FEVER AND PYREXIA WITH VERIFICATION OF THERMISTERS IN DOGS

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By

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The undersigned, appointed by the dean of the Graduate School, have examined the thesis entitled

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presented by Rebecca Greer a candidate for the degree of master of science, and hereby certify that , in their opinion it is worthy of acceptance.

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FEVER AND PYREXIA WITH VERIFICATION OF THERMISTERS IN DOGS

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ABSTRACT

An elevated body temperature (pyrexia) often accompanies disease. Body temperature measurement is one of the vital parameters in medicine. This thesis contains a literature review of the pathophysiology of temperature regulation, hyperthermia, fever, and treatments for hyperthermia and fever. Additionally, the thesis describes studies conducted to compare accuracy and precision of several methods of body temperature measurement in dogs.

The core body temperature can be difficult to measure and invasive techniques are required to make this measurement. In our original studies an auricular, subcutaneous, and rectal method of temperature measurement were compared to true core body temperature as measured by a thermister-tipped pulmonary artery catheter. Our results indicate that within the range of clinical application, predictive rectal thermometers in healthy dogs approximated core body temperature very well. At this time there is no other method of temperature measurement in routine use in veterinary medicine that approximates the core body temperature as well as rectal thermometers.

Chapter 1

Hyperthermia and fever: definitions and pathophysiology

Introduction

An elevated body temperature can occur when (1) physiological cooling mechanisms are overwhelmed or (2) the body thermostat is altered. Three scientific terms used to indicate an elevated body temperature are (1) pyrexia, (2) hyperthermia, and (3) fever. Pyrexia is a term commonly used to indicate that body temperature is elevated above reference range for the species, without inferring a cause. Hyperthermia denotes an exceptionally high body temperature, especially if it is artificially induced. Fever typically refers to increased body temperature resulting from an alteration upwards in the body thermostat.[1] By the strictest definitions none of these words indicate the mechanism for the increase in body temperature. By common usage and connotation in veterinary medicine, fever indicates an alteration in the body thermostat while hyperthermia implies that the cooling mechanisms have been overwhelmed. This thesis will apply these words according to their common usage.

Temperature Regulation

Body temperature is tightly controlled in mammals. In healthy mammals heat gain and loss is balanced so that the core temperature is maintained within a pre-determined, narrow range. The core temperature is the temperature deep within the body[1] and is considered the true measure of body temperature. Heat is gained primarily by basal metabolism, but muscle activity and radiation are also important.[2,3] Heat is lost by conduction, convection, radiation, or evaporation (Table 1).[3] Radiation is the emission of energy in the form of particles or waves and is important in both heat gain and heat loss. An example of heat gain by radiation is the heat gained by sunlight; heat

can be lost to the environment by radiation from the animal's skin/surface. Under normal environmental conditions radiation and convection are the primary mechanisms of heat loss in dogs. When the ambient temperature approaches body temperature, evaporation becomes more important than radiation and convection for cooling.[3,4]

The central nervous system is responsible for control and regulation of body temperature. Within the central nervous system the pre-optic region of the anterior hypothalamus is responsible for integrating signals from the periphery with central signals and initiating the appropriate response to warm or cool the body. Temperature is sensed by thermosensitive elements distributed over the skin surface, within the viscera, and in the hypothalamus. Input from the body and skin thermosensitive elements converge on the pre-optic area of the hypothalamus which in turn initiates the neurogenic compensatory response, primarily through the autonomic nervous system (Figure 1).[5]

Mechanisms of Cooling

When the hypothalamus senses that the temperature is above the accepted range, it signals vasodilatation of the peripheral blood vessels allowing increased flow to the cooler extremities resulting in cooler blood returning to the core and reducing the temperature. Cooling is also increased by evaporation (panting and hypersalivation in dogs, sweating in humans), posturing to increase the surface area for heat loss, and behavioral changes such as moving to a cooler environment.[6,7] The hypothalamic signals result in tachycardia; increasing cardiac output for increased flow to the cool periphery. Minute ventilation is also increased by the hypothalamus and causes more air to move past moist surfaces enhancing evaporation. Visceral perfusion is reduced and blood is shunted to the muscles and skin.[8] All of these mechanisms enhance heat loss.

Mechanisms of Warming

When the temperature sensed by the hypothalamus falls below the accepted range, heat conservation and heat production can be instituted. Heat conservation includes piloerection, peripheral vasoconstriction, and posture changes. Piloerection allows erect hairs to more efficiently trap warm air at the body surface. Peripheral vasoconstriction reduces blood flow to the cooler surface of the body. Posture and behavioral changes include curling to reduce surface exposure to the environment and moving to a warmer place.[9] Heat conservation is initiated before heat production, but if conservation is inadequate to maintain core temperature at the pre-determined set point, heat generation is initiated.

Additional heat is produced by shivering. The dorsomedial portion of the posterior hypothalamus contains the primary motor center for shivering. This area is excited by cold signals from the skin and spinal cord. When activated the posterior hypothalamus transmits signals through the brainstem and spinal cord to the anterior motor neurons. These signals are non-rhythmic and do not cause actual muscle shaking, but increase the tone of the skeletal muscles throughout the body; when the tone rises above a certain point, shivering begins.[10] Muscle activity (shivering) increases the use of ATP, resulting in the breakdown of chemical bonds and the release of energy (heat).[2] Although data is not available in dogs, in horses, 75-80% of the metabolic energy of muscles is lost as heat.[11]

Catecholamine and thyroxine production are increased when the body temperature is too low.[9] When the hypothalamus is cooled it increases the production of thyrotropin-releasing hormone resulting in increased thyroxine production. Increased

thyroxine production increases the rate of cellular metabolism throughout the body, which in turn increases heat production. This compensatory mechanism takes several weeks before new levels of thyroxine secretion are achieved.[10] Catecholamines (epinephrine and norepinephrine) and steroid hormones are increased in cold-exposed animals.[12] Steroid hormones act with the catecholamines to alter the cellular metabolism and increase heat production.[13] Increasing catecholamine and thyroxine activity leads to increased cellular metabolism and heat production.

The hypothalamus and its effector mechanisms are very good at maintaining core body temperature. Compensatory mechanisms are only invoked when the hypothalamus senses that the body temperature is outside the normal range.[14] In humans, a rise of less than 1° C of the blood will result in compensatory changes.[8] When the mechanisms to maintain body temperature are overwhelmed, hyperthermia or hypothermia will result. Hypothermia will not be discussed in this thesis.

Hyperthermia

Hyperthermia can be divided into two primary causes, exposure to a high environmental temperature (classical heat stroke) and strenuous exercise (exertional heat stroke). Heat stroke can also occur with a combination of classical and exertional conditions.[3,7] In human medicine hyperthermia is divided into multiple subcategories dependant on the severity of clinical signs and prognosis. Heat stress involves perceived discomfort and physiological strain associated with heat exposure. Heat exhaustion is a mild to moderate illness due to water or salt depletion from exposure to heat or strenuous exercise. Heat stroke is characterized by severe illness with a core temperature >40 °C (104 °F) and central nervous system abnormalities.[8] These definitions are difficult to

apply in veterinary medicine as mild central nervous system derangements are difficult to identify in non-verbal patients. Therefore, the term hyperthermia is applied to all illnesses where the cooling mechanisms are overwhelmed.

Environmental and medical factors contribute to decreased heat dissipation. Environmental factors that alter heat dissipation include increased ambient temperature, increased humidity, poor ventilation and inadequate water intake. Medical factors that impair the normal cooling mechanisms include obesity, upper airway obstruction (e.g., brachycephalic upper airway syndrome and laryngeal paralysis), toxins, drugs, cardiovascular disease, and pulmonary disease.[7] Bridging the gap between medical factors and exertional heat stroke are medical conditions such as seizures or tremors where heat is generated by muscular activity, often simultaneously with a reduction in the animal's ability to consciously seek a cooler environment or engage other mechanisms of heat loss. Increased muscle activity with its resultant large amount of heat production can lead to exertional heat stroke.

Dissipation of heat is improved by acclimation but this process may take several weeks. Acclimation includes enhanced cardiovascular performance, activation of the renin-angiotensin-aldosterone axis, salt conservation by the sweat glands and kidneys, increased ability to sweat (for species that sweat), expansion of plasma volume, increased glomerular filtration rate, induction of heat shock proteins, and an increased ability to resist exertional rhabdomyolysis.[8,15] Animals are capable of acclimation to both exertional and environmental conditions.

Heat stroke is commonly recognized in dogs and other animals,[3-6,11] but dogs are not considered a good model for human heat stroke because of the intrinsic thermal

resistance of the canine brain.[16] In humans, heat-related illnesses are first manifested by dizziness, delirium, or other cerebral signs[8] while in dogs cerebral signs do not occur without physiologic signs.[16] Nevertheless, heat stroke has similar physiologic manifestations and consequences in dogs and humans. The pathophysiologic derangements that occur with heat stroke are complicated and are associated with both direct cytotoxicity of heat and the acute physiological alterations associated with hyperthermia.[3]

Direct heat toxicity on intracellular function includes inhibition of DNA synthesis and transcription, inhibition of cell cycle processes, degradation and aggregation of proteins, cytoskeletal disorders, decreased ATP production, and alteration of membrane permeability. As cellular processes are hindered, the stability and fluidity of cellular membranes are altered with loss of surface receptors necessary for a variety of cellular functions.[17] Free radicals are released resulting in lipid peroxidation of tissues. Damage to cellular functions can lead to direct cellular necrosis or induction of apoptosis. The pathways of heat-induced apoptosis have not been identified, but the induction of heat shock proteins are protective in heat stroke[18] and against apoptosis.[8] In cellular models and rat studies, extreme temperatures of 49 to 50° C (120.2 to122.0° F) destroy all cellular structures and necrosis occurs in 5 minutes.[8] At lower temperatures cell death is primarily by apoptosis.

The physiologic changes caused by heat stroke start with the rise in core body temperature and are often first manifested as acid base and electrolyte abnormalities. With the rise in temperature, visceral perfusion is reduced because blood is shunted to the periphery. Decreased perfusion causes local hypoxia, lactic acidosis, and anaerobic

metabolism. As the perfusion deficits become widespread, metabolic acidosis occurs. Metabolic acidosis can directly decrease cardiac output.[19] Metabolic acidosis also inhibits the sensitivity of warm-sensitive neuron in the hypothalamus, blunting the cooling response.[20,21] As hyperthermia progresses, hyperventilation occurs. The hyperventilation can be severe enough to cause respiratory alkalosis. Respiratory alkalosis can lead to severe hypokalemia and eventual depression of the respiratory center.[6,7] A mixed acid-base disturbance can occur secondary to the metabolic acidosis and respiratory alkalosis. If the depression of the respiratory center becomes severe the animal can progress from hyperventilation and respiratory alkalosis to hypoventilation with respiratory acidosis.

Initially in heat stroke, the splanchnic vasculature is vasoconstricted, but vasodilation occurs as compensatory systems fail. When both the splanchnic and cutaneous vessels dilate, blood pools in the venous system. This pooling further contributes to decreased circulatory volume, decreased cardiac output, and failure of the cooling mechanisms. As a result of both blood pooling and direct heat-induced damage to the endothelium, coagulation abnormalities occur. Coagulation abnormalities frequently observed with heat stroke include thrombocytopenia, prolonged clotting times, and disseminated intravascular coagulation (DIC). The exact cause of these abnormalities is not known, but in vitro, heat damage promotes a prothrombotic state.[8] A prothrombotic state can lead to system-wide coagulation abnormalities, microthrombi, and DIC.

With epithelial damage from decreased perfusion and as a direct result of heat, the mucosal barrier of the gastrointestinal tract is compromised resulting in systemic endotoxin exposure.[17] Endotoxin contributes to the systemic inflammatory response-like

syndrome (SIRS) seen in heat stroke.[3,5-8,17,22] Inflammatory mediators are released without appropriate controls. Hypoxia, DIC, SIRS and microthrombi all contribute to multiple organ failure which makes advanced heat stroke a difficult condition to treat successfully.

There is no single temperature threshold that must be exceeded in order to cause heat stroke in dogs. Temperatures as low as 41° C (105.8° F) may cause permanent brain damage, but higher temperatures can be reached without any apparent adverse consequence. Temperatures above 43° C (109.4° F) cause severe organ damage with a high chance of mortality.[3] Both the maximum temperature and the length of time the animal is hyperthermic contribute to severity of systemic disease.

Fever

When the thermoregulatory set point is increased, the end result is fever. Elevation in core temperature occurs despite moderate ambient temperatures and fully functioning thermoregulatory mechanisms.[9] During fever, pyrogens act on the hypothalamus to elevate the set point range. When the core temperature is within the reference range, that normal temperature is perceived as too low by the hypothalamus. The hypothalamus then signals to increase the body temperature, thereby engaging all of the heat conserving and producing mechanisms used in non-disease states to increase the temperature of the animal. Fever is induced, maintained and resolved according to hypothalamic efferent signals.

Fever is a balanced physiologic reaction that involves cytokine release, generation of acute phase reactants (including heat shock proteins), and activation of both the endocrine and immune systems. Fever is induced and maintained by the pyrogenic

cytokines and molecules released from inflammatory and endothelial cells. These cytokines have multiple non-pyrogenic actions that integrate with the immune and neurohormonal systems (Figure 2). Simultaneously with release of pyrogens, anti-pyrogenic molecules are released that work to limit fever and inflammation. There are multiple causes for fever including infectious, inflammatory, autoimmune, drug or toxin related, neoplastic, and various disease processes;[23-25] and each of these causes of fever can incite a different cytokine, immune, or neurohormonal response.

During fever, certain cytokines (e.g., TNF-α, IL-1β, IL-6)[26,27] are released into the bloodstream where they are transported to the pre-optic anterior hypothalamic area. Once there, these cytokines induce prostaglandin E-2 (PGE_2) production from endothelial cells of the vasculature within the blood-brain barrier and the sensory circumventricular organs.[26] PGE_2 signals the hypothalamic neurons to increase the thermal set point. Alternately, PGE_2 may be produced in the periphery and pass through the blood-brain barrier to the thermosensitive neurons.[28] The first (earliest) phases of fever may be initiated not by cytokines but by parasymphathetic neurons. These neurons, located primarily in the liver, can send direct signals though the vagus nerve to the brain where norepinephrine signals the release of nitric oxide (NO) and the production of PGE_2. The fever can then be maintained by production of cytokines in the periphery.[28]

Pyretic cytokines are complex in their actions; for example, TNF-α has been shown to be both pyrogenic and antipyretic depending on the experimental conditions.[27,29] When pyrogenic stimuli are received endogenous anti-pyrogenic substances are also released.[29,30] Cytokines or hormones that are anti-pyrogenic include IL-10, arginine vasopressin, melanocyte-stimulation hormone and glucocorticoids. These

anti-pyrogenic substances work to limit the magnitude and duration of fever.[30] Other compounds such as epoxyeicosanoids produced by cytochrome P-450 enzymes also play a role in limiting fever and inflammation.[29,30] As cytokines have multiple actions, altering the expression of the cytokines may alter the course of fever and its associated inflammation. [28,29,31]

In human beings, fever is described as consisting of three clinical phases: chill, fever, and flush (induction, maintenance, and resolution). During the chill phase, core temperature is perceived as too low (thus the sensation of being chilled) and begins to rise to the new set-point. The body temperature is elevated by cutaneous vasoconstriction and increased muscle activity (shivering). In the fever phase the elevated target set point temperature is maintained. Clinically, the fever phase is manifested by an elevated body temperature and warm, dry skin. In the final phase, the set point temperature range is readjusted downward and heat dissipating mechanisms are invoked returning the body temperature to normal. During the final phase, vasodilation occurs resulting in the "flushed" skin appearance for which the phase was named.[29] These phases are not always recognized in animals.

Body temperature is tightly controlled in mammals. Both hyperthermia and fever are associated with disease as both cause and effect. Therefore, body temperature measurement is considered one of the vital parameters necessary to appropriately evaluate sick animals. In the next chapter, methods of temperature measurement will be discussed.

Table 1.1: Mechanisms of heat loss

Convection	Transfer of heat to a liquid or gas flowing past
Conduction	Transfer of heat without particle motion
Evaporation	Loss of heat due to converting water to vapor
Radiation	Emission of energy in the form of waves or particles

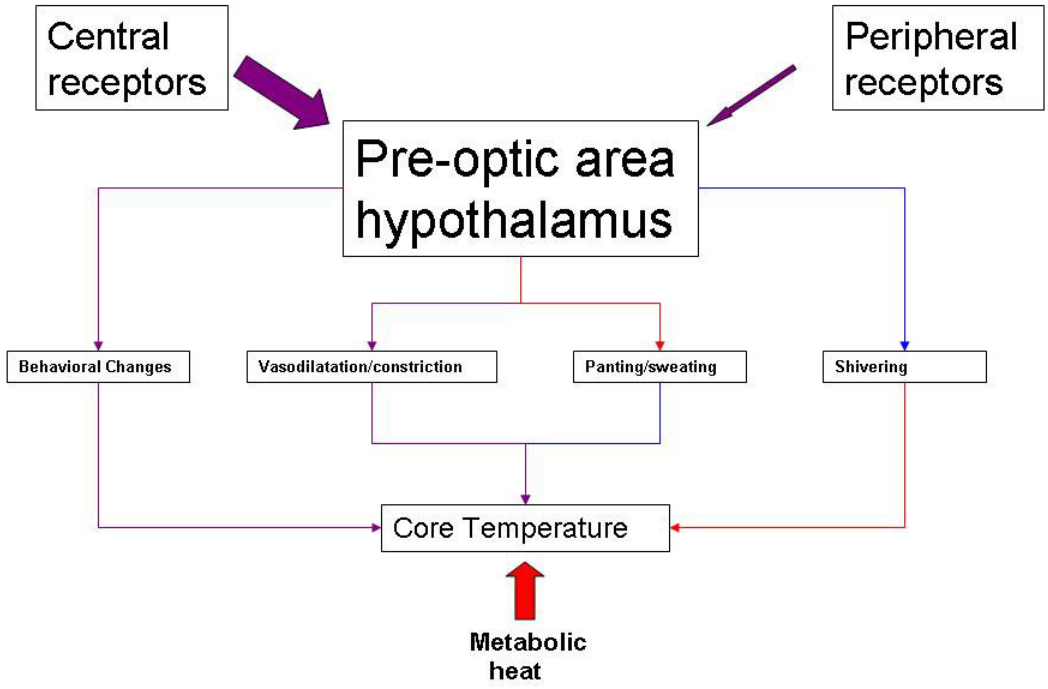

Figure 1.1: Normal temperature regulation
The pre-optic area of the hypothalamus integrates the signals from the central and peripheral thermo-receptors. It then signals for changes in the body that result in the heat loss or gain that maintains the core temperature. Metabolic heat is the primary heat source for the body.

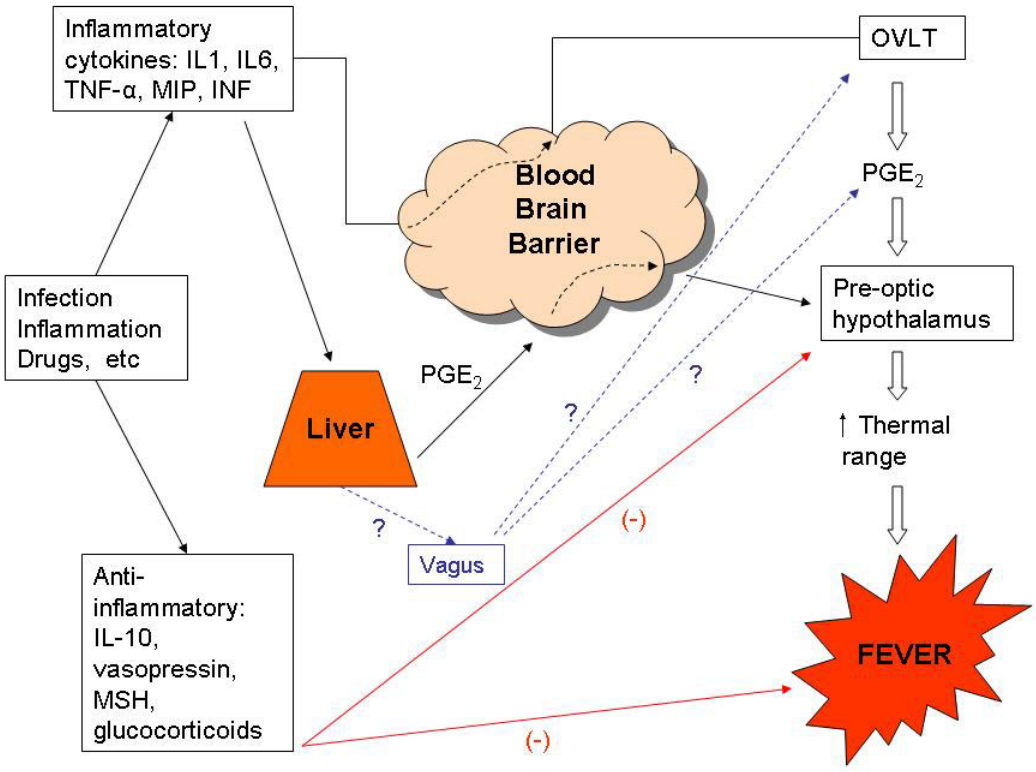

Figure 1.2: Fever regulation
OVLT: organum vasculosum laminae terminalis (located in the 4th ventricle)
IL: interleukins
TNF: tumor necrosis factor
MIP: macrophage inflammatory proteins
INF: interferons
MSH: melanocyte stimulating hormone
The current understanding of infection driven fever is that peripheral macrophages are activated by an infectious agent and release cytokines into the bloodstream where they are transported to the pre-optic anterior hypothalamic area. Once here prostaglandin E-2 (PGE_2) is induced by these cytokines and signals the neurons to increase the thermal set point. Alternately PGE_2 may be produced in the periphery and pass through the blood brain barrier to the thermosensitive neurons. The first (early) phase of fever maybe induced neuronally via parasymphathetic neurons in close relation to Kuppfer cells in the liver. The signal is then transmitted though the vagus to the brain where norepinephrine signals the release of nitric oxide (NO) and the production of PGE_2 resulting in the initial fever response. The fever is later maintained by production of cytokines in the periphery.[28] There is some evidence of direct transmission via the vagus nerve that influences fever. At this time it is unclear if there is neurotransmitter action on the OVLT or direct release of PGE_2 that induces an immediate fever.[28-30]

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Chapter 2

Methods of body temperature measurement

History

In the time of Hippocrates, the hand was used to subjectively detect the warmth of the human body. Alexandrine medicine placed more importance on pulse than temperature, but in the Middle Ages the concept of fever came back to importance with the assignment of the four humours; hot, cold, dry, and moist. Objective measurement of temperature was not possible until the invention of the first thermometer by Galileo in 1592. Body temperature was not measured in a quantitative way until Hermann Boerhaave (1668-1738) first used a thermometer at the bed side. In 1868 Carl Wunderlich used one foot-long thermometers requiring 20 minutes to obtain a temperature reading from the axilla of people and established a normal range of temperatures. Clifford Allbut (1836-1925) designed a 6-inch clinical thermometer that required 5 minutes to record a temperature, making temperature measurements a convenient bedside test[1] and leading the way for temperature measurement to become one of the vital parameters of physical examination.

In 1873, Professor Siedamgrotzky established normal body temperature ranges for dogs by using a 6-inch rectal thermometer. He also noted diurnal variation in body temperature. His original publication in German was re-published in English in 1875;[2] until recently there was little change in thermometer design and technique.[1]

Technology

Temperature can be measured with any of a number of devices that infer a temperature change based on some physical characteristic change in a sensor. There are

six common types of sensor devices: liquid expansion, resistive temperature, change of state, infrared sensing, thermocouple, and bimetallic.

The first thermometers were liquid expansion devices with a bulb containing liquid at one end and a tube connected to the bulb. As the temperature surrounding the bulb increased, the liquid would expand and rise in the tube. A scale printed on the tube allowed quantitative measurement of how high the liquid rose. All sealed glass thermometers work on this principle even today. Expansion of the liquid (mercury or alcohol) requires time; rectal temperature readings may take up to 5 minutes while as much as 11 minutes may be required for axillary readings.[3]

Resistive temperature devices work because the resistance of a substance changes with temperature. Resistance is an inherent physical property of a substance. Resistance thermometers contain a sensor (generally platinum) that contacts a body surface directly. The electrical resistance of a substance (the sensor) changes with temperature. When the sensor changes temperature, a circuit records the change in resistance to electricity and converts it to a temperature reading.[4] Many different thermometers use this technology; a common example is the digital rectal thermometer.

Change of state devices use temperature to cause a change in a substance. Most commonly a temperature sensitive dye is used. The dye is impregnated on a material (fabric, plastic or paper) that can be placed against a body surface. The dye changes color as the temperature changes.[5] The dye impregnated material is placed on the body (often the skin of the forehead) and is left in place for 1 to 3 minutes. At the end of that time, a visible color change indicates the approximate body temperature. Many brands of

pediatric thermometers using this technology are available, but to the author's knowledge there is no published data on their use in dogs.

Infrared devices are based on Planck's Law of thermal emission of radiation. Plank's law is expressed as a mathematical calculation for energy emitted when a black body is heated. The mathematical calculation is complex but uses the principle that a substance will emit energy when heated and that that energy can be measured as flow. Passive infrared detectors measure how fast thermal energy flows through the sensor (pyroelectric detectors). Because flow is being measured, a shutter or gate is necessary to control the infrared heat flow. Infrared thermometers work similarly to a camera. A reflective barrel is used instead of a lens, there is a shutter, and the pyroelectric detector replaces the film.[6] The device takes a snap shot of the heat emanated from an object. Prior to the clinical use of this device, a sensitive calibration system had to be developed.[6] Medical infrared thermometers use pyroelectric sensors to detect heat as infrared wavelengths emanating from an object. The common medical example is the tympanic membrane thermometer.[4,7,8]

Thermocouple devices consist of two wires made of different metals that are connected at one end. Changes in the temperature of the joined end induce a change in electromotive force (voltage) between the other ends. The electromotive force at the non-joined ends can be measured. As the temperature increases, the electromotive force also increases, but not in a linear fashion. Many types of thermometers use this technology; the thermocouple on a pulmonary artery catheter is an example.

Bimetallic devices are not commonly used in medicine because they are not as accurate as thermocouples or resistance devices. Bimetallic devices use the difference in

expansion rates between types of metals. Strips of two types of metals are bonded together. When heated, one metal will expand more rapidly than the other, causing bending. The metal is mechanically linked to a pointer that displays the temperature.

The technology in the temperature sensing microchips used in the research conducted for this thesis was proprietary and not disclosed to the researchers.

Modes of Operation

Resistance thermometers may work in one of two modes of operation, either in a "monitoring" mode or a "predictive" mode. In the monitoring mode, the sensor is placed in contact with tissue such as the rectal mucosa. In humans, the tissue might be the area under the tongue when using the thermometer for oral temperature measurement or the skin of the axilla (with the arm held close to the body) for axillary temperature measurement. The sensor is allowed to reach temperature equilibrium with the surrounding tissues. The change in resistance generated within the sensor is then calculated and converted into a temperature reading displayed digitally on the thermometer. In the predictive mode, the sensor does not reach temperature equilibrium with surrounding tissue. Instead, the thermometer is held in place for a set length of time (often 10 to15 seconds). The rate of change in resistance of the sensor is measured, and a mathematical algorithm is used to calculate (i.e., predict) what the temperature would be if the sensor were allowed to equilibrate with the surrounding tissues.[3] The obvious advantage to the predictive mode is the rapidity of temperature readings.[9]

Classification of measurements

Temperature measurements can be described by the type of thermometer and by the method used to obtain a temperature measurement. Typically, these descriptions are

classified as invasive or non-invasive, and contact or non-contact methods. During an invasive temperature measurement, the thermometer enters the body in some manner. Invasive measurements can be further divided into minimally invasive and invasive. Minimally invasive thermometers enter the body through normal orifices, such as the mouth or rectum. Invasive thermometers penetrate deeper into the body; these thermometers measure temperature in blood vessels, organs, or body cavities. Examples of invasive thermometers include pulmonary artery thermistors, esophageal thermistors, bladder thermistors, and subcutaneous thermistors. Non-invasive thermometers do not enter the body. Colorimetric skin sensors are examples of such non-invasive thermometers. Contact thermometers actually touch the body where the temperature is to be measured. All invasive methods are contact methods. Non-contact thermometers, like the infrared aural thermometer, do not touch the body at the site of measurement.

Sites of temperature measurements

Temperature can be measured from a variety of sites on and in the body, and the best choice depends on factors such as species and ability to restrain or handle the patient, local disease process, and available equipment. The potential sites include skin (axillary and forehead areas are common for humans), mucus membranes (oral [human] and rectal [many species] sites are common), tympanic membrane, subcutaneous tissues, viscera, and body cavities. The most common sites used to measure body temperature in dogs are listed along with advantages and disadvantages associated with each site (Table 2.1).

In medicine a core temperature (the temperature of the internal organs) is frequently desired. Direct measurement of a core temperature requires an invasive

method. Accurate substitutes for an invasive core temperature are actively being sought and are the research focus of this thesis.

Site	Device	Advantage	Disadvantage	Uses
Rectum	Glass mercury Electronic predictive Phase-change (dot-matrix) Deep rectal probe	Easy access Minimally invasive Familiar Established	Site records the highest temperature in the body Lags behind core body temperature	Routine
Ear	Infrared ear thermometer Veterinary Human	Easy access Choice of two sites Minimally invasive Reflective of brain temperature	Technique dependant	Routine
Pulmonary artery	Electronic sensor	True core temp	Affected by the temperature of infused fluids	Surgery Critical care Research
Esophageal	Electronic sensor	True core temp	Anesthesia required	Surgery Anesthesia Research

Table 2.1: Common sites of temperature measurements in dogs

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Chapter 3

Comparison of three methods of temperature measurement in hypothermic, euthermic, and hyperthermic dogs

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Body temperature determination is an important component of the physical examination of an animal.[1] Traditionally, veterinary practitioners have depended on equilibrium-type rectal thermometers to determine body temperature.[1,2] Although usually well tolerated, rectal thermometry can be difficult in fractious animals or in animals with rectal disease and can be influenced by the presence of feces or certain disease states.[1-3] Predictive rectal thermometry measures the rate of temperature change in the first few seconds after thermometer placement to mathematically predict the final temperature; to our knowledge, this method of temperature measurement has not been evaluated in euthermic or hyperthermic dogs. Auricular thermometers were developed to provide temperature measurements less invasively.[2,4,5] As with rectal thermometry, some animals resent the auricular procedure and local pathologic changes may affect the reading obtained.[2,3] A subcutaneous identification microchip with a temperature sensor has been developed for dogs and is currently marketed in Europe and Asia. To our knowledge, there are no published studies regarding accuracy or reliability of the subcutaneous microchip device for temperature determination, while results of some studies [6,7] have indicated that rectal and auricular temperatures correlate with core body temperatures in dogs. However, core body temperature is still considered the most accurate method of temperature assessment. Such core temperature measurements can be achieved by use of thermistors placed in the esophagus, urinary bladder, or central vascular compartment.[8-12] Despite the tremendous importance of accurate temperature measurement for clinical

management of dogs, there is a paucity of scientific comparison of any of the minimally invasive methods of temperature assessment with core body temperature. The purpose of the study reported here was to assess the reliability and accuracy of 3 temperature measuring devices (a predictive rectal thermometer, an infrared auricular device designed for veterinary use, and a subcutaneous temperature-sensing microchip) for measurement of core body temperature (determined by use of a thermistor-tipped PA catheter) over a variety of temperature conditions in dogs. We hypothesized that, in dogs, rectal thermometry would provide the most reliable and accurate estimate of core body temperature among these temperature sensing methods.

Material and Methods

Eight mixed-breed sexually intact purpose-bred hounds aged 8 months to 5 years (mean age, 1.5 years) and weighing 19.1 to 26 kg (42.0 to 57.2 lb; mean weight, 22.5 kg [49.5 lb]) were used in the study. The group included 3 male and 5 females. Body condition scores were 4 or 5/9 for all dogs; coat length was short in 7 dogs and medium in 1 dog. All dogs were considered to be in good health on the basis of findings of physical examination, including an aural examination. Dogs were housed in a routine manner in animal facilities accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International. All experimental procedures were reviewed and approved by the Animal Care and Use Committee of the University of Missouri, Columbia. Dogs were adopted to private homes after completion of the study.

For each dog, temperature was measured by use of 4 thermometry devices during 4 study periods over 3 days. To provide a range of body temperatures at which the thermometry devices could be assessed, conditions were manipulated during each study

period so that dogs were euthermic or developed hypothermia or hyperthermia. Hypothermia was induced during the first study period without manipulation other than induction of general anesthesia, while hyperthermia was induced during study periods 2, 3, and 4 via administration of a low dose of endotoxin. Temperature readings during euthermia occurred prior to onset of either hypo or hyperthermia during each study period.

Two temperature-sensing microchips[a] were implanted in each dog a minimum of 7 days prior to temperature measurements to allow resolution of any inflammation that might result from device implantation. The microchips were placed according to the manufacturer's recommendations in either the suggested or an alternate location in the body. For 5 dogs, a microchip was placed in the deep subcutaneous tissues of the dorsum between the shoulder blades (interscapular location) as suggested by the manufacturer. Three of the 8 dogs had non-temperature sensing microchips placed in the typical interscapular location prior to enrollment in the study. To avoid interference from that existing microchip and evaluate use of the microchip when placed in an alternate location, the temperature-sensing microchip was placed in the subcutaneous tissues of the dorsal aspect of the sacral area in those 3 dogs. Also, all dogs had a microchip placed SC over the distal aspect of the scapula and proximal portion of the humerus (designated the lateral shoulder location) to mimic migration of a microchip from the suggested interscapular location.

When possible, accuracy of thermometer devices was evaluated in vitro. The microchips were evaluated at the site of manufacture before shipping and were accurate to within 0.3ºC (0.54^{o}F) of environmental temperature. Rectal thermometers[b] were tested

just prior to use in 40ºC (104°F) and 25ºC (77°F) water baths; prior to testing the rectal thermometers, the water bath temperatures were determined with a digital thermometer[c] that was traceable to the bureau of standards. Rectal thermometer readings were within 0.1ºC (0.18°F) of agreement with water bath temperatures in each instance. After removal of the PA catheter[d] at the end of data collection, the thermistor unit of each catheter was checked in an identical manner and all readings were accurate to within 0.1ºC of water bath temperatures. Accuracy of the auricular thermometer[e] was not evaluated in vitro.

Thermometers were used according to the method for which they were designed. The rectal thermometers were of an electronic predictive type. Prior to temperature measurements, the temperature probe was covered with an unused plastic sheath made for the device. The thermometer was inserted approximately 3 cm (1.5 inches) into the rectum and held there until a digital reading was obtained on the thermometer. For use of the auricular thermometer, a plastic sheath made for the device was fitted onto the probe prior to temperature measurement. As suggested by the manufacturer, the ear was manipulated to straighten the ear canal and allow a more direct alignment of the probe with the tympanic membrane. The temperature-sensing microchips (2/dog) were placed via SC injection in the same fashion as traditional identification microchips. Temperature readings from the microchips were accomplished by slowly moving an electronic hand-held scanning device designed for use with the microchips over the area of microchip implantation. Ease of use for each device was assessed subjectively.

At least 7 days after microchip placements, each dog was anesthetized for placement of a thermistor-tipped PA catheter. All dogs were administered butorphanol

(0.5 mg/kg [0.23 mg/lb]), xylazine (0.25 mg/kg [0.114 mg/lb]), and glycopyrrolate (0.01 mg/kg [0.005 mg/lb]) IM. Once sedated, a cephalic IV catheter was placed and an IV infusion of physiologic saline (0.9% NaCl) solution was begun at 10 mL/kg/h (4.5 mL/lb/h). Anesthesia was induced with thiopental to effect (approx 10 mg/kg [4.5 mg/lb], IV) to allow endotracheal intubation. Anesthesia was maintained via inhalation of isoflurane in oxygen. During anesthesia, periodic monitoring included subjective assessment of the depth of anesthesia, respiration rate, heart rate, hemoglobin oxygen saturation, and exhaled CO_2 concentration. The coat over a jugular vein was clipped and the area was prepared by use of standard aseptic technique. With fluoroscopic guidance, a percutaneous sheath introducer was used to place the thermistor-tipped catheter in the PA. The catheter was sutured in place and the neck was bandaged.

Once instrumentation was complete, study period 1 was initiated. Temperature readings from the PA catheter, rectal and auricular thermometers, and both microchips were obtained in duplicate as near simultaneously as possible (all 10 readings were accomplished within 90 seconds in each dog). Because the PA catheter-derived temperature was provided as a continuous digital reading, it was recorded first and then again last among the temperature assessments; otherwise, the order of measurements was random. A single scribe recorded temperature measurements from the PA catheter as well as measurements obtained for the other devices by 2 or 3 other investigators. Auricular temperatures were measured by a single investigator (RJG). Readings from the rectal and auricular thermometer in each dog were obtained every 10 minutes during a 40-minute period. Hypothermia, defined as a core body temperature < 37.8°C (100°F), was achieved in 7 of 8 dogs during the first study period. Following completion of study

period 1, dogs were allowed to recover from anesthesia in the University of Missouri Veterinary Medical Teaching Hospital's intensive care unit and remained there until the PA catheters were removed at completion of study period 4.

Study period 2 began later the same day after the dogs were fully recovered from anesthesia and alert and their core body temperature (assessed via the PA catheter) was at least 38.3°C (101.0°F). A low dose of endotoxin[f] (2 μg/kg [0.9 μg/lb]) was administered to the dogs to induce fever.[13,14] Hyperthermia was defined as core body temperature > 39.17 ºC (102.5°F). Temperature readings from the PA catheter, rectal and auricular thermometers, and both microchips were obtained in duplicate as near simultaneously as possible immediately prior to endotoxin administration and every 10 minutes thereafter until core body temperature reached a plateau for 3 consecutive readings or began to decrease. At the conclusion of study period 2, physiologic saline solution (20 mL/kg [9.1 mL/lb]) was administered IV to each dog over 4 hours. Arterial blood pressure and clinical evidence of illness were monitored until the dogs appeared clinically normal after endotoxin administration.

Study period 3 was conducted the following day and study period 4 was conducted the day after that. On the basis of increases in body temperature and subjective assessment of degree of illness (vomiting, diarrhea, marked lethargy, or signs of depression) during study period 2, subsequent doses of endotoxin were reduced for several dogs (lowest dose administered was 1 μg/kg [0.45 μg/lb]). As during study period 2, temperature readings from the PA catheter, rectal and auricular thermometers, and both microchips were obtained in duplicate as near simultaneously as possible immediately prior to endotoxin administration and every 10 minutes thereafter until core body

temperature reached a plateau for 3 consecutive readings or began to decrease. The PA catheters were removed at the end of study period 4 and cephalic catheters were removed following infusion of physiologic saline solution.

In 1 dog, the interscapular microchip device was surgically removed after completion of the described studies. The device itself was re-evaluated by the manufacturer, and the tissues surrounding the device were evaluated via histologic examination; tissue samples underwent aerobic and anaerobic microbiologic cultures by use of standard techniques at the Veterinary Medical Diagnostic Laboratory of the University of Missouri.

Statistical analysis

Data were analyzed by use of a statistical software package.[g] Repeatability (variability) for each device or device location was described as the mean difference in near simultaneous (duplicate) measures obtained by use of the same device and standard deviation (SD) of the difference in duplicate measures. The range of temperature difference for duplicate measurements by each device was also calculated. A formal test to compare the variances of measurements made close together in time was conducted by using a mixed model approach. The response variable used was the sample variance of the duplicate measures. Since measurements were taken on different devices on the same dog under the same conditions (or study period), the dog was included as a random effect. The device and the study period were included as fixed effects. Measurements taken 10 minutes apart in time were treated as repeated measures and the correlation structure for these measurements was modeled as autoregressive of order 1. Heterogeneous variances for the response variable across different devices were included

in the model. Pair-wise comparisons of mean responses for different devices were made using Least Squares Means. For other comparisons, the first reading from each device was compared with the core body temperature as measured by the first PA catheter reading at the same time. The agreement between each of the other devices and the core body temperature (determined via the PA catheter) was assessed in 2 ways. First, simple descriptive statistics were used to determine how frequently the measured temperature agreed with the core body temperature within 0.5°C (0.9°F), 0.75°C (1.35°F), 1.0°C (1.8°F), and so forth at 0.25°C (0.5°F) increments to the level of 3.5°C (6.3°F). Second, Bland-Altman scatterplots were used to provide visual assessment of agreement between readings for the thermistor-tipped PA catheter and each of the other devices or device locations. Although commonly reported in similar studies, correlation and regression are not appropriate analytic tools with which to determine accuracy of a method of measure, compared with a gold standard technique.[15] For all analyses, a value of P<=0. 01 was considered significant.

Results

Placement of the indwelling thermometry devices (ie, microchips and PA catheters) was achieved without complication in all dogs. No adverse reactions were detected; there was no evidence of swelling, redness, or signs of pain at the site of microchip insertion. Temperature readings were obtained in duplicate from all 8 dogs on 297 separate occasions (594 recorded temperature readings). Temperature readings obtained from the PA catheter (core temperature), rectal and auricular thermometers, and microchips from the lateral shoulder location were each recorded in duplicate on all 297 occasions. Because only 5 dogs had the thermistor microchip implanted in the interscapular region, temperature readings were recorded in duplicate on 180 occasions. Because 3 dogs had the thermistor microchip implanted in the subcutaneous tissues in the dorsal aspect of the sacral region, sacral temperature readings were recorded in duplicate on 117 occasions.

Core temperatures from 35.3°C (95.5°F) to 41.4°C (106.5°F) were recorded. As determined by PA catheter readings, hypothermia was accomplished in 7 of 8 dogs during study period 1; core body temperature readings were in the hypothermic range on 36 occasions. During all 4 study periods combined, temperatures were within reference limits on 110 occasions. As expected, administration of endotoxin to the dogs during periods 2, 3, and 4 resulted in increases in core body temperature with only mild to moderate systemic signs of illness. Core body temperature in the hyperthermic range was achieved on 151 occasions during the entire study. During study period 2, 6 dogs became hyperthermic (24 readings in the hyperthermic range); during periods 3 and 4, all 8 dogs became hyperthermic (61 and 66 readings in the hyperthermic range, respectively). All

dogs became lethargic within an hour of endotoxin administration, and vomiting and diarrhea developed in several dogs. All dogs appeared to recover fully from endotoxin administration and returned to apparently normal activity within 4 hours.

Ease of use and rapidity of results differed with each device. Placement of the PA catheter required anesthesia and was an invasive procedure. The PA catheter provided continual temperature readings. Rectal thermometry was easily accomplished in the dogs, but during much of the study period, the dogs were either anesthetized or lethargic. Unlike equilibrium rectal thermometry, results were obtained rapidly via predictive rectal thermometry (a period of only 10 to 15 seconds was required to obtain each reading). Although the response time of the auricular thermometer was extremely rapid (approx 1 second), correct positioning of the probe required a period of some seconds and, frequently, an interval of ≥ 15 seconds elapsed before the thermometer provided a second reading. If the foldable arm of the auricular thermometer was not closed completely between temperature readings, the device would display an error message during attempts to obtain a second reading and required another 15-second interval for recalibration. This often resulted in a 30- to 45-second time lapse before a second auricular temperature reading could be obtained. It was our subjective impression that several dogs resented positioning of the auricular probe more than they resented positioning of the rectal probe. Although initial placement of the microchip required SC injection, actual temperature readings were completely non-invasive and required no restraint. Once the scanner device was passed over the site of the implant, the temperature reading was displayed instantaneously.

Variability between successive readings from the same thermometry device or device location at the same time period was assessed (Table 1). Variability was least for the thermistor-tipped PA catheter and greatest for the auricular thermometer. A formal test of the null hypothesis of equal variances across devices was done using the mixed model approach. Initial results based on all observations showed that the variance for the auricular thermometer was significantly greater than that of any other device ($p<0.001$ for all paired comparisons). Examination of residuals showed some extreme values for one dog at one site. When the analysis was re-run with those extremes excluded, the results were the same. The mixed model analysis was done again with the auricular thermometer excluded. There was a significant device effect ($p<0.001$). Pair-wise comparisons showed that the PA device had a significantly smaller variance than all other devices ($p<0.001$ for all comparisons). No other differences were significant at the 0.01 level, suggesting reliability of the rectal thermometer and microchip device was similar. Both the rectal thermometer and microchip device were more reliable than auricular thermometry in these dogs.

Agreement between the core body temperature and temperatures determined by use of the rectal or auricular thermometers or thermistor microchip in any location was also assessed (Table 2). Of the 3 thermometry devices and microchip locations evaluated in the study dogs, the smallest difference between core body temperature and temperature readings was achieved by use of the rectal thermometer; 94.28% (280/297) of rectal temperature readings were within 0.5ºC of the PA catheter measurement of core body temperature. Agreement between core body temperature and the temperature derived from the thermistor microchip placed in the interscapular location was similar to that

between core body temperature and the temperature derived from the auricular thermometer; 50% (90/180) of temperature readings obtained from the interscapular microchip and 45.5% (135/297) of readings obtained by use of the auricular thermometer were within 0.5°C of the PA catheter measurement of core body temperature. Differences of approximately 3.5°C between core body temperature and some temperature readings from the microchip (in any location) and from the auricular thermometer were detected. The worst agreement between core body temperature and temperature determined by any other device or device location was associated with the thermistor microchip in the sacral location.

Agreement between core body temperature (assessed by use of the PA catheter) and the other thermometry devices or device locations was also examined graphically (Figure 1). Temperature assessments derived from the rectal thermometer were in best agreement with core body temperature. Auricular thermometer readings and interscapular microchip temperature readings also provided a reasonable assessment of core temperature in most dogs, but were less accurate than the rectal thermometer temperature readings. For all devices other than the rectal thermometer, temperature readings from the device generally underestimated core body temperature.

Differences between core temperature and interscapular microchip temperature were relatively consistent from time to time in each dog, but varied greatly among dogs. The mean absolute difference between core temperature and interscapular temperature was calculated for each dog. The readings that differed most greatly from the core temperature at hypothermic, euthermic, and hyperthermic temperatures were associated with 1 dog; each occasion in which the interscapular microchip temperature reading and

core body temperature differed by 1.5°C (3.2°F) or more was attributed to data obtained from this single dog. The dog was not dissimilar to the other dogs with regard to coat length, body condition score, weight, and breed. When this dog was removed from consideration, agreement between interscapular microchip temperature readings and core body temperatures improved greatly (Table 3).

For the single dog with the greatest discrepancy between interscapular microchip temperature readings and core temperature readings, the interscapular microchip was removed. Radiographically, appropriate placement of the microchip in the subcutaneous tissues between the scapulae was confirmed. The microchip was palpable in the subcutaneous tissue, but the implantation site was not discolored, swollen, warm, or in any other way grossly abnormal. The microchip itself was returned to the manufacturer for further evaluation and was reported to be undamaged and provided temperature readings in vitro that were within 0.3°C of ambient temperature.[h] Specimens of the tissue surrounding the microchip were examined histologically and findings were unremarkable. Microbial culture of tissue samples yielded no growth.

Discussion

In the present study, 3 clinical temperature-measurement devices were compared with core body temperature in dogs during periods of hyperthermia, hypothermia, and euthermia. Because high body temperature is a much more common clinical problem than low body temperature, greatest emphasis was given to evaluation of these thermometry devices during hyperthermia rather than hypothermia. Core body temperature represents the standard to which other measures of body temperature are

compared, but measurement of core temperature is invasive and therefore not suitable for daily clinical application. Rectal temperature is assessed most often clinically as a substitute for core body temperature. Recently, digital rectal thermometers have largely supplanted the use of glass mercury thermometers. Digital thermometers are of either the equilibrium or predictive type. In our study, a predictive thermometer, in which the rate of temperature change during the first few seconds after thermometer placement is measured and used to mathematically predict the final temperature, was evaluated. We are aware of only 1 study[6] involving comparison of core body temperature with temperature readings derived from predictive rectal thermometers in dogs and that study was conducted only under conditions of hypothermia. Auricular thermometry was developed as a rapid and less invasive alternative to rectal thermometry for use in humans. Auricular thermometers use infrared technology to sense heat emanating from the tympanic membrane; because the tympanic membrane shares blood flow with the hypothalamus via the carotid artery, these temperature readings are purported to approximate core temperature. Because the anatomic features of humans and other animals differ, thermometry devices have been developed specifically for use in the ear canal of domestic pet animals. Although multiple studies[1,2,16-19,i] have been performed to evaluate auricular and rectal temperature measurements in several species, data regarding comparisons of auricular temperature readings with core body temperature are sparse.[6] To our knowledge, comparison of temperature assessments by use of a subcutaneously placed temperature-sensing microchip with either rectal temperature readings or core body temperature in dogs has not been reported. This microchip device is already marketed for use in dogs in Europe, and is being considered for market in the United

States. Further assessment of reliability and accuracy of the device is warranted before its routine use in dogs can be advocated.

Reliability of a measuring device refers to the degree of stability among measurements when those measurements are repeated under identical conditions and does not refer to the dependability of the measuring device.[20] In the present study, reliability of each device was evaluated as repeatability of device-derived temperature readings via calculation of the SD of the difference in duplicate measures and description of the range of differences for duplicate measures from each device. As expected, reliability was greatest for the thermistor-tipped PA catheter device that was used to assay core body temperature in the study dogs. Repeatability was markedly worse for the auricular thermometer than for any other temperature measuring device. The positioning of the measuring device critically influences results of auricular thermometry, whereas appropriate positioning of a rectal thermometer is simple and easy to achieve; after initial placement, appropriate positioning of the thermistor-tipped PA catheter or microchip for temperature measurements is established for subsequent occasions. Therefore, user variability in positioning of the auricular thermometer might have contributed to the poor repeatability of temperature measurements for this device, compared with the others.[19] However, to minimize such user variability, auricular temperature measurements were obtained by a single investigator.

Compared with core body temperature determined via the thermistor-tipped PA catheter, the accuracy of temperature readings obtained by use of the predictive rectal thermometer was highest among the thermometry devices. Rectal temperature change often lags behind changes in core body temperature in humans.[11,21] Because the

conditions applied to the dogs in the present study resulted in a rapidly changing core temperature, a similar lag effect may have biased the results and caused the rectal thermometer to appear less accurate than it actually is. Despite the lag effect, rectal thermometry provided an accurate estimation of core body temperature in the dogs of the present study. There are conditions in which this may not be the case. Fecal material could interfere with the juxtaposition of the temperature probe with the rectal mucosal wall, thereby affecting the temperature reading.[5] Rectal inflammation might result in local increases in temperature, whereas thrombotic conditions that interfere with local blood flow could result in decreased local temperature, compared with core body temperature. In individuals with these conditions, an alternative means of temperature measurement would be required. As reported elsewhere,[4,21] the rectal thermometer used in the present study was the only device that frequently (189/297 [63.6%] readings) gave results that were higher than the true core body temperature.

Previous studies of auricular thermometry[1,2,6,16-19] in animals have revealed varied estimates of accuracy. Because of the anatomic differences in the ear canal of dogs and humans, infrared auricular thermometers made for use in people are likely to detect the temperature of the skin of the external ear canal rather than of the tympanic membrane when used in dogs, thereby underestimating core body temperature among canids. Auricular thermometers designed for use in veterinary patients, such as the one used in our study, supposedly provide more accurate results.[19] Although auricular temperature has been found to correlate closely with rectal temperature in dogs with or without otitis externa,[7] correlation does not imply accuracy. Other studies[2,17] have failed to demonstrate accuracy of auricular as compared to rectal temperatures, and comparisons

of auricular temperature with core body temperature in euthermic or hyperthermic dogs have not been conducted, to our knowledge. Similarly conflicting results regarding accuracy of auricular thermometry were obtained in studies[1,16-19] of humans, cats, and other species, all of which leaves clinicians unsure as to the usefulness of the auricular technique. Typically, auricular temperature readings are lower than the core body temperatures.[19] This could be related to improper device positioning, but might also be related to actual temperature differences at different sites within the body.[19] Interestingly, auricular thermometry may be more accurate at hypothermic than hyperthermic temperatures in dogs, cats, and children.[6,19,22] Although the number of readings obtained during each temperature condition prevented meaningful statistical analysis of each different temperature subset in the present study, our data would appear to be in agreement with that finding.

Instrumentation placed within the subcutaneous space for measurement of body temperature has been used in research settings for many years.[23,24] The subcutaneously placed device evaluated in the present study is the only identification microchip combined with temperature-sensing technology that is currently marketed for purchase by owners of pet dogs in Europe. Although the product has been available in Europe since 2004, it is not yet marketed in the United States. To our knowledge, there are no published studies regarding either the reliability or accuracy of the device. Once the microchip is in place, the temperature measurement is obtained simply by moving an electronic scanning device over the area of microchip implantation. In the present study, microchip temperature readings were obtained rapidly and with no objection from any dog. When placed in the suggested interscapular location, the microchip provided a

reasonable approximation of core temperature in most dogs but was not as accurate as rectal thermometry. Although agreement between core body temperature and temperature readings obtained from the thermistor microchip in the interscapular region was good for most dogs, temperatures recorded from the PA catheter and microchip were widely different in 1 dog. For this dog, there were no obvious differences in conformation or coat, compared with the other dogs, and no evidence of pathologic changes or infection within the tissue surrounding the microchip. The microchip itself was returned to the manufacturer for evaluation, and was reportedly accurate in vitro to within 0.3°C. We do not have an explanation for why the microchip provided far less accurate results in this particular dog. Although not part of the present study, the authors placed an identical microchip in the interscapular location of another dog taking part in a different research study; in that dog, rectal temperature and microchip temperature readings were also widely discrepant, again without obvious cause.

The temperature-sensing microchip provided the most accurate results when placed in the recommended interscapular location. In studies[23-25] involving other types of subcutaneous temperature transponders in humans, differences in temperature readings were associated with location of microchip implantation and amount of subcutaneous adipose tissue. There may be inherent differences in subcutaneous temperatures in difference body locations. Likewise, there may be an inherent difference between the subcutaneous temperature and the core or rectal temperature. In the present study, environmental conditions, body condition, and hair coat, or possibly lag time between changes in core and subcutaneous temperatures might account for some of the disagreement between subcutaneous temperature readings and core body temperature. All

of our experiments were performed in the climate controlled environment of a veterinary teaching hospital and in dogs of similar body condition and coat type.

During hypothermia, hyperthermia, and euthermia in the study dogs, temperature readings obtained from all thermometry devices in all locations followed the changes in core body temperature (determined via the thermistor-tipped PA catheter). However, predictive rectal thermometry provided the most accurate approximation of core temperature in dogs. Although rapidity of results is an advantage of auricular or microchip thermometry over equilibrium thermometry, use of predictive digital thermometers provides results nearly as quickly. We suggest that neither the thermistor microchip nor auricular thermometer used in the present study should be relied on as the sole means of temperature measurement in dogs when hypothermia or hyperthermia is suspected. For routine use in most dogs, predictive rectal thermometry is reliable and appears to provide the most accurate estimation of core body temperature of any of the devices evaluated.

[a]Temperature-sensing microchips, Digital Angel Corporation, St Paul, Minn.
[b] Welch Allyn predictive digital thermometer, Welch Allyn Inc., San Diego, Calif.
[c] Traceable digital thermometer, Fisher Scientific, Pittsburgh, PA
[d] Argon flow directed thermodilution catheter, Argon Medical, Athens, Tex.
[e] Vet-Temp model VT-110, Advanced Monitors Corporation, San Diego, Calif.
[f] Purified LPS, Sigma, St. Louis, Mo.
[g] SAS version 9.1, SAS Institute Inc, Cary, NC.
[h] Personal communication, Debra Skoog, Digital Angel, September 2005.
[i] Sharp PE, Sanow CT, Oteham CP, et al. Use of the Thermoscan® thermometer in determining body temperature in laboratory rabbits, rodents, dogs, and cats. Contemp Top Lab Anim Sci 1993;32:28.

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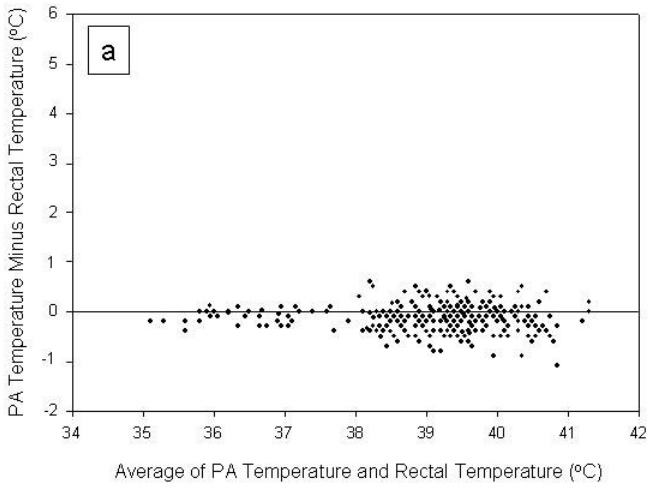
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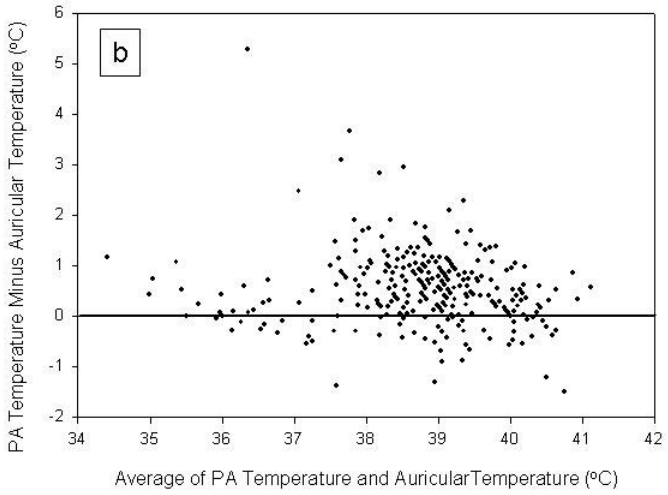
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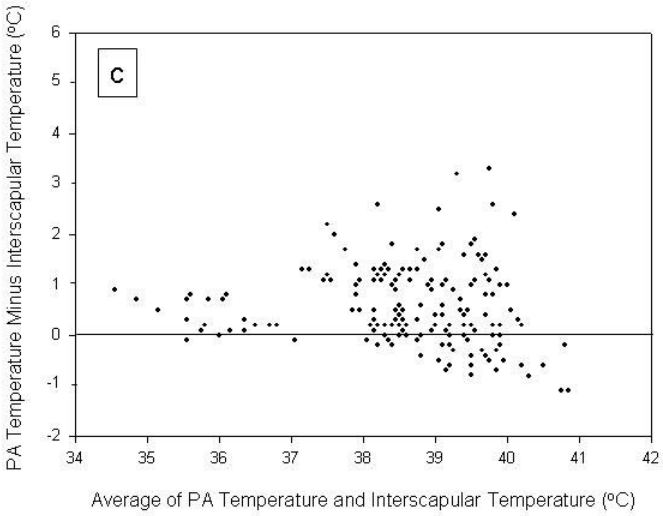
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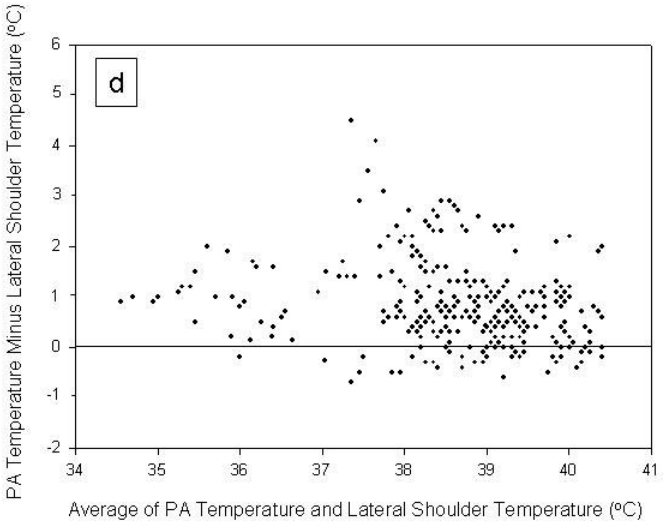
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PA Temperature Minus Lateral Shoulder Temperature (ºC)
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Average of PA Temperature and Lateral Shoulder Temperature (ºC)

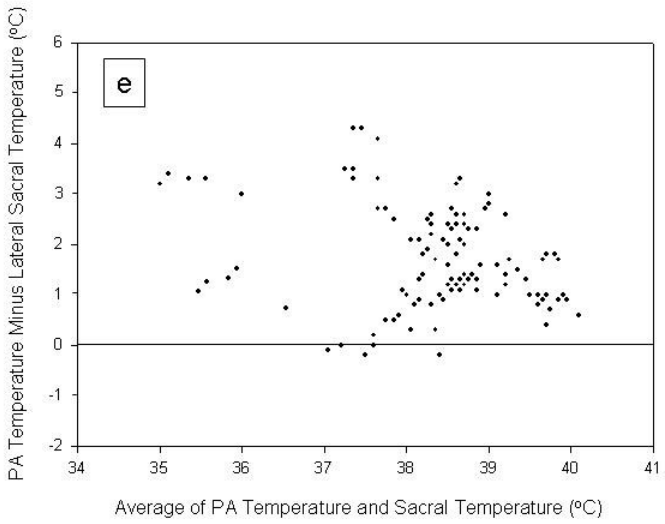

Figure 3.1: Bland-Altman plots are presented for each device or device location. For each plot, the Y-axis represents the difference between temperature measured by the PA catheter and the temperature measured by the device or device/location while the X-axis represents the average of the temperature as measured by the PA catheter and the temperature measured by the device or device/location. The reference line shown corresponds to zero differences (i.e., if the reading from the described device/location matched the core reading perfectly, then all points would fall on this line). Figure a = rectal thermometry, b = auricular thermometry, c = subcutaneous microchip thermometry (interscapular location), d = subcutaneous microchip thermometry (lateral shoulder location), e = subcutaneous microchip thermometry (sacral location). Points located

above the reference line represent an underestimation of temperature by the device in comparison to core body temperature (as measured by PA catheter temperature).

Device or location	Mean difference between readings	SD of the difference	Range of differences
PA catheter	0.004	0.059	-0.30–0.30
Rectal thermometer	0.009	0.235	-0.90–0.80
Auricular thermometer	0.300	0.776	-2.45–5.34
Microchip			
Interscapular region	0.016	0.189	-0.50–0.80
Lateral shoulder region	0.011	0.249	-1.30–1.90
Sacral region	0.018	0.236	-0.50–0.90

Table 3.1: Variability between duplicate temperature measurements

Variability between duplicate temperatures measurements obtained from 8 dogs by use of a thermistor-tipped PA catheter, rectal and auricular thermometers, and a thermistor microchip (in 3 body locations). Variability is measured by the SD of the differences, and was calculated based on 297 duplicate measures for PA catheter, rectal thermometer, auricular thermometer, and lateral shoulder region microchip. Variability was calculated based on 180 duplicate measures from the interscapular microchip location and 117 duplicate measures from the sacral microchip location. Variability was least for the PA catheter and greatest for the auricular thermometer; other temperature measuring device or device locations did not significantly differ in regards to variability.

	Thermometry device				
Range of agreement (^{o}C)	**Rectal thermometer**	**Auricular thermometer**	**Thermistor microchip**		
			Interscapular region	**Lateral shoulder region**	**Sacral region**
≤0.5	94.28 (280/297)	45.45 (135/297)	50.00 (90/180)	38.38 (114/297)	9.40 (11/117)
≤0.75	98.32 (292/297)	63.97(190/297)	57.78(104/180)	52.19(155/297)	12.82 (15/117)
≤1.0	99.66 (296/297)	78.11(232/297)	65.00(117/180)	68.35(203/297)	27.35 (32/117)
≤1.25	100.00 (297/297)	87.21(259/297)	81.11(146/180)	76.43(227/297)	35.04 (41/117)
≤1.5	100.00 (297/297)	93.60(278/297)	88.33(159/180)	82.83(246/297)	48.72 (57/117)
≤1.75	100.00 (297/297)	95.96(285/297)	92.22(166/180)	85.52(254/297)	56.41 (66/117)
≤2.0	100.00 (297/297)	97.31(289/297)	96.11(173/180)	88.89(264/297)	64.10 (75/117)
≤2.25	100.00 (297/297)	97.64(290/297)	96.67(174/180)	91.25(271/297)	69.23 (81/117)
≤2.5	100.00 (297/297)	98.32(292/297)	97.78(176/180)	95.29(283/297)	79.49 (93/117)
≤2.75	100.00 (297/297)	98.32(292/297)	98.89(178/180)	96.97(288/297)	86.32 (101/117)
≤3.0	100.00 (297/297)	98.99(294/297)	98.89(178/180)	98.65(293/297)	88.89 (104/117)
≤3.25	100.00 (297/297)	99.33(295/297)	98.89(178/180)	98.99(294/297)	90.60 (106/117)
≤3.5	100.00 (297/297)	99.33(295/297)	100.00(180/180)	99.33(295/297)	97.44 (114/117)

Table 3.2: Agreement between temperature readings

Agreement between temperatures readings obtained from 8 dogs by use of rectal and auricular thermometers and a thermistor microchip (in 3 body locations) with core body temperature (determined by use of a thermistor-tipped PA catheter). Agreement is presented both as percentage of all readings for each device or location which agreed within the given range of temperature intervals, and parenthetically as the actual number of readings which agreed within the given range.

Range of agreement (°C)	All dogs (n = 8)	Single dog excluded (n = 7)
≤ 0.5	50.0 (90/180)	62.0 (90/146)
≤ 0.75	57.8 (104/180)	71.2 (104/146)
≤ 1.0	70.0 (117/180)	85.0 (123/146)
≤ 1.25	81.1 (146/180)	94.5 (138/146)
≤ 1.5	88.3 (159/180)	100.0 (146/146)

Table 3.3: Comparison of agreement without discrepant dog

Comparison of agreement between temperatures readings from the microchip in the interscapular location with core body temperature (determined by use of a thermistor-tipped PA catheter) with and without the inclusion of a single dog responsible for the greatest discrepancy in agreement. Agreement is presented both as percentage of readings which agreed within the given range of temperature intervals, and parenthetically as the actual number of readings which agreed within the given range

Chapter 4

Treatment of hyperthermia and fever

Hyperthermia

Hyperthermia, in the form of heat stroke, is an emergency and should be treated as such. As with any emergency patient, airway, breathing, and circulation (ABCs) are assessed immediately and interventions taken as needed. Interventions may include oxygen therapy, sedation, intubation and mechanical ventilation.[1,2]

Once the ABCs have been addressed the mainstay treatments of hyperthermia are rapid cooling, volume replacement, and management of secondary complications. Prompt cooling is the only known effective measure against hyperthermia.[3] Owners should be instructed to cool their pet on-site or in transit because dogs that were cooled prior to presentation to a veterinary facility had improved survival over dogs cooled on arrival.[4] Cooling can be achieved by many methods including, but not limited to: cool water baths, fans, placing wet towels on the animal, or placing ice packs over major superficial vessels. One cooling technique has not been proven superior to another, but tepid or tap water will cool as effectively as ice water[5] without the risk of vasoconstriction; tepid water improves human patient comfort.[6] Active cooling should be continued or initiated at presentation until a mild hyperthermia of 39.4 to 40° C (103 to104°F) is achieved, then active cooling should be stopped as the body temperature may drop precipitously[6] causing hypothermia.

While external methods of cooling are applied, room temperature intravenous fluids should be started. Resuscitative crystalloid fluids have the dual role of being an effective cooling method and the primary treatment for shock that often accompanies heat

stroke. The animal should be fluid resuscitated to standard endpoints assessed via arterial blood pressure measurement, heart rate, pulse rate and quality, mucus membrane color, capillary refill time, urine output, lactate concentrations, packed cell volume, and total solids. Central venous pressure is a useful way to evaluate fluid volume in animals without cardiac disease,[1,2,6,7] providing another measurable endpoint of resuscitation. If the fluid volume is appropriate but hypotension is still present, vasopressor therapy with dobutamine, dopamine, or vasopressin maybe be necessary.[2]

Colloids are an effective way to expand and maintain plasma volume and may improve outcome as hetastarch improved survival in a rat model of heat stroke.[8] Plasma has the advantage of being both a colloid and containing proteins such as coagulation factors that maybe needed to treat disseminated intravascular coagulation (DIC).[1] Plasma and other blood products or hemoglobin-based oxygen carriers are given based on the oxygen saturation, hemoglobin concentration, packed cell volume, coagulation profile results, and the need for colloid support.

Once cooling and volume replacement have been addressed, treatment of secondary complications is undertaken. Secondary complications are addressed as they arise. Commonly encountered complications include electrolyte abnormalities, glucose aberrations, acute renal failure, sloughing of the intestinal tract with bacterial translocation, systemic inflammatory response syndrome (SIRS), sepsis, fulminant liver failure, DIC, thromboemboli, neurologic abnormalities, cardiac arrhythmias, and rhabdomyolysis.[2,9] Because heat stroke has many pathophysiologic similarities with sepsis[9] and SIRS, treatment beyond cooling is similar among the conditions.

Hypoglycemia and electrolyte abnormalities often occur very early in the course of heat stroke. Either hyper- or hypoglycemia can be seen on presentation and can change with the course of the disease necessitating frequent evaluation. Hypoglycemia is treated with intravenous dextrose solutions. Mild hyperglycemia may not need to be treated, but if hyperglycemia is sustained or pronounced, insulin therapy with short acting insulin may be warranted. Dependent on the animal's recent intake of water, hyper- or hyponatremia may be present. In humans that have been drinking pure water, hyponatremia is the presenting sodium abnormality, but if access to water has been restricted, hypernatremia will be the presenting sodium abnormality.

Potassium may be normal or altered in either direction. Both hyper- and hypokalemia are reported as the presenting abnormality in human medicine. In an experimental swine model hyperkalemia was the primary abnormality due to a direct action of heat on the K-Cl cotransporter in the plasma membrane, resulting in an increase in extracellular potassium.[10] But, during initial hyperthermia the kidney excretes the elevated plasma potassium and additional potassium is lost in sweat (humans) or saliva (panting); therefore, dependent on the timing of the electrolyte sample hyper-, hypo-, or normokalemia maybe recorded.[10] Hypophosphatemia, hypocalcemia, and hypomagnesemia may all be observed.[11] Because electrolyte and blood glucose abnormalities are common, blood glucose and electrolytes should be evaluated frequently and any abnormalities corrected.

Acute renal failure often occurs a day or two after heat stroke. The mainstay treatment of acute renal failure is fluid diuresis; other treatments such as furosemide, mannitol, diltiazem, peritoneal dialysis or hemodialysis may be necessary.[1,2,12]

Furosemide and mannitol are only used in oligouric or anuric renal failure; diltiazem has shown promise in treatment of infectious renal failure due to its reversal of renal vasoconstriction,[12] but needs further evaluation before its use can be recommended. Dialysis is used when medical treatment (fluids and diuretics) of renal failure is not successful and oliguria/anuria persist, or azotemia is extreme.

Gastrointestinal sloughing occurs quickly in animals with heatstroke; bloody diarrhea with sloughed tissue is often observed during the initial cooling and fluid resuscitation stages. Treatment with antibiotics is initiated in an attempt to control bacterial translocation from the gut. A common choice of antibiotic is injectable ampicillin, although other antibiotics maybe used. Gastrointestinal complications are also treated with anti-emetics, antacids, gastrointestinal protectants (such as sucralfate), and nutritional supplementation.[2] Enteral administration of the amino acid, glutamine improves survival after hyperthermia.[2,13]

Liver insult as evidenced by alterations in liver enzymes is very common. Liver enzyme elevations may be present on arrival and liver failure may develop over the next 24-72 hours of treatment.[11] Treatment for liver injury is supportive only. A role for antioxidants such as S-Adenosyl-L-Methionine (SAMe) has not been demonstrated but may be speculated.

Coagulation abnormalities may occur immediately or may be delayed, showing up days after the hyperthermic episode. Animals may have petechial hemorrhage resulting in part from thrombocytopenia and in part from vasculitis. DIC can also develop quickly both from direct heat injury and from complications that often accompany heat stroke such as sepsis/endotoxemia. Coagulation defects are generally

treated with fresh frozen plasma and blood products. A role for heparin administration in prevention or treatment of DIC remains speculative.

Many other complications of heat stroke may develop, often requiring complex and multi-drug therapy. Neurologic deficits can change rapidly. Anti-convulsant medications are given as needed. Lidocaine is used if significant ventricular arrhythmias develop, and has the additional potential benefit of antioxidant activity.[1,2,6,7] Rhabdomyolysis is treated with fluid diuresis (to prevent acute renal failure) and analgesics.

Oxidative damage is thought to play an important role in secondary tissue damage seen in heat stroke patients,[14] but no pharmacological interventions have been found to prevent or treat the damage. Drugs that have been used to treat the oxidative and secondary tissue damage include steroids and non-steroidal anti-inflammatory drugs (NSAIDs). Steroids have not shown benefit in an experimental model of heat stroke[15] despite their membrane stabilization anti-oxidant properties. Non-steroidal anti-inflammatory drugs are not recommended; these drugs lower temperature during fever by lowering the hypothalamic set point, which is not abnormal in animals with heat stroke. NSAIDs are actually contraindicated in animals with gastrointestinal or renal disease, which are both common complications of heat stroke.[1,16] At this time no one specific pharmacologic agent has been shown to increase survival,[13] therefore treatment of heat stroke is limited to rapid cooling and aggressive supportive care for the secondary complications.

Fever

Fever is orchestrated by the hypothalamus and involves a complex interaction of the endocrine and immunologic systems.[17] Of itself, fever is seldom an emergency and the goal in fever treatment is to identify and eliminate the underlying cause. There are many causes for fever including infection, inflammation, neoplasia, toxins, drugs, and autoimmune diseases. Because there are many etiologies for fever, a careful systematic evaluation is necessary to identify the underlying cause.[18-20]

Interestingly, scientific studies have not proven if fever is beneficial or detrimental, and in fact this may depend on the specific situation.[21-25] Fever is a protective mechanism to help the body fight infection. Multiple experiments have demonstrated better outcomes when fever is not abated. In experimental models, increasing body temperature artificially has been shown to enhance the resistance of mice to multiple viruses including herpes simplex virus, poliovirus, Coxsackie virus, and rabies virus; and when dogs were tested, the increased body temperature rendered them more resistant to herpesvirus virus.[23] In select human viral infections, virus shedding and morbidity was prolonged in those who received antipyretics.[26-28] In humans with sepsis, antipyretic therapy appears to increase mortality rates.[29] Based on these studies it would appear that fever is beneficial.

Fever also increases the metabolic rate, and an increased metabolic rate in a critically ill individual can increase the demands on the heart, as well as increase oxygen and nutrient consumption.[23] Fever can cause mental dysfunction and is associated with increased mortality in humans with traumatic brain injury.[28,30,31] Febrile seizures are well described in young children. This condition is not necessarily related to magnitude of fever, and appears to have a genetic susceptibility. Antipyretic therapy does not

influence the seizure or recurrence rate of the seizures.[32-34] To the author's knowledge, fever-associated seizures have not been documented in dogs or cats. While human beings are more comfortable after medical fever reduction, this may be related as much to analgesic properties and other anti-inflammatory effects of the drugs used to reduce fever (NSAIDS, acetaminophen) as to the normalization of temperature itself.

Antipyretics

Because it is unclear if fever is beneficial or detrimental, antipyretic therapy is controversial. Antipyretic therapy is often used in human medicine both to increase patient comfort and because of the perception among patients themselves that fevers are dangerous.[35] While pet owners seldom take their pet's temperature, it is common for humans to take the temperature of themselves or their children and to self-medicate to control fever. Currently, there is evidence for benefit of fever suppression in only a small subset of human patients with acute brain injury;[36] even here it is controversial as antipyretic therapy may decrease cerebral perfusion pressure.[37] The decision to use antipyretic therapy should be evaluated on an individual animal basis. If the animal is still eating and drinking antipyretic therapy is rarely necessary. If the fever is high, >40 °C (105 to 106° F) in-patient treatment with intravenous crystalloid fluids is often recommended because these animals are typically anorexic and are not taking in enough fluids to meet the increased metabolic demands of fever. Intravenous fluids alone often reduce the fever slightly while a definitive diagnosis is sought and specific treatment begun. If the fever becomes dangerously high despite intravenous fluids and treatment aimed at any known underlying cause, antipyretic medication or external cooling maybe warranted. Since temperatures in excess of > 41 °C (106 °F) can cause direct cellular

damage, this value represents a reasonable temperature at which treatment of fever should be initiated.

External cooling can be achieved by all the methods described to cool a hyperthermic animal. Care should be taken not to cool the animal to the point of shivering as the benefits of cooling are lost once the animal starts shivering.[35] External cooling works directly against the body as the hypothalamus is signaling the animal to retain heat; external cooling may therefore increase patient discomfort.

There are many types of antipyretic medications. Corticosteroids are effective antipyretics which act by several mechanisms. These compounds decrease pro-inflammatory cytokine production as well as inhibiting arachidonic acid liberation from cell membranes, thereby reducing production of leukotrienes and prostaglandins. Because corticosteroids affect many cytokines, their use, even at anti-inflammatory doses, may affect the entire immune system. Corticosteroids are essentially never used specifically to reduce fever but may be the most appropriate treatment for some inflammatory causes of fever such as immune-mediated polyarthropathy.

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used in human and veterinary medicine to reduce fever. All NSAIDs work primarily by inhibiting the cyclooygenase (COX) enzymes. There are multiple COX enzymes and the different NSAIDs have different affinities for the major COX enzymes. Despite their differences all NSAIDs reduce fever by reducing the prostaglandins (specifically PGE_2) and other end-products of the arachidonic pathway (Figure 1).

Because of their action on COX, all NSAIDs have potential adverse affects including gastrointestinal bleeding and/or ulceration, nephrotoxicity, hepatotoxicity and

platelet dysfunction.[38] These risks must be taken into account prior to the use of NSAIDs. NSAIDs should generally not be given to dehydrated, poorly perfused animals, animals with pre-existing gastric ulcers, animals with renal insufficiency, or pregnant animals.[39] Cats are exquisitely susceptible to the side effects of NSAIDs due to a decreased ability to metabolize NSAIDs.[39,40] The half-life of carprofen and aspirin (acetylsalicyclic acid) in cats is long, 20 and 22 hours respectively after IV injection. Because NSAIDs have a long duration of action and reduced metabolism in cats they should be used cautiously in this species.

Once the decision to use an antipyretic has been made the choice of the specific drug will depend on dosing route and availability. Any of the Federal Drug Administration (FDA) approved NSAIDs at the appropriate dose will likely be effective in reducing fever.[41] Mixing types of NSAIDs or combining them with corticosteroids potentiates the detrimental side effects.[42]

There are several anti-inflammatories commonly used in humans that deserve special consideration for dogs and cats. Acetaminophen (Tylenol®) is highly toxic to cats due to their reduced ability to glucuronidate the toxic metabolites. An acetaminophen dose as small as 10 mg/kg can be fatal in cats; acetaminophen should never be used in this species.[43] Acetaminophen can be used with caution in dogs, but the therapeutic range is very narrow making it easy to overdose and cause liver damage.[44] Ibuprofen also has a very narrow therapeutic range; it can cause severe gastrointestinal ulcers in dogs and cats are considered twice as sensitive. Therefore, ibuprofen is rarely used in dogs and cats.[44] Aspirin can be used with caution in dogs and cats. It is used in ultra low doses (0.5 mg/kg) as an anticoagulant[45] due to its platelet effects but at

analgesic or antipyretic doses (10-40 mg/kg)[46] it can cause significant gastrointestinal ulcers; the effects are prolonged (2-3 days) in cats.[41]

Appropriate treatment of fever requires identifying an underlying cause. The underlying cause should be treated or eliminated if possible. If treatment for the underlying cause and supportive care does not resolve the fever or the fever elevates to a dangerous level, antipyretic therapy is indicated.

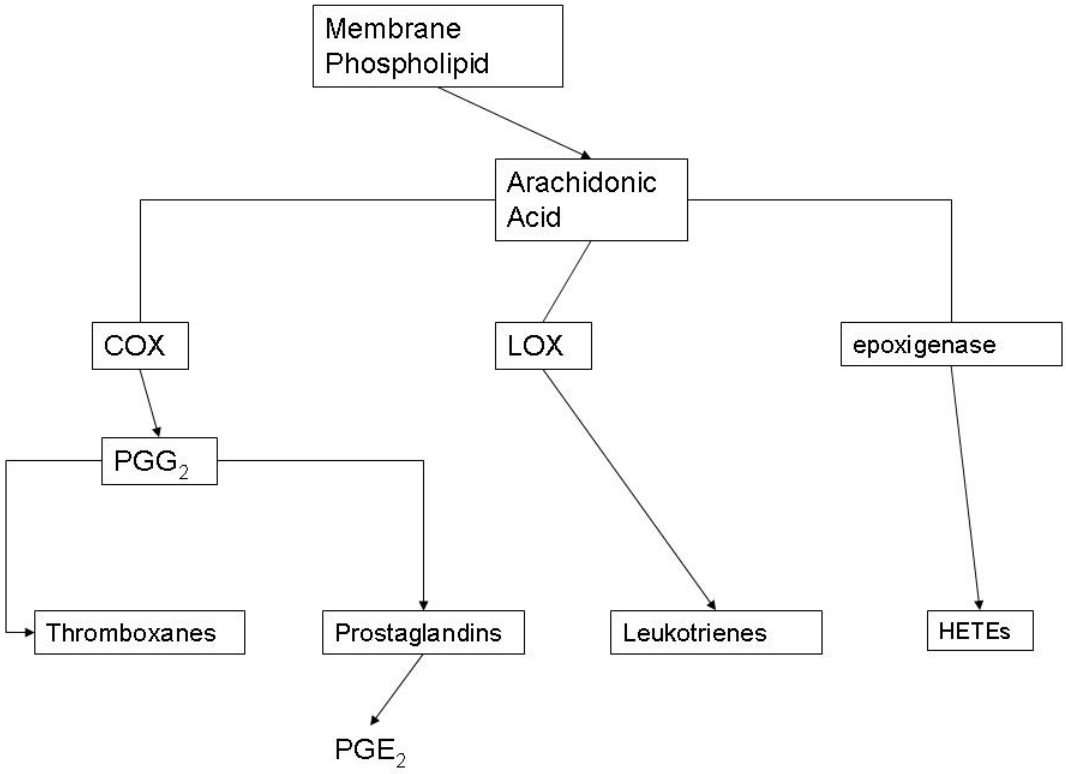

Figure 4.1: The arachidonic acid pathway
COX: cyclooxygenases
LOX: lipoxygenases
PGG_2: prostaglandin G_2, the precursor to the rest of the prostaglandins and thromboxanes
HETEs: endogenous monohydroxy-eicosatetraenoic acids
PGE_2: prostaglandin E_2

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Chapter 5

Conclusions and future directions

Body temperature regulation requires coordination among many systems including the nervous, endocrine, immune, and musculoskeletal systems. Because so many systems are involved, body temperature measurement allows a global assessment of a patient and is considered one of the vital parameters.

A perfect method to measure core body temperature would be non-invasive, accurate, rapid, and technically simple. All current methods of measuring core body temperature are invasive and, therefore, require some technical expertise. In this thesis it was shown that predictive rectal thermometers approximate core body temperature over a wide range of temperatures in healthy dogs. This gives clinicians an accurate, rapid, minimally invasive, simple method to approximate core temperature.

An accurate, rapid, non-invasive method to determine core body temperature would be beneficial since rectal temperature measurements are often distasteful to the owner and resented by the dog. The subcutaneous site offered an exciting option. After the initial microchip placement via simple subcutaneous injection, measurements literally come at the wave of a wand. Unfortunately, the subcutaneous measurements were not sufficiently accurate to consider as a replacement for rectal thermometry. While the microchip was very accurate in some dogs, it was very inaccurate in other dogs. Our research did not reveal why the subcutaneous site was inaccurate in some dogs. We found no obvious explanation: no differences in size, build, condition, or coat of the dog, no evidence of improper placement, pathology around the microchip, and no evidence of

infection at the site of the microchip. The device itself was removed from one dog and re-evaluated by the manufacturer, but no problem was identified with the device itself.

It might be that the subcutaneous site itself is not conducive to rapid and accurate estimates of core temperature. To help determine if the subcutaneous compartment itself, rather than the particular device used in our projects was the problem, a different thermistor could be tested in this site. There are several thermistor-tipped catheters that could be placed subcutaneously and readings compared to core temperature. Using a different thermistor could help determine if it was the device or location that caused the inaccuracy.

The skin and subcutaneous tissues are effectors the body uses to control temperature. When the core is too hot the vessels in the periphery dilate to allow more blood flow, warming the subcutaneous tissue while allowing the blood from the core to cool. When the core is too cool the vessels in the periphery constrict shunting warm blood away from the periphery and to the core. This vasoconstriction and dilation are thought to be more effective in non-haired species. It is possible in haired species that the peripheral temperatures will not change as drastically and the subcutaneous site maybe an acceptable approximation of core body temperature. This could be tested by exposing dogs to different ambient temperatures and comparing the subcutaneous temperature to core or rectal temperatures.

The infrared auricular thermometer was the most inaccurate at approximating the core temperature. Because the dog has a bend in the external ear canal the auricular thermometer may be obtaining skin temperature measurements rather than tympanic membrane measurements leading to readings below the core temperature. Often the

readings were above the core temperature. The brain in humans is maintained at approximately 1° C above the core body temperature; readings higher than core may indicate a true tympanic temperature that is actually closer to the brain temperature than the core temperature. An infrared device that measures a site known to approximate core body temperature could be developed. For example, an infrared device could measure the temperature of the oral cavity in dogs. Most dogs will allow a brief oral exam and if the device could be pointed towards the back of the throat the temperature reading may correlate with core body temperature. If this device were made it would require developing a black box temperature reference in the size and shape of a dog's mouth. The size and shape of dogs' mouths varies greatly, so developing this reference may be challenging. Another possible site would be the retina. The retina is in direct connection with the central nervous system and has minimal differences in size and shape among dogs.

Many of the devices used in human medicine contact the skin. Most dogs are haired over all of the body making skin contact devices ineffective. The haired skin can be shaved, but that does not guarantee good contact with a thermistor device. Skin contact methods are likely to be less accurate in veterinary patients than in humans. To the authors knowledge there is no published data on the use of skin contact devices in dogs.

There is a minimally invasive core thermistor for short-term used in humans. This thermistor is swallowed and measures temperature from inside the gastrointestinal tract until it is passed out of the body in the stool. It can be used to monitor core temperature during experimental conditions such as exercise. It has been used to monitor

the core temperature in athletes running marathons.[1] This type of device would be useful in dogs in the research setting but may not be useful in the clinical setting.

Of the methods measured in our study, the rectal site using predictive resistance thermometer was the most accurate minimally invasive method to obtain an accurate approximation of core temperature. It is expected that equilibrium rectal thermometry would be similarly accurate, but would require additional time for an accurate reading to be registered. While tympanic or subcutaneous thermometry might be used as a screen, when accurate and precise temperature readings are required for practical clinical use, rectal thermometry is preferred over other minimally invasive methods in dogs.

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