FEVER VS. HYPERTHERMIA

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Determining if a patient's elevated body temperature is a true fever (pyrexia), or hyperthermia can be difficult. There are many ways to treat an elevated body temperature and understanding the physiology of both is important. An elevated body temperature is considered to be a core body temperature of over 102.5°F (39.2°C). There are many ways to take a body temperature, but it is important to note that rectal temperatures are the most accurate in our veterinary patients. Most patients that have an elevated body temperature have a true fever, but there can be other instances where a patient is hyperthermic. These instances can include heat stroke and medication reactions.

Thermoregulation is the balance between heat loss and heat production in the body. Once the fever starts, the body's need for oxygen increases, heart rate increases, respiratory rate increases, and protein usage increases. Fevers also increase white blood cell activity and stimulate immune system function. They also inhibit some microbial growth. If a fever gets too high, the brain, liver, kidneys, and other organs do not function appropriately and can start to fail. The body's temperature control center is located in the central nervous system, in the preoptic area of the anterior hypothalamus (AH). The specific area that controls body temperature in the hypothalamus is the organum vasculosum of the laminae termalis. The body also has peripheral and central thermoreceptors that can sense when the body is above or below its normal temperature. When the thermoreceptors are activated, they send a signal through the nervous system to the AH. The AH then stimulates the body and it either releases heat through dissipation or conserves heat. Body heat is mostly produced through muscle activity.

When the body has a fever, thermoreceptors are activated by exogenous pyrogens or pyrogenic cytokines. Exogenous pyrogens are substances that are formed outside the body that have a capability of introducing interleukins into the body. Interleukins are cytokines. Cytokines are proteins that control inflammatory responses and typically induce a fever. In the initial acute phase of a true fever, or pyrogenic hyperthermia, an outside source or antigen invades the body. Macrophages are then activated. Once the macrophages are activated, interleukin-1 is produced which initiates T-cell activation. Other interleukins are then activated, which in turn, activates plasma cells, other T-cells, stem cells, and natural killer cells. Interferon (INF) then stimulates the macrophages to produce Interleukin -1,(IL1). Tissue necrosis factor, (TNF), as an endogenous pyrogen, triggers the AH to stimulate the temperature set-point of the body to increase. True fevers can be caused by viruses, bacteria, fungi, and protozoal infections.

Heat loss can occur in four ways: radiation, evaporation, convection, and conduction. Radiation is the most common method; 60% of the body's heat is lost through radiation. An example of heat loss through radiation would be like feeling heat from a fire without being inside the fire. Convection heat loss is when air or water moves across the skin surface. Conduction heat loss is when you are in direct contact with the heat source, when one touches a hot stove, for example. Evaporation is heat loss through respiration. So, in our patients, this can be heat lost through panting.

Non-pyrogenic hyperthermia is not due to an introduction of an exogenous pyrogen or pyrogenic cytokines. The patient's body temperature set point has not be altered and the outside temperature exceeds the patient's ability to dissipate heat. Examples of non-pyrogenic hyperthermia are heat stroke, exercise induced hyperthermia, hyperpyrexic syndrome, and medicated induced hyperthermia.

A good way to differentiate a true fever versus hyperthermia is with a patient history and physical exam. Usually, if a patient has a true fever, they will not be presenting with a history of being in hot environments or exercising with the owner in very high heat or humidity. The patient's breed can also predispose them of having hyperthermia. Some examples of this are any brachycephalic breeds, like bulldogs and boxers.

Heat stroke occurs when a patient is exposed to elevated environmental temperatures that can cause their body temperature to elevate. Heat loss tries to occur but is unsuccessful due to the elevated temperature of the environment. When the environmental temperature increases, the body's natural responses are to vasodilate the blood vessels to get the heat to the surface, panting to increase dissipation, tachycardia to increase blood flow to the surface of the skin, and constriction of the blood vessels of the spleen and kidneys to keep them cool. Heat stroke can occur very quickly in enclosed spaces with no ventilation, or even when a patient is not used to exercising.

Heat stroke is usually characterized by the patient having a core body temperature of over 106°F (42°C). When these patients present at the hospital, they are usually past the initial stages of heat stress, which includes increased cardiac output and panting. They usually present laterally recumbent, panting, and have brick red mucous membranes.

During the initial, or acute, stages of heat stroke, cardiac output increases, thus increasing heart rate. The vessels then become vasodilated, and because of an inflammatory response and cytokine release, vessels become less resistant and blood pools in the spleen. This blood pooling can cause less blood to circulate. Less blood circulation combined with vasodilation can lead to hypotension. This can also cause the kidneys, brain, gastrointestinal tract, and liver to not receive enough oxygen. This in turn causes ischemia and signals an inflammatory response. Cells have a natural compensatory mechanism to protect themselves from the heat. They produce heat shock proteins. These proteins protect the cells from breaking down and help maintain cellular function. They also limit the production of pro-inflammatory cytokines. Cytokines, reactive oxygen and nitrogen species, and endothelial injury can cause increased vascular permeability. Once this happens, edema forms.

The first organ to be affected by hyperthermia is the gastrointestinal tract. Once the inflammatory response is activated and hypoxia sets in, reactive oxygen and nitrogen species are produced. The gastrointestinal tract then becomes leaky which can lead to bacteria translocation. Bacteria can then enter the blood stream, which then can predispose the animal to sepsis. Acute kidney injury also happens in heat stroke from cytotoxicity, vasoconstriction, and hypoxia. The lungs also are affected during a heat stroke event. The endothelial cells in the lungs are broken down as a direct effect of thermal injury. This can quicky result in acute respiratory distress syndrome, (ARDS). As the organs start failing, hemostasis is affected. Endothelial damage causes von Willibrand factor, platelets, and leukocytes to try and repair the damage. It activates the coagulation cascade but because of liver damage, tissue factors are then used up which can create a more serious problem, disseminated intravascular coagulation (DIC). Patients can then start having petechia formation or bleeding from the nose, bladder, rectum, and mucous membranes.

There are definitely problems with a fever present; increased metabolism, water requirements, and oxygen consumption are just a few. However, even with all of the negatives, there are benefits to a fever. Viruses and bacteria cannot handle warm environments making a true fever a necessary defense mechanism against disease.

Diagnostics

Diagnostics are an important tool in diagnosing a true fever versus heatstroke. The first diagnostic tool is the history and physical exam. A rectal temperature should be obtained. Then, a packed cell volume and total protein, (PCV/TP), should be drawn. The next step would be to obtain stat bloodwork, glucose, lactate, complete blood count, (CBC), and a serum biochemistry profile. PCV/TP are usually elevated usually due to dehydration during the first stages, but during late stages of heat stroke PCV may be decreased. If the patient has a true fever, PCV/TP may not be abnormal. Glucose can be affected depending on what disease process is happening. In a true fever or heat stroke, glucose can be very low. Lactate in heat stroke is usually very high which is over 2 mmol/L. Stat bloodwork usually shows electrolyte imbalances for both true fever and heat stroke. Heart rate is usually elevated in both heat stroke and true fever situations. Bloodwork results are the most important tool in diagnosing heat stroke versus a true fever. When a patient has a true fever, neutrophil count can be very low or have white blood cell count changes. In heat stroke patients, on CBC, nucleated red blood cells are elevated. They are elevated because there is heat damage to the bone marrow. In both fever and heat stroke dogs, there may be multiple organ systems that are affected and multiple values on bloodwork will be decreased or increased. Another tool that can be used is blood cultures. Blood cultures can tell you what kind of bacteria is present in the blood stream. Unfortunately, blood cultures can take 24-48 hours for results. So, even though effective, this test would not be suitable for patients that are critical. Prothrombin time and partial thromboplastin time, or PT/PTT, can help assess clotting times in heat stroke patients. If the PT/PTT results are elevated, it can be an indicator of clotting issues and the patient can be at risk of DIC. In a patient with a true fever, if the CBC/Chem, PT/PTT are normal, more blood tests may be warranted. For example, in felines, a Feline Leukemia virus and Feline Immunodeficiency Virus test can tell you a cause of a fever.

Radiographs are also another tool to help diagnose patients with a true fever. Chest and abdomen radiographs can detect the presence of pneumonia, cancer, or other abnormalities that cannot be seen with the naked eye. In heat stroke patients, radiographs might not be warranted immediately due to their critical nature.

Treatments

It is important to remember that patients with a true fever have a fever for a reason. It is an appropriate physiologic response to a foreign material entering the body. Bacteria, viruses, and fungi cannot survive in high temperature environments. After diagnostics, it is important in these patients to find out why they have a fever and treat the underlying cause of that fever. Antibiotics should be started if the patient's bloodwork warrants it.

IV fluids should be started on patients with a fever. This will help perfusion of organs as well as correct any electrolyte abnormalities. Depending on the disease process that is causing the fever, fluid bolus' may be warranted. Dextrose solutions should also be given to patients who are hypoglycemic due to possible sepsis.

There are multiple treatments to avoid when working with patients that have a true fever. Antipyretics such as non-steroidal anti-inflammatory drugs have been shown to not have any real benefit unless the patient also has a neurologic component to their disease process. These drugs have side-effects that can sometimes cause gastric bleeding or perforation, AKI, liver damage, or red blood cell damage. External cooling should be avoided in true fever patients. This can include room temperature baths, fans, alcohol on paw pads, and ice packs in axillary areas. This can cause significant patient discomfort and have no effect on decreasing the fever.

Heat stroke treatment is quite different than fever patients. Active cooling must be initiated immediately. Tepid water baths should be initiated. Once the water is on the patient, a fan should be placed near the patient so that evaporation of heat can happen. Temperatures must be taken every 2-5 minutes, and once the patient's temperature reaches 103°F, or 39°C, active cooling should be stopped. Patients with thick fur coats can be shaved to promote evaporation. Intravenous fluids given quickly can also decrease a patient's temperature. Oxygen therapy should also be administered. Dextrose should be given to patients with heat stroke if they are hypoglycemic. Mannitol can be given if cerebral edema is expected due to oxidative damage from elevated temperatures, for an extended period of time. Benzodiazepines can be beneficial in the heat stroke patient if they are seizing. Gastroprotectants and anti-emetics can also be used in these patients to help prevent further gastric damage. Broad-spectrum antibiotics should be used to treat patients with suspected GI-translocation of bacteria or sepsis. In heat stroke patients that have coagulopathies, whole blood, fresh frozen plasma, or packed red blood cells, will be warranted to prevent the patient from bleeding.

Ice packs, alcohol, and ice baths should be avoided in heat stroke patients. When these treatments are done, vasoconstriction happens, forcing the warm blood back into the core of the body. This will not cool down the patient.

Pain management is important in both patients with a fever and heat stroke. It is important to access each patient and clinicians should prescribe pain medications accordingly.

Nursing Care

In both patients, nursing care is important. Full physicals, blood pressures, and pain scores should be assessed frequently. Bloodwork, including CBC/Chemistry should be assessed at least once a day. A urinary catheter could be a helpful tool in monitoring hydration status and kidney function. Physical therapy is also a major part in patient care. Making sure the patient's muscles contract and move so that they do not build up lactate. Keeping the patient clean, dry, and comfortable is also key to the patient's survival.

Prognosis

Prognosis for true fever depends on what the underlying cause of the true fever is. Prognosis for patients with heat stroke leaving the hospital is around 50%. If the patient comes in quickly after the owner recognizes the signs of heat stroke, they have a better prognosis.

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