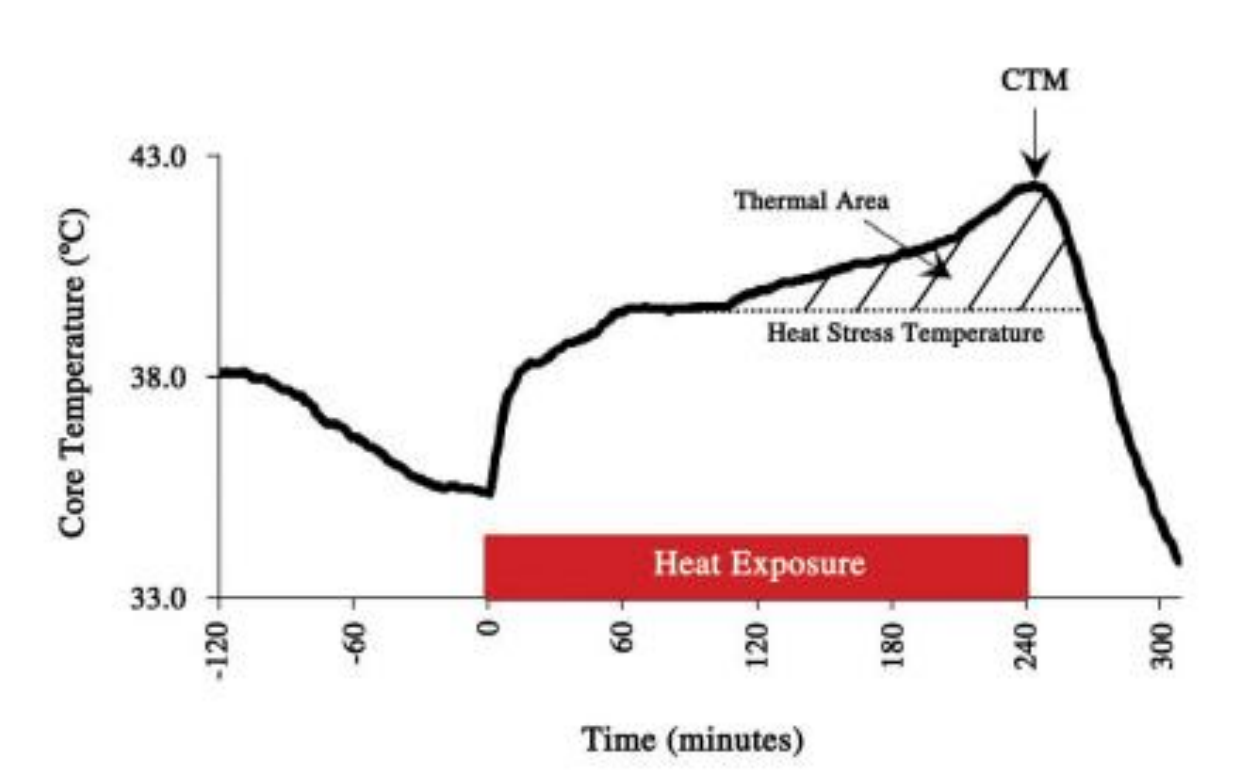



Leon, Lisa R., and Abderrezak Bouchama. "Heat stroke." Comprehensive Physiology (2015).

# Temperatures That Risk Heat Stroke

| | Relative humidity (%) | | | | | |
|---|---|---|---|---|---|---|
| Temperature (°F) | 90 | 80 | 70 | 60 | 50 | 40 |
| 90 | 121 | 113 | 105 | | | |
| 95 | | 133 | 122 | 113 | 105 | |
| 100 | | | 142 | 129 | 118 | 109 |
| 105 | | | | 148 | 133 | 121 |
| 110 | | | | | | 135 |
| Heat index | Heat disorder seen in humans | | | | | |
| 105–130°F | Heatstroke possible | | | | | |
| >130°F | Heatstroke highly likely with continued exposure | | | | | |

# Thermal Area

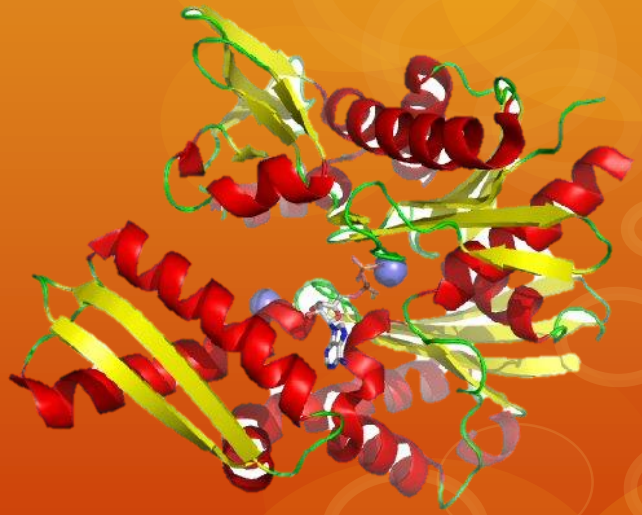



Leon, Lisa R. "Pathophysiology of Heat Stroke." Colloquium Series on Integrated Systems Physiology: From Molecule to Function to Disease. Vol. 7. No. 2. Morgan & Claypool Life Sciences, 2015.

# Cellular adaptive response to heat

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

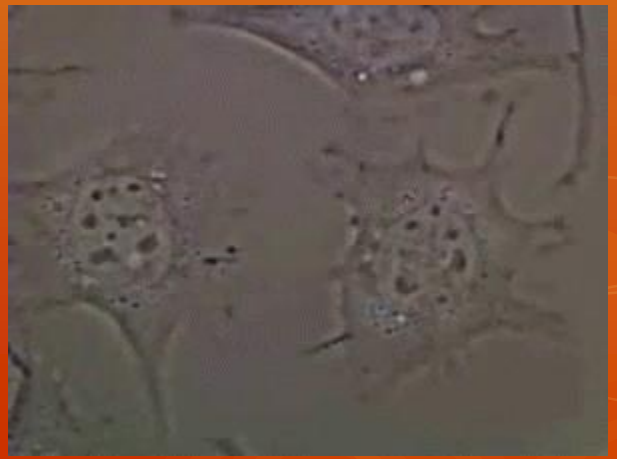
- Chaperonin activity
- Modulation of inflammatory responses (decreased IL-1, IL-6, TNF-α NF-$\kappa$B)
- Regulation of the acute physiological alterations
- Antioxidant effect
- Antiapoptotic effect



# Cellular Response to Hyperthermia

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

- IL-6 and NF-$\kappa$B is greatly increased
- Temperatures above 106.7$^{o}$F for as little as a few minutes can induce cellular apoptosis
- Temperatures above 109.4$^{o}$F uncouples oxidative phosphorylation and enzymes are denatured

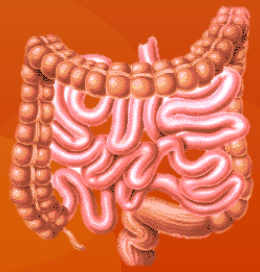


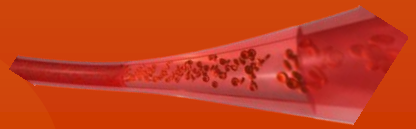
# Cellular Response to Hyperthermia

- Temperature dependant electrolyte channels are altered
- Potassium flows extracellularly leading to increased plasma [K+]
  - Rarely seen in veterinary patients
- Severe hyperthemia 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





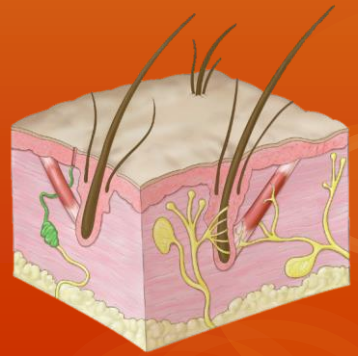


**TABLE 3:** Adaptations and functional outcomes in response to heat acclimatization

| PHYSIOLOGICAL RESPONSE | EFFECT |
|---|---|
| *Thermoregulatory* | |
| Core temperature (rest and exercise) | Reduced |
| Skin flow | Earlier onset; higher rate |
| Skin Temperature | Reduced |
| Sweating | Earlier onset; higher rate |
| *Cardiovascular* | |
| Heart rate | Reduced |
| Blood pressure | Better defended |
| Stroke volume | Increased |
| Cardiac output | Improved sustainment |
| Cardiac efficiency | Increased |
| Cardiac compliance | Increased |

**TABLE 3:** Adaptations and functional outcomes in response to heat acclimatization

| PHYSIOLOGICAL RESPONSE | EFFECT |
|---|---|
| *Metabolic* | |
| Metabolic rate | Reduced |
| Muscle lactate | Reduced |
| Muscle lactate threshold | Increased |
| Muscle glycogen | Spared |
| Muscle force generation | Increased |
| *Fluid-Electrolyte* | |
| Fluid balance | Improved |
| Sweat electrolyte losses | Reduced |
| Plasma volume | Increased |
| Total body water | Increased |
| Thirst | Improved |

# Maladaptive Physiologic Response to Heat Stress

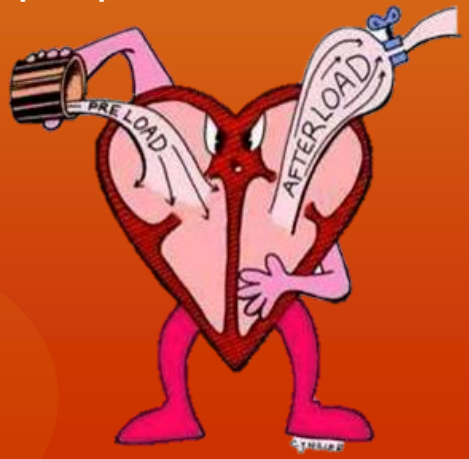
- As blood continues to get shunted to the peripheral circulation, perfusion to the gut is compromised
- Direct heat injury to the gut also causes breakdown of tight junctions and bacterial translocation
- Direct cytotoxic injury to liver limits ability to overcome portal bacteremia
- Cerebral blood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

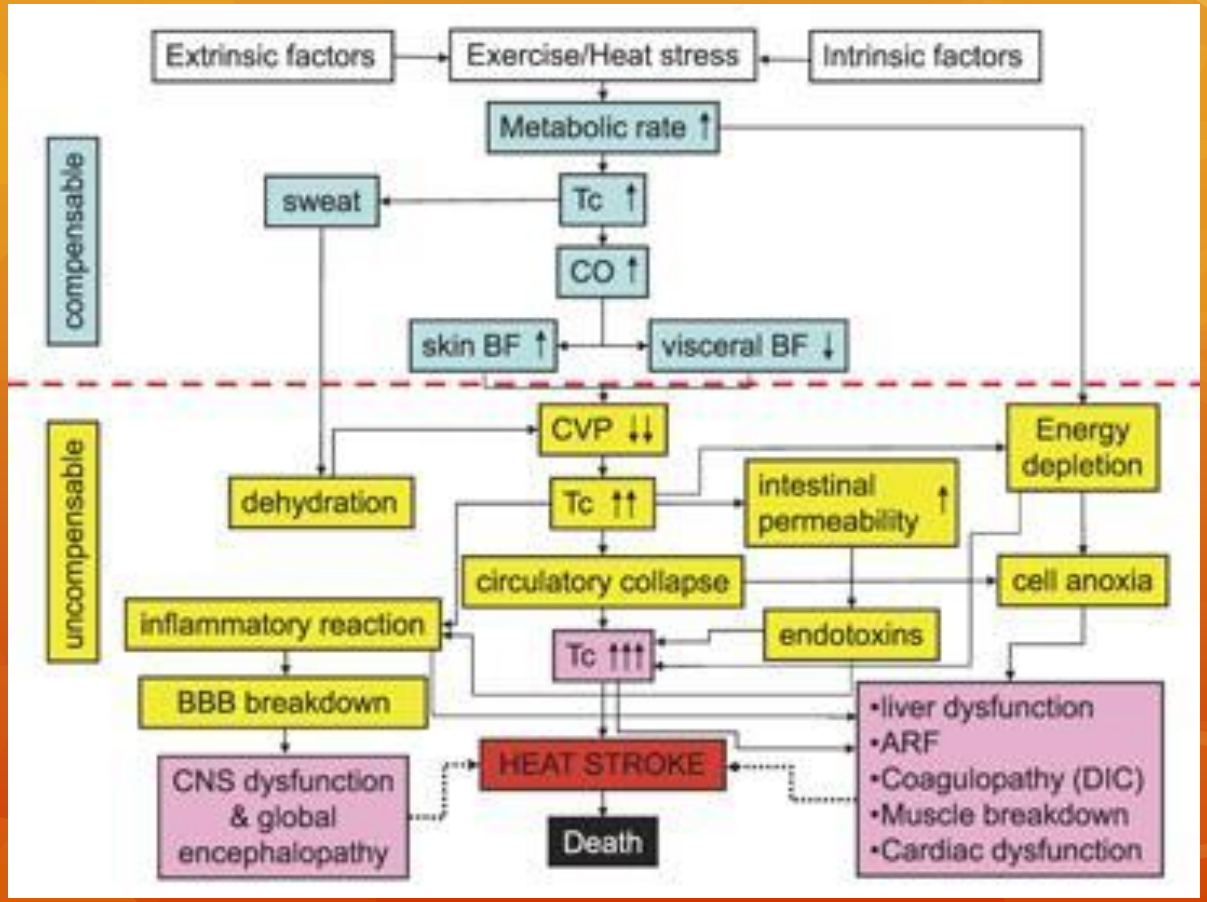
# Maladaptive Physiologic Response to Heat Stress

- 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






Epstein, Y., and W. O. Roberts. "The pathopysiology of heat stroke: an integrative view of the final common pathway." Scandinavian journal of medicine & science in sports 21.6 (2011): 742-748.

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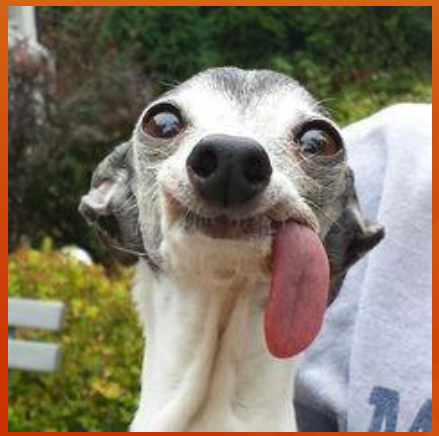
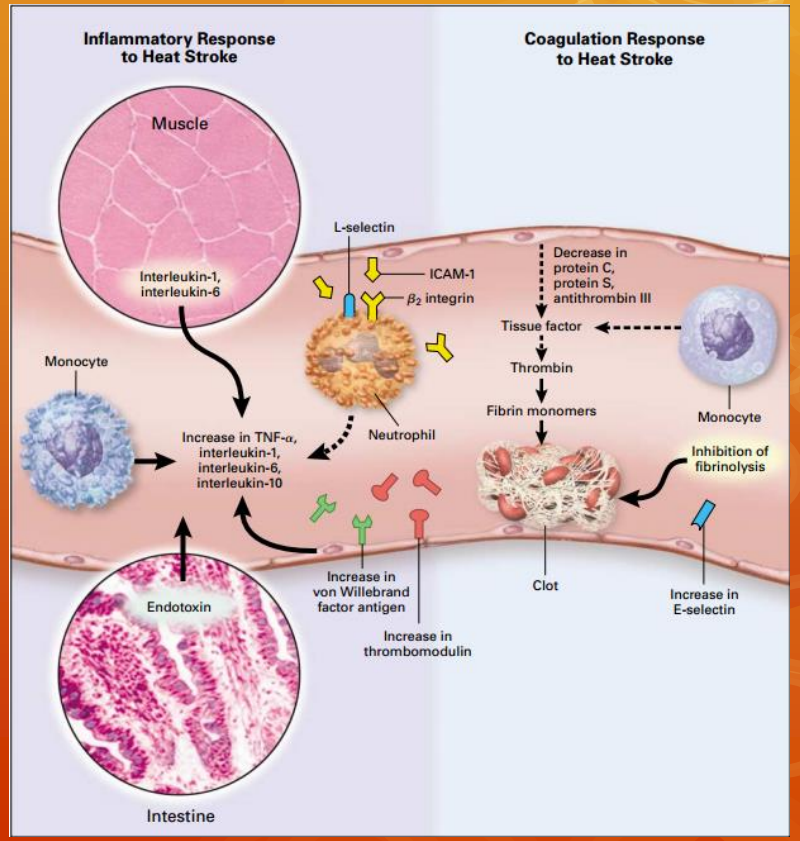
# Brain Effects of Hyperthermia

- 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

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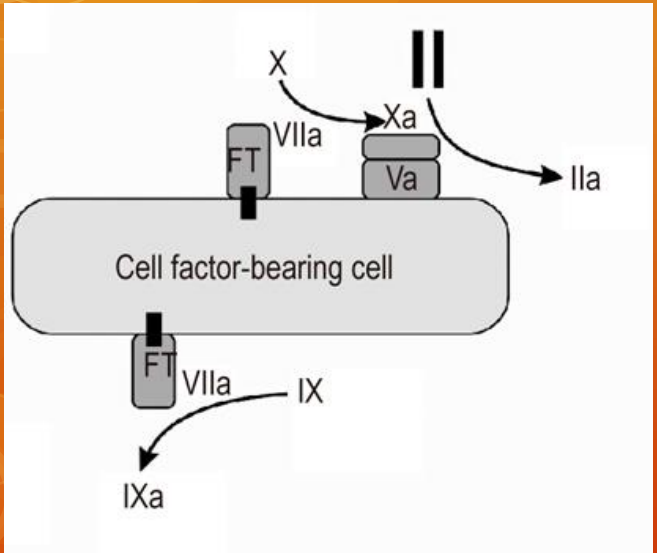
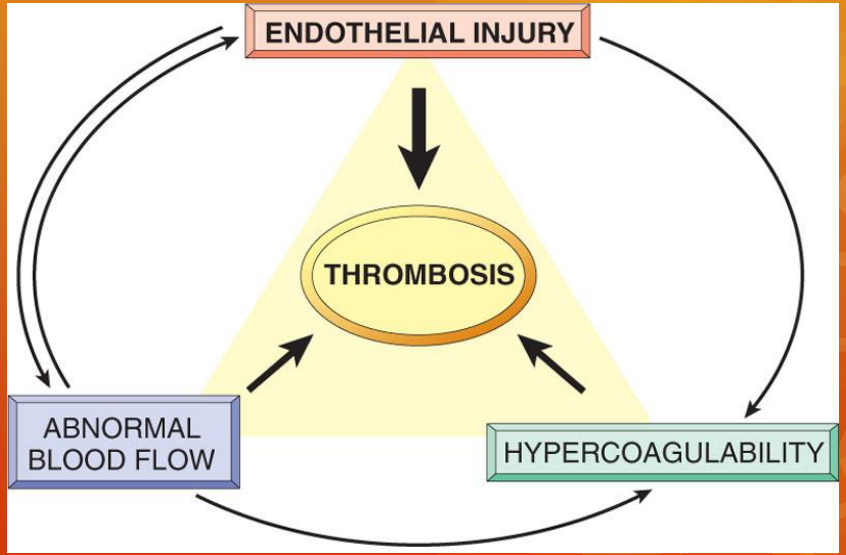
# Virchow's Triad and Tissue Factor



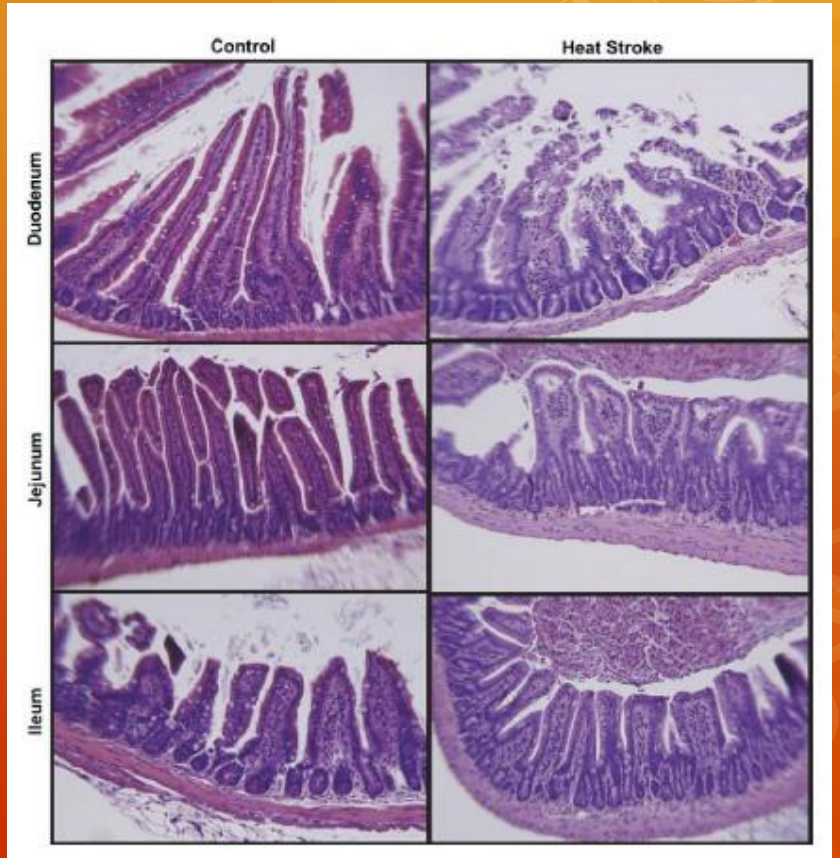



# Coagulopathies associated with Heatstroke

Within hours to days, hypercoagulable phase of DIC progresses to hypocoagulable state and clinical bleeding

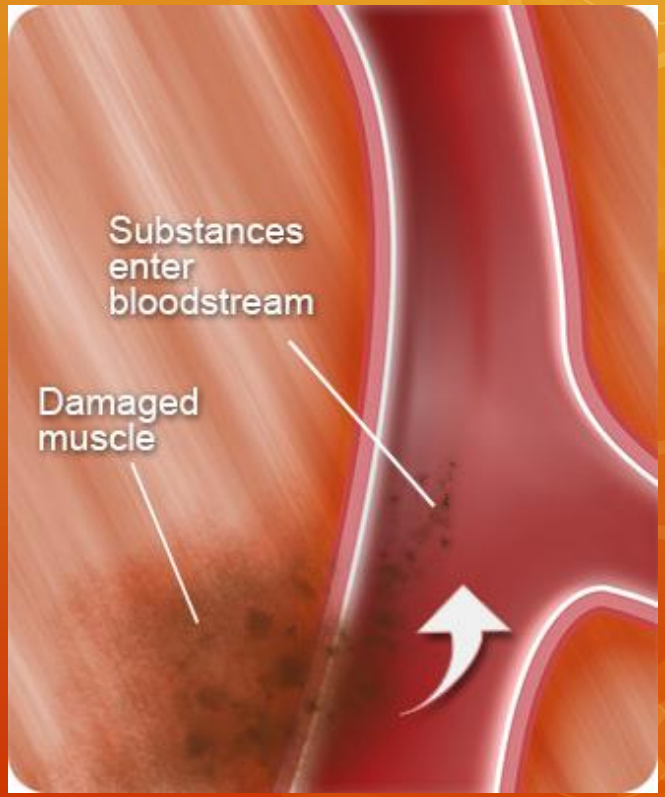
# Effects of Hyperthermia on the GI Tract

- 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

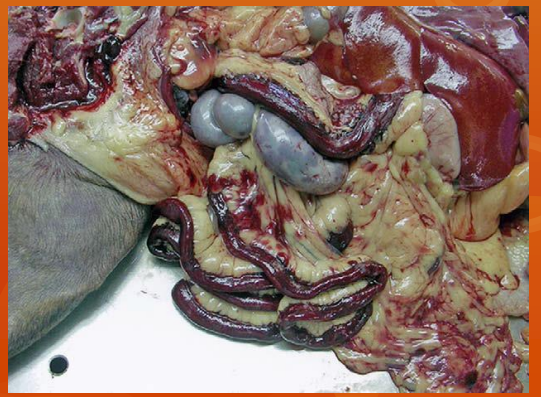
- Necropsy findings confirm pre-mortem findings
  - Microthrombosis
  - Multi-organ necrosis
  - Increased endothelial permeability
- Did not find blood-bone marrow barrier defects
  - Not-detectible by light microscopy
  - Response to cytokines

**Pathological Findings in Dogs with Fatal Heatstroke**

**Y. Bruchim*, E. Loeb*, J. Saragusty† and I. Aroch***

** Koret School of Veterinary Medicine, Emergency and Critical Care Unit and † Department of Reproduction Management, Leibniz Institute for Zoo and Wildlife Research, Germany*

J. Comp. Path. 2009, Vol. 140, 97–104



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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

| **Predisposing factor** | **Mechanism of action** |
|---|---|
| Exogenous | |
| Lack of acclimatization | Decreased neurohormonal responses |
| Confinement and/or poor ventilation | Decreased conduction, convection, radiation, and evaporation |
| Increased humidity | Decreased evaporative heat loss |
| Water deprivation | Decreased blood volume that leads to decreased cutaneous vasodilation and cooling |
| Furosemide | Fluid losses that lead to hypovolemia |
| | Electrolyte losses that lead to altered electrical activity |
| Negative inotropic drugs (β-blockers) | Impair cardiac contractility |
| Phenothiazines | Hypohidrosis (in humans) |
| | Altered autonomic function |

| **Predisposing factor** | **Mechanism of action** |
|---|---|
| Endogenous | |
| Brachycephalic anatomy | Inadequate ventilatory capacity |
| Laryngeal paralysis | Inadequate ventilatory capacity |
| Obesity | The insulating effect of fat leads to decreased heat dissipation and decreased ventilation |
| Cardiovascular disease | Decreased cardiac output |
| Neurological/neuromuscular | Altered thermoregulatory function |
| | Decreased ventilatory capacity |
| Age (geriatric) | As extrapolated from humans, poor acclimatization, compromised cardiovascular response, and deficient voluntary control |
| Hair coat and color | Darker coats absorb more heat |
| | Thicker coats decrease radiation and convection |

# Factors that Increase Heat Production

| **Exogenous** | **Endogenous** |
|---|---|
| Amphetamines | Exercise |
| Metaldehyde | Pyrexia (febrile disease) |
| Macadamia nuts | Hormonal hyperthermia (hyperthyroid) |
| Organophosphates | Seizures |
| Halothane | Eclampsia |

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# Historical Findings

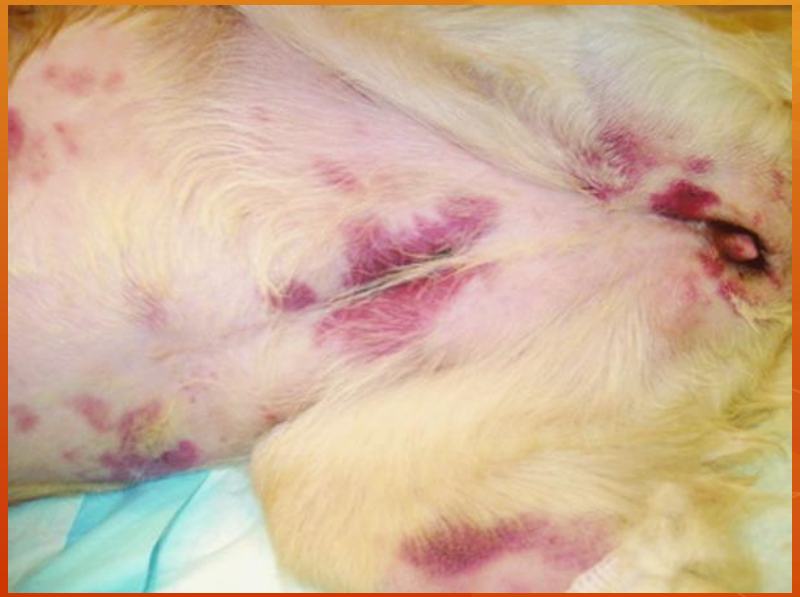
- Most cases occur early in the summer
  - Owner lack of vigilance?
  - Lack of acclimation?
- June (28%), July (31%), and August (19%)
- Exertional heat stroke - Heavy exercise prior
- Classic heat stroke - left in car, laryngeal paralysis, brachycephalic breeds
- Dogs may or may not have been cooled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

# Physical Examination Findings

- Rectal temperatures ranges 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

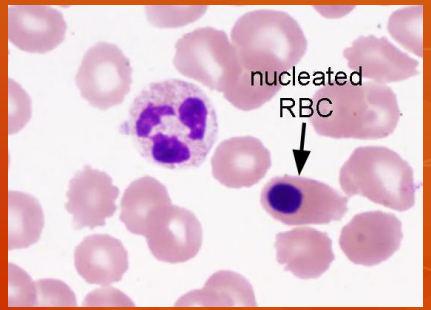
# Physical Examination Findings

- 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

| Increased Value | Decreased Value |
|---|---|
| ALT | Glucose |
| AST | Platelet count |
| CK* | |
| ALP | |
| BUN | |
| Creatinine | |
| Neutrophils | Neutrophils |

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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

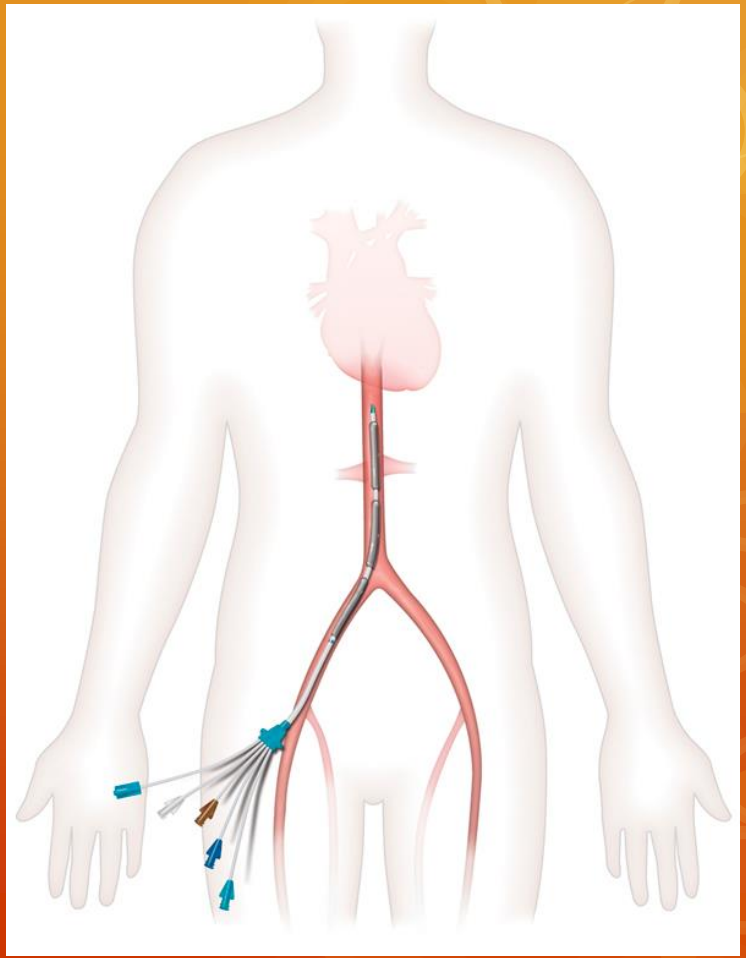
# Invasive Cooling Methods

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

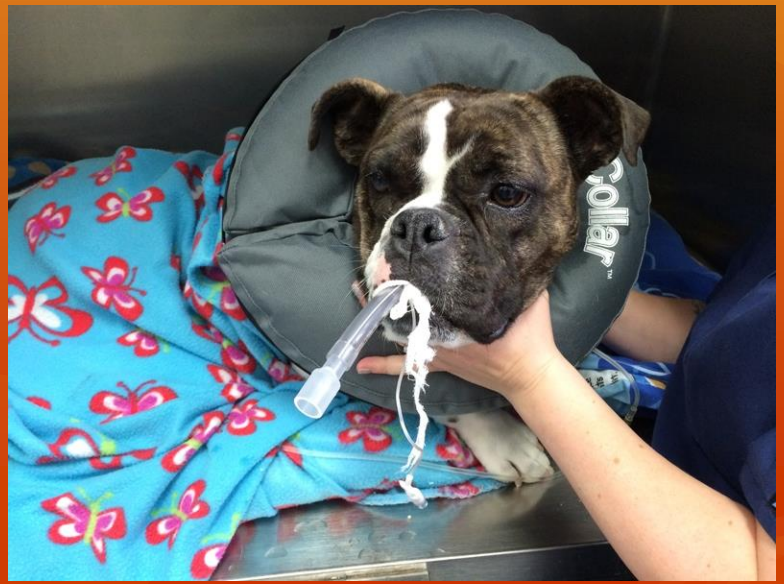
- Dantrolene in malignant hyperthermia
- Reduces release of calcium from sarcoplasmic reticulum
- Studies only support in cases of malignant hyperthermia


# 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 patiens will breath on their own once intubated
- Wake up SLOWLY

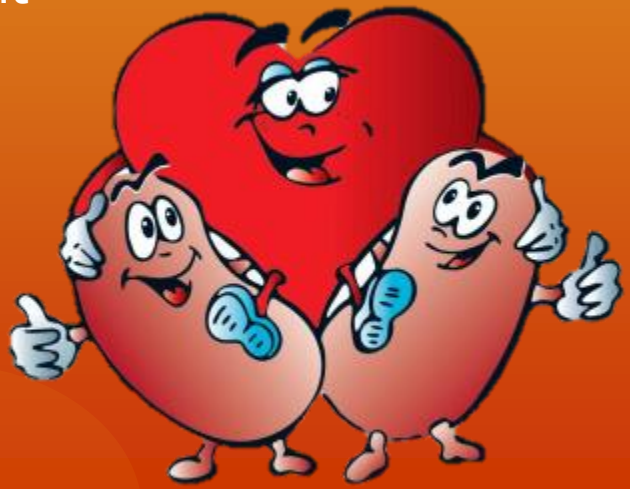


# Neurologic Support

- 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

*J Vet Intern Med* 2009;23:544–551

**Peripheral Nucleated Red Blood Cells as a Prognostic Indicator in Heatstroke in Dogs**

I. Aroch, G. Segev, E. Loeb, and Y. Bruchim

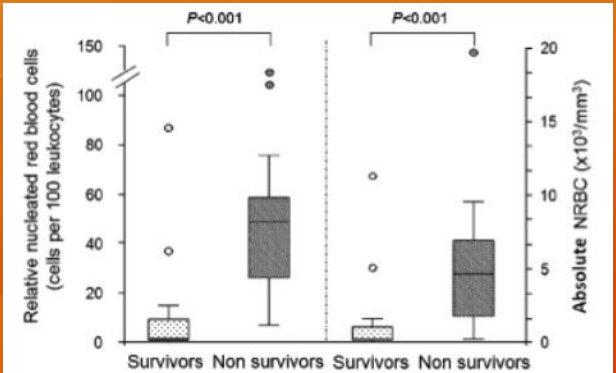
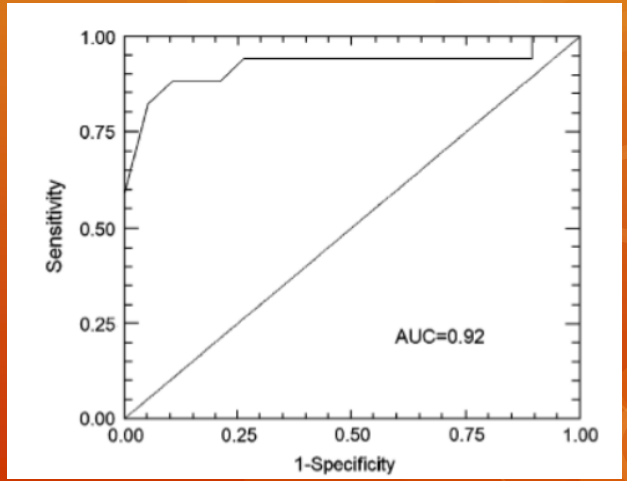



**Fig 1.** Relative nucleated red blood cells (NRBC) (cells per 100 leukocytes) at presentation and absolute NRBC in 17 survivor and 21 nonsurvivor dogs with heatstroke.



# Prognosis

- Persistent neurologic abnormalities are less likely to survive
- Seizures are assossaited 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

# Summary

- Heat stroke is a complex disease processes that shares many similarities with sepsis
- Heat stroke is life threatening if not threated 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

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# Questions?