Thermal injury is a relatively uncommon presentation in veterinary medicine. Contact with an electric heating pad, a hot muffler of a motor vehicle, or an open flame is the most common inciting cause. Severe thermal injuries, particularly full-thickness burns exceeding 30% of total body surface area, provoke a profound systemic inflammatory response characterized by leukocyte activation and plasma leakage in the microvasculature of tissues or organs remote from the wound. 

Thermal Injury Characterization

Thermal injury is characterized by the depth of affected tissue. Superficial (first-degree) burns involve only the epidermis. The skin is hyperemic, painful, and nonblistered and often heals in 5 days without scarring. Partial-thickness (second-degree) burns involve the epidermis and the dermis and are further subcategorized as superficial or deep partial-thickness burns. A superficial partial-thickness burn involves the epidermis and one-half of the dermis. It is characterized by blisters, pain, blanching upon pressure, and intact hair and takes 2 to 3 weeks to heal. A deep partial-thickness burn leads to destruction of deep dermal layers and may be dry or moist and blistered; the area does not blanch, and the hair falls out easily. Deep partial-thickness burns heal slowly with scarring and potential loss of function. Full-thickness (third-degree) burns involve all dermal layers. The skin is often dry and leathery and may appear white or charred. This type of burn results in loss of sensation and therefore may be nonpainful, although the tissue has been irreversibly damaged. A third-degree burn heals by contracture and epithelial migration or via excision and grafting. Third-degree burns may result in the formation of eschar, a hard, leathery product.

Local Response to Thermal Injury

Thermal injury results in the disruption of cell membrane integrity, activation of cytokines, and cessation of local blood flow. At the cellular level, cytoskeletal components are disrupted, resulting in increased membrane permeability. The cell membrane is extremely vulnerable to thermal injury because its bilayer lipid component is held together by forces of hydration. The disruption in cell membrane permeability is speculated to be the most important pathophysiologic event leading to tissue death.

The severity of a thermal injury depends on the temperature of the heat source, the size of the affected area, and the duration of contact. Jackson originally outlined three different zones evident on visual examination immediately following a burn injury: the zone of coagulation, the zone of stasis, and the zone of hyperemia.

The zone of coagulation is the area of a burn nearest to the heat source. This zone suffers the most damage, sustaining blood clotting and thrombosis of vessels. Tissue properties are irreversibly altered secondary to extensive protein denaturation. The zone of stasis surrounds the zone of coagulation and is characterized by decreased blood flow (blood stasis). Edema forms in this zone due to vasodilation and increased microvascular permeability. Excessive local edema is followed by hypoperfusion, further exacerbating local tissue ischemia. The tissue in this zone is potentially salvageable.
and is therefore the focus of most burn resuscitation therapies, which are aimed at restoring perfusion to the affected area to prevent irreversible damage. The zone of hyperemia is the peripheral area around the burn and is characterized by increased blood flow. The tissue in this zone is likely to recover as long as sepsis or prolonged hypotension do not ensue.

The body’s response to thermal injury may be described in four stages. Stage 1, the emergent phase, occurs within minutes to hours of the initial injury and is characterized by a pain response, catecholamine release, and subsequent tachycardia, tachypnea, and mild hypertension. Stage 2, the fluid shift phase, lasts for 18 to 24 hours. During this phase, damaged cells initiate the inflammatory response. This local phenomenon results in a shift of fluid from the intracellular space to the extracellular space, causing capillary leakage and substantial edema. Stage 3, the hypermetabolic phase, may persist for days to weeks, and may be thought of as a period of profound increase in nutritional needs for proper tissue healing. Stage 4 is the resolution phase and results in scar formation with a gradual return to normal tissue function. These stages typically follow a consecutive pattern, although some overlap between stages may occur.

**Systemic Response to Thermal Injury**

When a thermal injury affects more than 30% of total body surface area (TBSA), the release of cytokines and other inflammatory mediators at the site of the injury has a profound systemic effect. The inflammatory response is initiated immediately after the burn and may persist for several months, affecting the cardiovascular system at many levels. Myocardial contractility is decreased, likely secondary to release of tumor necrosis factor-α (TNF-α) from injured tissue. Increased capillary permeability leads to loss of intravascular proteins and fluid into the interstitial compartment. The combination of hypovolemia and negative inotropy results in hypotension and hypoperfusion. Inflammatory mediators such as leukotrienes, histamine, and interleukin may induce bronchoconstriction, leading to acute lung injury and respiratory distress. All of these factors contribute to systemic inflammatory response syndrome (SIRS). The mainstay of treatment for patients with SIRS consists of treatment of the underlying disease process and aggressive supportive care (see Treatment of Thermal Injury, below).

Hypoalbuminemia develops as a result of increased vascular permeability and is exacerbated by up-regulation of acute-phase proteins and subsequent decreased hepatic production of albumin. Hypoalbuminemia perpetuates edema formation, hypotension, and hypoperfusion. Colloid support with synthetic colloids such as hetastarch is frequently necessary in these patients, and if hypoalbuminemia is severe (<1.5 g/dL), the administration of canine or human albumin solution should be considered.

Vasoconstrictive substances such as thromboxane A2/B2, prostaglandins, cytokines, and reactive oxygen species produced at the burn site may produce a normal or increased blood pressure in thermal injury patients despite profound hypovolemia. A normal blood pressure should not preclude treating a thermal injury patient with aggressive intravenous fluid therapy, as the patient may be in a state of compensated shock. Additionally, hypertension may be the result of pain, and appropriate analgesics should be administered (see Treatment of Thermal Injury, below).

The hyperalgesia of a thermal injury is the result of a complex inflammatory response. Numerous cytokines, including interleukin-1 (IL-1), interleukin-6 (IL-6), and TNF-α, have been evaluated and used as markers of the severity of thermal injury in people. Hyperalgesic cytokines IL-1β, IL-6, and TNF-α are synthesized and released in response to injury, in addition to several other inflammatory mediators. The increase of these proinflammatory cytokines leads to pain, hypermetabolism, and tissue catabolism.

The hypermetabolic response that follows thermal injury is characterized by an elevated body temperature, augmented oxygen and glucose consumption, and increased carbon dioxide production, glycoegenolysis, proteolysis, and lipolysis. The elevation in body temperature is often mild and should be distinguished from fever secondary to infection, which is often more pronounced (>103.5°F) and may be accompanied by other changes, such as elevated white blood cell count or an obvious source of infection. In people, the hypermetabolic response following thermal injury has been reported to last up to 24 months. During this phase, there is loss of lean body mass and bone density, muscle weakness, and delayed wound healing.

**Potential Complications of Thermal Injury**

Insulin resistance associated with hepatocyte damage is common in thermal injury patients. In human medicine, insulin administration has been shown to improve survival and decrease the rate of infection. Insulin decreases the synthesis of proinflammatory cytokines and aids in the restoration of hepatic homeostasis by modifying damaged signaling pathways after thermal injury. Hyperglycemia is common in burn patients and is secondary to an increased rate of glucose production with impaired extraction of glucose by the damaged tissues. Jeschke et al found that patients with poor glycemic control had significantly higher rates of bacteremia, fungemia, and mortality. Interestingly, the current practice of tight glycemic control in critically ill humans stems from early research evaluating glycemic control in thermal injury patients. Tight glycemic control remains a very controversial topic in both human and veterinary medicine and cannot be recommended as a therapy for veterinary patients at this time.

Adrenal insufficiency (AI), or critical illness–related corticosteroid insufficiency, is a relatively uncommon complication of thermal injury in human patients. The development of AI in people appears to be associated with burns affecting a greater TBSA and older age. After a severe burn, a diagnosis of AI greatly increases the risk of death. AI after thermal injury results from severe systemic inflammation leading to sepsis, thrombosis, and coagulopathy with hemorrhage into the adrenal glands. No studies have examined the incidence of AI in veterinary burn patients. Thus, routine monitoring of adrenal function in veterinary thermal injury patients cannot be recommended at this time, but could be considered in hypotensive patients that are not responding to standard fluid resuscitation therapy.
Sepsis is a major cause of death in burn patients. Sepsis may result from wound infection, respiratory infection, catheter infection, bacterial translocation from decreased gastrointestinal perfusion, and decreased mucosal integrity. Diagnostic criteria for sepsis include fever, hypothermia (especially in cats), tachycardia, bradycardia (especially in cats), tachypnea, altered mental status, significant edema or positive fluid balance, hyperglycemia in the absence of diabetes, and hypoglycemia. Identification and treatment of septic patients is discussed elsewhere in the veterinary literature.

**Treatment of Thermal Injury**

The current practice of burn care in people is focused on antimicrobial control of wound infection, enteral nutrition, analgesia, early surgery, initiation of anabolic steroid and β-blockade therapy, and use of artificial/cultured skin where appropriate. The same level of care may be applied to veterinary patients.

**Acute Management**

All veterinary burn patients should be provided with oxygen, intravenous fluids, and analgesia as well as assessed for shock and treated accordingly. If inhalation injury is suspected, oxygen therapy should be continued and fluid therapy should be more conservative to prevent exacerbation of possible pulmonary capillary leak syndrome.

The corneal epithelium is sensitive to temperature, and corneal ulcers are common secondary to thermal injury. Therefore, in patients that have sustained burns from fires and were exposed to smoke and high temperatures, the eyes should be treated with lubricating and antibacterial ophthalmic medications.

Immediately following a thermal burn, the area should be cooled with water or damp towels for 10 minutes to help prevent further thermal injury in the absence of heat. Even once the heat is removed, tissue may continue to burn. However, cold water or ice should be avoided, as they may cause vasoconstriction and increased wound depth. Due to the increased risk for hypercoagulability in burn patients, jugular catheters should be avoided if possible. Patients with burns involving more than 20% of their TBSA may develop severe metabolic derangements, and appropriate diagnostic samples should be obtained once the patient is stabilized. Initial diagnostic tests should include a complete blood count, serum biochemical profile, urinalysis, prothrombin time (PT), activated partial thromboplastin time (aPTT), and orthogonal thoracic radiography. In patients with burns involving >50% of their TBSA, the prognosis is poor to guarded, and euthanasia should be discussed with the owner.

**Fluid Therapy**

The greatest amount of fluid loss in thermal injury patients occurs during the first 24 hours, secondary to increased microvascular permeability. Patients receiving IV fluids should be monitored closely for changes in body weight and abnormalities detected on physical examination (skin turgor, heart rate and pulse quality, mucous membrane color, and capillary refill time). If an indwelling urinary catheter is in place, urine output can be compared with fluid input to help guide fluid therapy and prevent hypervolemia or hypovolemia secondary to fluid administration. Blood urea nitrogen and creatinine should be assessed, along with urine specific gravity. Blood lactate should be measured, as inadequate tissue perfusion may result in hyperlactatemia secondary to anaerobic metabolism. Moderate to marked elevations in blood lactate should alert the clinician that more aggressive fluid therapy is warranted. Additional parameters for monitoring patient fluid requirements include packed cell volume/total solids, electrolytes, and central venous pressure (maintain between 3 and 7 cm H₂O). Colloid oncotic pressure (COP) should be measured if possible, and colloid therapy (such as hetastarch) should be instituted if COP is <15 mm Hg. Central venous pressure is regarded as the gold standard for practical assessment of intravascular volume in veterinary patients. However, this measurement requires placement of a central catheter, which may be risky in a patient that is predisposed to hypercoagulability.

In addition to replacing the tremendous volume of fluid lost within the first 24 hours, high fluid rates should be used to protect the renal tubules from myoglobin-induced injury and other waste products from damaged tissue. Fluid therapy should be tailored to patient needs, and changes should be made based on patient monitoring.

**Monitoring**

Between days 2 and 6 after the injury, patients should be closely monitored for anemia, immune dysfunction, SIRS, early burn wound infection, and disseminated intravascular coagulation (DIC). Early laboratory changes associated with DIC include thrombocytopenia, prolonged PT, prolonged aPTT, hypofibrinogenemia or hyperfibrinogenemia, low antithrombin levels, and presence of fibrin degradation products or D-dimers. The diagnosis and treatment of DIC are discussed in depth elsewhere.

**Pain Management**

Inadequate pain management is detrimental to burn patients. Immediate pain is due to stimulation of skin nociceptors, and thermal injury causes the release of chemical mediators that sensitize active nociceptors at the site of injury. Burn patients may experience both nociceptive and neuropathic pain. Continuous or repeated peripheral stimulation of nociceptive afferent fibers induces an increase in dorsal horn excitability via N-methyl-d-aspartate (NMDA) receptors, leading to increased sensitivity in the undamaged skin surrounding a burn. Peripheral and central sensitization contribute to the pathophysiology of burn pain; therefore, analgesia should address both of these pain mechanisms.

Analgesia should be provided with pure µ agonists such as fentanyl (3 to 10 µg/kg/h CRI), hydromorphone (0.025 mg/kg/h CRI), and morphine (0.5 to 1 mg/kg SC q4h). Lidocaine (1.5 to 3 mg/kg/h CRI) may be used as an adjunctive analgesic and as a free radical scavenger in dogs and may be used cautiously in cats. Ketamine (loading dose: 0.5 mg/kg IV; maintenance dose: 2 to 5 µg/kg/min CRI) and gabapentin (7 to 10 mg/kg PO q12h) are also particularly beneficial in canine and feline thermal injury patients. Ketamine has been used for more than 40 years in the treatment of burn pain in people. Ketamine inhibits...
Thermal Injury

γ-aminobutyric acid and may also block serotonin, norepinephrine, and dopamine in the central nervous system. Ketamine can also inhibit NMDA receptors in the central nervous system and decrease the wind-up effect.16 Gabapentin is an antihyperalgesic drug that selectively affects central sensitization.17 In people, gabapentin has been shown to reduce opioid consumption and lower pain scores secondary to its ability to prevent central hyperalgesia.17 Appropriate analgesia in thermal injury patients should be multimodal, incorporating antagonism of nociceptive and neuropathic pain pathways.

Wound Management

Early excision and closure of the burn wound has been a major advancement in treating human patients with severe thermal injuries in the past 20 years.18 Although early wound closure is ideal, it should not take place for the first 3 to 7 days until the full extent of the wound is apparent.1 Wound care is best provided by first cleaning the area with a mild, water-based antiseptic such as povidone-iodine solution or 0.25% chlorhexidine solution, and then applying silver sulfadiazine.3 Alternatively, aloe vera cream may be used for its antithromboxane effects to prevent vasoconstriction and thromboembolic seeding of the microcirculation.1 Unpasteurized honey has also been used with favorable outcomes in thermal injury management. Honey reportedly decreases inflammatory edema, accelerates sloughing of necrotic tissue, and provides a good energy source for development of granulation tissue.1 Other topical agents that may be used in thermal injury wound management are mafenide acetate (a sulfonamide) and Polysporin (polymyxin B sulfate and bacitracin; Johnson & Johnson).18 Sterile gloves should be worn at all times to protect the patient, and the wound should be cleaned on a daily basis until excision and closure can take place.

Provision of moisture to the affected area(s) following the application of topical agents is crucial and may be accomplished by applying a bandage with a nonadherent, porous inner layer that allows the passage of fluids and exudates and an absorbent gauze/pad outer layer. Full-thickness burns should be excised at the end of the first week if possible. Before excision, conservative management of burn wounds should entail hydrotherapy, removal of necrotic tissue, topical therapy, and bandaging.1 This helps to prevent wound sepsis and SIRS as well as to decrease morbidity and mortality and down-regulate the hypermetabolic response.3

Another option for more conservative management is enzymatic debridement. This procedure entails the use of topical agents such as trypsin-balsam of Peru castor oil to soften, loosen, and digest necrotic tissue. This facilitates easy removal of necrotic tissue with gentle lavage. Enzymatic debridement should only be considered in the very early stages of burn management and must be discontinued once a healthy granulation bed has formed.1 Full-thickness burns typically require skin grafts or flaps in order to achieve complete closure.

Antibiotic Therapy

Significant thermal injuries induce a state of immunosuppression that predisposes patients to infectious complications. Most deaths in severely burned human patients are due to burn wound sepsis.19 Topical antibiotics are the antimicrobial of choice in thermal injury patients; systemic broad-spectrum antibiotics are not indicated unless there is evidence of immunosuppression, wound infection, pneumonia, and/or sepsis. Examples of antibiotics commonly used in the management of wound infections are listed in TABLE 1.

<table>
<thead>
<tr>
<th>Key Drug</th>
<th>Drug Class</th>
<th>Dosage</th>
<th>Frequency</th>
<th>Route</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin or ampicillin</td>
<td>Extended-spectrum penicillin</td>
<td>15–22 mg/kg</td>
<td>q6–8h</td>
<td>PO (amoxicillin), IV/IM (ampicillin)</td>
<td>Infection, dirty wound</td>
</tr>
<tr>
<td>Amoxicillin–clavulanic acid</td>
<td>Extended-spectrum penicillin with β-lactamase inhibitor</td>
<td>13.75–20 mg/kg</td>
<td>q8–12h</td>
<td>PO</td>
<td>Superficial wound</td>
</tr>
<tr>
<td>Amoxicillin–sulbactam</td>
<td>Extended-spectrum penicillin with β-lactamase inhibitor</td>
<td>13.75–20 mg/kg</td>
<td>q8–12h</td>
<td>IV, IM</td>
<td>Superficial wounds</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>Cephalosporin</td>
<td>22 mg/kg</td>
<td>q6–8h</td>
<td>IV, SC</td>
<td>Infection, dirty wound</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>Fluoroquinolone</td>
<td>5–20 mg/kg (do not exceed 5 mg/kg q24h in cats)</td>
<td>q24h or divided q12h</td>
<td>IV</td>
<td>Infection, dirty wound</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Antimicrobial</td>
<td>7–10 mg/kg</td>
<td>q8–12h</td>
<td>PO, IV</td>
<td>Anaerobic infection, dirty wound</td>
</tr>
</tbody>
</table>

Metabolic Management

Due to burn patients’ extreme state of catabolism, nutritional support is vital for a positive outcome. Additionally, enteral nutrition may decrease the risk of translocation by promoting GI motility.
Several therapies have been developed in attempt to attenuate the hypermetabolic response to thermal injury. Pharmacologic interventions such as administration of growth hormone, insulin-like growth factor-1 (IGF-1), oxandrolone (an anabolic steroid), testosterone, insulin, and propranolol have been successfully used to dampen the catabolic state that results from thermal injury in people. Many studies using propranolol and IGF-1 to address the hypermetabolic phase in human burn patients have shown promise. Jeschke et al recently reported that propranolol administration attenuated lipolysis and the hepatic acute-phase response; furthermore, β blockade decreased urinary nitrogen loss, peripheral lipolysis, whole body urea production, and resting energy exposure. These therapies are in the early phases of use in people, and it is possible that veterinarians might achieve the same beneficial results with propranolol, insulin, and oxandrolone in patients in the future. However, no veterinary studies evaluating the use of these drugs in thermal injury patients have thus far been performed, and recommendation of their use is premature at this time.

Conclusion
Treatment of thermal injury is an active area of research in human medicine. Novel treatment strategies continue to develop as investigation continues into the inflammatory component of burn pathophysiology. Although very little has been published in the veterinary literature on this topic, much can be extrapolated from human studies. Further research is warranted to investigate a variety of novel therapies, particularly the use of oxandrolone, propranolol, insulin, and IGF-1β in veterinary burn patients. Understanding the pathophysiology of thermal injury is vital to developing effective treatment strategies and highlights the myriad roles the immune system plays in critical illness.

References
1. Pain response, catecholamine release, and mild hypertension are characteristics of the _______ phase in the body's response to thermal injury.
   a. emergent
   b. fluid shift
   c. hypermetabolic
   d. resolution

2. Which is speculated to be the most important pathophysiologic event leading to tissue death after thermal injury?
   a. disruption in cell membrane permeability
   b. temperature of the heat source causing the burn
   c. inhibition of DNA synthesis and transcription
   d. ischemia

3. Jackson's burn model includes the
   a. zone of coagulation.
   b. zone of stasis.
   c. zone of hyperemia.
   d. all of the above

4. Which zone in Jackson's burn model sustains the most damage?
   a. zone of stasis
   b. zone of hyperemia
   c. zone of coagulation
   d. zone of necrosis

5. The zone of hyperemia is characterized by
   a. increased blood flow.
   b. decreased blood flow.
   c. increased microvascular permeability.
   d. clotted blood and thrombosis of blood vessels.

6. For cytokines and other inflammatory mediators released at the site of injury to have a systemic effect, more than ____ of the TBSA must be burned.
   a. 10%
   b. 30%
   c. 66%
   d. 75%

7. A full-thickness burn is characterized by
   a. blanching upon pressure.
   b. destruction of deep dermal layers.
   c. presence of blisters and pain.
   d. hyperemic, painful skin.

8. Which is not a potential complication of thermal injury?
   a. sepsis
   b. hyperadrenocorticism
   c. hyperglycemia
   d. adrenal insufficiency

9. Burn patients experience the greatest amount of fluid loss during the first ____ after injury.
   a. 4 hours
   b. 24 hours
   c. 48 hours
   d. 72 hours

10. Which analgesics are recommended for IV administration in burn patients?
    a. pure μ agonists
    b. lidocaine
    c. ketamine
    d. all of the above