Systemic Inflammatory Response Syndrome

Angela Randels, CVT, VTS (ECC, SAIM)

Systemic inflammatory response syndrome (SIRS) is a complex series of events that may occur in veterinary patients due to an infectious or a noninfectious cause. Veterinary technicians are often the first to visually assess patients and measure their vital signs. Through regular patient monitoring, technicians have the opportunity to quickly identify subtle changes in a patient's status. Therefore, technicians are often in a key position to identify patients at risk for developing SIRS and the early clinical signs of SIRS. Early identification of at-risk patients and the clinical signs can allow treatment to be instituted as early as possible. This is associated with improved outcomes in patients with SIRS.[1]

The term *SIRS* was introduced by the American College of Chest Physicians and the Society of Critical Care in 1992 to describe the systemic activation of inflammation that eventually leads to organ failure in critically ill patients.[2] SIRS is associated with many diseases (e.g., pancreatitis), trauma, burns, and major surgery, and it may not be associated with sepsis.[2] Specific systemic signs must be present to diagnose SIRS (**TABLE 1**).[2]

Does My Patient Have SIRS or Sepsis?

SIRS and sepsis are underrecognized.[1] Consider the following examples:

Case 1: A 6-year-old, spayed cat presents with stranguria, a temperature of 98.4°F, a heart rate of 120 bpm, a white blood cell (WBC) count of 32,000, and large numbers of bacteria and WBCs on urine cytology.

Case 2: An 8-year-old, intact female Labrador retriever mix presents with purulent vaginal discharge (for 36 to 42 hours), vomiting, anorexia, lethargy, a temperature of 104.2°F, a heart rate of 152 bpm, and large numbers of rods and neutrophils on vaginal cytology.

Cases like these are seen in practices every day, so these patients can seem "normal"—unaffected by sepsis or SIRS. However, if the parameters in these cases are compared with those in **TABLE 1**, they *do* meet the criteria for SIRS, which increases the severity of these cases. It is vital for technicians to maintain a high suspicion of SIRS or sepsis in all critically ill patients.

Table 1. Diagnostic Criteria for SIRS

	Dogs Must Meet Two of the Following Criteria	Cats Must Meet Three of the Following Criteria
Temperature (°F)	<100.6 or >102.6	<100 or >104
Heart rate (bpm)	>120	<140 or >225
Respiratory rate (breaths/min)	>20	>40
White blood cell count (×103); percentage of bands	<6 or >16; >3%	<5 or >19

Pathophysiology of SIRS With Sepsis

The body produces an inflammatory reaction as part of the normal immune response to an insult, whether noninfectious (e.g., trauma, hyperthermia, hypothermia, gastric dilatation-volvulus) or infectious. The five primary signs of inflammation are heat, redness, pain, swelling, and loss of function.[1,3] Usually, these responses are localized, serving as protective mechanisms for the body. When the body experiences a second insult (a "second hit"; e.g., surgery, hypoperfusion, tissue hypoxia, reperfusion injury), an overzealous or exaggerated inflammatory response can ensue, resulting in an imbalance of proinflammatory and antiinflammatory mediators.[3]

In the presence of an infectious or inflammatory disease, pathogen- or damage-associated molecular patterns (PAMPs or DAMPs, respectively) activate immune cells.[1] PAMPs from gram-negative pathogens include lipopolysaccharides and endotoxins.[4] PAMPs from gram-positive pathogens include peptidoglycans. DAMPs result from damaged cells and include heat shock proteins, high mobility group box 1 protein, ATP, and DNA.[4] PAMPs or DAMPs initiate the inflammatory cascade. Monocytes and macrophages become activated, activating nuclear factor κβ, which undergoes nuclear translocation.[4] This results in transcription of various inflammatory mediators (e.g., tumor necrosis factor α; interleukins [ILs], including IL-1β, IL-6, and IL-10; CXC chemokine ligand 8; leukotrienes). Some of these are proinflammatory (e.g., cytokines, IL-1, IL-6, IL-8, interferon-γ),[1] and others are anti-inflammatory (e.g., IL-4, IL-10, IL-13, transforming growth factor

Box 1. Effects of Systemic Inflammation

- Loss of vascular tone
- Disruption of the endothelial permeability barrier
- Fibrin deposition in the microvasculature of organs

β,[1] glucocorticoids).[3] Normally, the antiinflammatory mediators keep the proinflammatory mediators localized to the affected area through the compensatory antiinflammatory response syndrome.[3] However, when a second hit occurs, the proinflammatory mediators increase at a scale and rate beyond the control of the compensatory antiinflammatory response syndrome, and homeostasis is disrupted.

This disruption results in several effects on the body (**BOX 1**),[2] the first of which is a loss of vascular tone. Some loss of vascular tone is secondary to excessive inducible nitric oxide synthase (NOS) production,[2] which is a precursor to nitric oxide release.[5] Studies in humans have shown that inhibition of NOS results in increased blood pressure (BP).[6] Additionally, patients with SIRS often experience a deficiency in vasopressin. Vasopressin stimulates peripheral vasoconstriction during shock and stress in order to shunt blood toward vital organ systems. Vasopressin deficiency in patients with sepsis or SIRS prevents vasoconstriction, often resulting in widespread vasodilatory shock.

Next, cytokines cause disruption of the endothelial permeability barrier.[2] On a localized scale, this disruption helps move macrophages to the area of insult or infection. However, in SIRS, this occurs on a systemic scale, resulting in third spacing of fluids. Edema may form peripherally and in organs and in body cavities (i.e., third spacing). Edema of organs contributes to their dysfunction as SIRS and/or sepsis progresses.

Finally, the coagulation system is stimulated by expression of cytokine-mediated tissue factor on the surface of leukocytes. This leads to fibrin deposition in the microvasculature of organs, which also contributes to development of organ dysfunction.[2]

Causes and Clinical Signs

Many diseases and their processes predispose patients to developing SIRS (**BOX 2**).[2]

The clinical signs of SIRS depend on the underlying disease or cause and, therefore, vary widely. In addition, the signs vary between cats and dogs. Common, nonspecific signs include depression, loss of appetite, bounding peripheral pulses, and vomiting and/or diarrhea. Dogs commonly develop injected (brick red) mucous membranes; cats do not.[2] It is important to remember the diagnostic criteria for cats and dogs.[2] Dogs must have two of the four signs for a diagnosis of SIRS to be considered (**TABLE 1**). Cats must have three of four signs for a diagnosis of SIRS to be considered.

Systemic Inflammation in Dogs

While no clinicopathologic findings are pathognomonic for SIRS, dogs with SIRS typically have some laboratory irregularities. Complete blood cell counts frequently reveal neutrophilic leukocytosis, with or without a left shift.[2] Toxic changes in neutrophils are commonly found, with or without leukocytosis or a left shift. Biochemical testing may reveal hyperglycemia or hypoglycemia, which is secondary to altered carbohydrate metabolism.[2] Hyperglycemia occurs early in the course of SIRS due to increased gluconeogenesis. Later in the disease process, glucose utilization exceeds its production, resulting in hypoglycemia. Hypoalbuminemia commonly occurs due to decreased albumin production by the liver. During the course of these inflammatory processes, the liver favors production of acute-phase proteins, such as C-reactive protein (CRP), instead of albumin.[2] Hypoalbuminemia is exacerbated by increased losses due to changes in endothelial permeability (leaking proteins). If the patient also has concurrent diarrhea or another disease, further albumin losses may occur (i.e., gastrointestinal [GI] ulcer resulting in blood loss). Liver enzyme changes may be found as well. Alterations in systemic perfusion affect the liver, causing decreased oxygen delivery to hepatic tissue.[2] This can result in elevated alanine transaminase and aspartate aminotransferase levels. Hyperbilirubinemia is not as common but may be found in some dogs; if it is present, the cause should be investigated because it may indicate cholestasis, the presence of endotoxins, immune-mediated hemolysis, or a combination of these.[2]

Box 2. Conditions That Predispose Patients to SIRS

- Sepsis
- Heatstroke
- Acute pancreatitis
- Immune-mediated disease
- Neoplasia
- Severe polytrauma
- Burns
- Peritonitis
- Parvoviral enteritis

Systemic Inflammation in Cats

SIRS should be suspected in weak or collapsed cats. Cats that appear sicker on presentation than on "paper" should raise concern for SIRS. Cats with SIRS are called *systemic inflammatory cats* (SICs).[7] SICs typically present in lateral recumbency with hypotension and icterus. Instead of presenting with tachycardia, which might be expected, they commonly have bradycardia. SICs that are nonhyperthyroid are usually anorexic on presentation, so early nutritional intervention is required but should not be initiated when these patients are hypotensive or "shocky."[7] SICs typically appear to be near death for several days before they begin to improve.

Anemia is common in SICs.[7] This is due to various feline-specific factors; for example, cats have smaller intravascular volumes than dogs. Sick cats also have a poor regenerative capacity to replace red blood cell losses. Additionally, feline hemoglobin is susceptible to oxidative stress, which may result in hemolysis. Therefore, the number of blood draws and the volume of blood taken should be minimized, as iatrogenic anemia can result.

Hyperbilirubinemia is common in cats with SIRS and often found in conjunction with anemia, resulting in icterus. Causes

may be prehepatic (hemolysis), hepatic (hepatic lipidosis, cholangiohepatitis), or posthepatic (pancreatitis or "triaditis"—a combination of liver, GI, and pancreatic dysfunction). It should be assumed that icteric cats are coagulopathic until proven otherwise.[7] Coagulation testing (especially the prothrombin time) should be evaluated and vitamin K_1 supplemented, when indicated. Azotemia is commonly seen in SICs; concurrent hyperkalemia may indicate acute kidney injury. Pyelonephritis should be ruled out.

Severe Sepsis

Severe sepsis occurs when SIRS is present and at least one organ system is dysfunctional.[8] Because SIRS affects every organ system, dysfunction may occur in any of them. Acute kidney injury is occurring if the patient's creatinine concentration has increased more than 0.5 mg/dL.[9] The glomerular filtration rate is also altered in these patients. The cardiovascular system is affected when vasodilation and cytokine-induced myocardial depression result in decreased cardiac output, which contributes to decreased tissue perfusion and shock (septic shock). Severe sepsis is evidenced by respiratory distress that requires supplemental oxygen or ventilation. Affected patients are at risk for developing acute respiratory distress syndrome. A total bilirubin concentration of >0.5 mg/dL and/or elevated liver enzymes are suggestive of hepatic dysfunction. The coagulation system is considered an "organ" system in veterinary critical care. Thrombocytopenia, increased prothrombin time, increased activated partial thromboplastin time, increased activated clotting time, and evidence of disseminated intravascular coagulation are indicators of coagulation dysfunction. Vomiting, regurgitation, ileus, constipation, and diarrhea are indicators of altered GI perfusion and function. Endothelial permeability changes are evidenced by vascular leaking, resulting in third spacing, both peripherally and within organs and body cavities. If more than one organ system is affected/injured, the patient meets the criteria for multiple organ dysfunction syndrome (MODS). Left untreated, MODS can progress to multiple organ failure (MOF).

Additional Diagnostics

Various biomarkers[10] are being studied to see if they can be used to detect the development of SIRS or sepsis before clinical signs present. These biomarkers might be used to identify the severity of the inflammatory response and to monitor improvement. A few of the biomarkers being investigated are CRP,[2,11] calcitonin precursor,[1] and other cytokines. The usefulness of biomarkers seems to vary between cats and dogs, so further investigation is required.

Treatment

Early intervention can improve outcomes in patients with SIRS.[1] Once initiated, SIRS cannot be immediately halted. Treatment involves addressing the underlying disease or cause and providing supportive care.[1] The goal is to prevent progression of SIRS to MODS or the more severe MOF. Aggressive fluid therapy is warranted. Antibiotic therapy should be initiated immediately if sepsis is suspected. Cultures of potential sources of infection (i.e., blood and other body fluids) should be performed early so that antibiotic administration is not delayed.[12] Source control (surgery) should not be postponed if sepsis is suspected or confirmed.[2]

When sepsis is recognized in a patient, the source of infection should be determined. Point-of-care infectious disease testing should be performed (e.g., FeLV, FIV, and heartworm testing in cats; heartworm, *Ehrlichia*, Lyme disease, and parvovirus testing in dogs). Thoracic radiographs need to be evaluated for the presence of pneumonia. Checking urine sediment for the presence of bacteriuria and pyuria may be considered. Abdominal ultrasonography (focused assessment with sonography for trauma)[12] is recommended to detect free fluid. If free fluid is found in the abdominal or thoracic cavities, a sample should be obtained for culture and cytology. Enough abdominal fluid should be obtained for paired testing of the glucose and lactate levels and for comparing these levels to the peripheral blood levels. Abdominal fluid with a glucose level that is lower (a difference of ≥20 mg/L)[13] and a lactate level that is higher (>2 mmol/L) than the patient's peripheral blood levels is suggestive of septic peritonitis.

Once all samples for culture and cytology are obtained, antibiotics should be administered immediately to all patients with suspected sepsis.[1] Delayed implementation of antibiotic therapy is associated with increased mortality.[12] The antibiotic should have a broad spectrum of antimicrobial activity, and combination therapy is typically preferred. Common combinations include a β-lactam with an aminoglycoside or a fluoroquinolone. Metronidazole may be added if an anaerobic infection is suspected. Aminoglycosides should be considered only after the patient has been fluid/volume resuscitated and only if there is no evidence of renal disease. Other examples of antibiotic combinations include (1) cephalosporin (second- or third-generation cefoxitin or cefotaxime) with enrofloxacin and metronidazole or (2) ampicillin and enrofloxacin.[14]

Fluid therapy is mandatory in all patients with SIRS or sepsis.[14] The amount of fluid administered depends highly on the individual. Aggressive fluid resuscitation should continue until acceptable perfusion goals are met.[2] If hypotension or hypovolemia is present, crystalloid boluses of 20 mL/kg (in dogs) and 10 to 15 mL/kg (in cats) should be administered and repeated as needed.[14] The addition of a colloid (5 mL/kg bolus to start) may be necessary, especially in patients with changes in endothelial permeability and/or with hypoalbuminemia.[14] Perfusion parameters (i.e., mentation, mucous membrane color, capillary refill time, pulse quality, heart rate, urine

Glossary

Dysoxia—altered cellular oxygen consumption

Sepsis—the presence of systemic inflammatory response syndrome and a confirmed or suspected infectious cause[3]

Septic shock—the presence of sepsis and nonresponsive hypotension despite fluid resuscitation[3]

Severe sepsis—the presence of sepsis along with dysfunction of one or more organs[3]

output, and extremity and core temperatures) should be monitored during resuscitation. Crystalloid/colloid boluses should be repeated until the systolic BP is >80 to 90 mm Hg (mean arterial pressure [MAP]: >70 mm Hg).[14] Once the patient is resuscitated, the dehydration deficit must be calculated as follows[15]:

Deficit replacement volume (mL) =
% Dehydration (e.g., for 5%, use 0.05) ×
Body weight (kg) × 1000 × 0.8

The deficit replacement volume should be administered over the first 24 hours in addition to the maintenance fluid rate (45 mL/kg/d, or 30 × body weight [kg] + 70) and the replacement of ongoing losses. Care must be taken when fluid resuscitating SICs—during initial resuscitation and throughout hospitalization.[7] Fluid intolerance, or overload, is common in SICs. Confirming that a feline patient is truly hypotensive before treating it is important.[7] Severely peripherally vasoconstricted cats can have falsely reduced BP readings. A cat that has a low BP measurement but is walking around and producing an adequate urine volume is likely to be falsely hypotensive.[7] Cats should be monitored for signs of respiratory distress throughout treatment because fluid intolerance/overload typically occurs after several days of fluid therapy, resulting in pleural effusion or in edema. Previously unknown/undiagnosed cardiomyopathy and/or endothelial permeability changes may also play a role in this. Central venous pressure (CVP) and ingoing and outgoing fluids, body weight (once or twice daily), and urine output should be monitored in affected cats. If the cat is truly becoming volume overloaded, stopping or decreasing intravenous fluid therapy, possibly administering diuretics to manage volume overload, and performing intermittent thoracocentesis may be necessary.

What if a patient has received maximum doses of a crystalloid (60 to 90 mL/kg in dogs; 40 to 60 mL/kg in cats) and a colloid and is still hypotensive and hypovolemic? This patient is in septic shock and is likely deficient in vasopressin and other mediators that regulate vascular tone. In dogs, this results in clinical findings of bounding pulses (thready in late sepsis) and injected mucous membranes (pale in late sepsis). These patients require vasopressor or inotrope therapy. Dopamine (5 to 15 µg/kg/min CRI) or norepinephrine (0.05 to 0.3 µg/kg/min CRI)[14] is commonly used in these patients. Patients should be started at the low end of the dose range and titrated upward until a MAP of 70 mm Hg is achieved. Dobutamine is a positive inotrope that may help treat cardiac depression and decreased contractility associated with sepsis.[14]

Monitoring and Care

Technicians can play a vital role not only during the initial identification and treatment of a patient with SIRS but also through continued care. It is important for technicians to quickly identify subtle changes in a patient's vital signs. Typical monitoring involves evaluation of "upstream" macrovascular[16] parameters, such as temperature, pulse, respiration, BP, CVP, and urine output.[1] Frequent monitoring of vital signs (temperature, pulse, respiration) is mandatory. Fever may indicate development or recurrence of SIRS or sepsis. Tachycardia may indicate compensatory or early decompensatory shock as well as pain. Cardiovascular function should be monitored through various means, including electrocardiography, echocardiography, BP monitoring (MAP: >70 mm Hg), and CVP (target: 7 to 10 cm H_2O).[16] Tachypnea, increased respiratory effort, or a decreased blood oxygen saturation (Spo_2) indicates respiratory dysfunction.

All personnel handling SIRS patients must be diligent about washing their hands between every patient. Gloves should be worn when handling SIRS patients.[1] Strict aseptic protocols must be followed when using central lines and other invasive devices, which can be colonized by pathogens.[9] Bandages and catheter insertion sites should be changed and inspected daily. Urinary catheters must be cared for attentively. Chlorhexidine solution should be used to clean the catheter and the collection set lines every 8 hours.[9] The vaginal vault or prepuce should be flushed with sterile saline every 8 hours. Recumbent patients should be turned every 2 to 4 hours to prevent decubital ulcers and to limit the development of pulmonary atelectasis.[14] Patients should be kept clean, dry, and comfortable. The ins/outs must be closely monitored, and urinary output should not fall below 1 to 2 mL/kg/h[14] but should not exceed the ins.

SIRS patients should be given GI protectants to help prevent GI "stress" ulcers. Sucralfate, along with ranitidine or famotidine, should be administered. If ileus is present, it should be treated with a prokinetic drug (unless GI hemorrhage or obstruction is suspected). Early nutritional support is necessary for all SIRS or sepsis patients because they are prone to developing a low protein level. Once the patient is adequately fluid resuscitated, a nutritional plan should be implemented. Enteral feeding should be used, when possible, to support the enterocyte level and help maintain GI integrity. If the patient cannot tolerate enteral feeding, partial parenteral nutrition or total parenteral nutrition (TPN) should be implemented. TPN must be administered through a dedicated central line using strict sterile technique. A combination of enteral and parenteral support should be considered if partial enteral feedings are tolerated but full resting energy requirements cannot be met. Although sepsis is a potential complication in any patient receiving TPN, this feeding method is not contraindicated!

Laboratory Monitoring

Multiple laboratory tests should be routinely repeated in SIRS patients. The blood glucose level should be checked every 2 to 12 hours as needed to detect hypoglycemia (which may indicate bacterial consumption of glucose or sepsis) or to monitor dextrose supplementation. Urine specific gravity should be monitored to assess hydration status and renal function. The creatinine level should be monitored for resolution or development of acute kidney injury. Electrolyte levels and acid-base balance should ideally be checked one or two times daily. Any abnormal parameters at presentation should be rechecked and monitored for resolution and improvement.

Monitoring of SIRS patients should also include testing to assess microvascular, or "downstream," parameters.[16] Microvascular monitoring involves tests that measure the blood after it has

Key Points

- Maintain a high suspicion for SIRS at all times!
- Know the diagnostic criteria for SIRS.
- Early, aggressive treatment is vital for a positive outcome in SIRS patients.

flowed to oxygen beds; therefore, this testing pertains to tissue oxygenation. Microcirculation is the network of vessels that are <100 microns in diameter (arterioles, capillaries, and venules), representing the largest endothelial surface in the body.[16] This is where oxygen exchange, waste collection, and nutrient deposition occur. Local mediators (nitric oxide, partial pressure of oxygen [Po_2], pressure gradients) control microvascular circulation and make changes based on macrocirculatory changes.[16] Microvascular circulation must be healthy to ensure tissue survival in critically ill patients.

A common method of microvascular monitoring is measurement of the blood lactate level.[16] Under anaerobic conditions, pyruvate is converted to produce energy, creating a by-product called *lactate*. Under normal conditions, some lactate is produced daily in the body and is subsequently cleared by the liver. Type A and type B hyperlactatemia result in accumulation of lactate, or hyperlactatemia (lactate level: >4 mmol/L).[16] Type A hyperlactatemia occurs when oxygen delivery (Do_2) to the tissues is inadequate to meet demand. Shock, heart failure, local thromboembolism or torsion, hypoxemia/altered oxygen-carrying states (carboxyhemoglobin, methemoglobin), or anemia may decrease Do_2. Exercise, seizures, or muscle tremors may also lead to inadequate oxygen delivery to the tissues, resulting in excessive lactate production. Type B hyperlactatemia is not associated with tissue hypoxia but is due to (1) insufficient clearance of lactate from the liver (e.g., in liver failure), (2) abnormal mitochondrial function (e.g., SIRS/sepsis, diabetes mellitus, renal failure, neoplasia, thiamine deficiency, alkalemia, short bowel syndrome), (3) drugs/toxins (ethylene glycol, acetaminophen, xylitol in dogs, terbutaline, carbon monoxide, salicylates, bicarbonate), or (4) hypoglycemia. SIRS or sepsis patients may have both type A and type B hyperlactatemia: these patients experience tissue hypoperfusion through hypovolemia, cardiovascular derangements, and microvascular thrombosis (type A) as well as microvascular shunting and mitochondrial dysfunction (type B). The lactate level should be checked before initial treatment, if possible, and then monitored throughout resuscitation. The initial lactate value does not mean as much as the rate of clearance, the response to treatment/fluid resuscitation, and the return to a normal level. It is important to note, however, that a normal lactate level does not always mean that tissue perfusion is normal. A patient's plasma lactate level may initially be normal and may then rise after fluid resuscitation, before clearing. This is because fluid resuscitation allows mobilization of accumulated lactate in the tissue and the lactate becomes detectable after initial intervention or therapy.

Central venous oxygen saturation ($S_{CV}O_2$)[16] is a measurement of the oxygenation of blood in the vena cava. This parameter can be determined by placement of a central line in the jugular vein, with the catheter tip extending into the thoracic cavity and ending cranial to the right atrium. The oxygen saturation (So_2) level (%) of a venous blood sample from the central line is tested. $S_{CV}O_2$ testing measures the amount of oxygen used by tissues, as this parameter is the remaining amount of Do_2 minus the amount of extracted oxygen consumption (Vo_2). In normal patients, the amount of oxygen delivered to tissues exceeds what could ever be used or needed. However, when Do_2 is decreased—whether through anemia, hypoxemia, or hypoperfusion—the percentage of oxygen extracted (i.e., the oxygen extraction ratio) is increased to maintain tissue oxygenation. A normal $S_{CV}O_2$ is 65% to 75%. A low $S_{CV}O_2$ means there is ongoing tissue dysoxia and, therefore, an oxygen debt. A high $S_{CV}O_2$ (≥80%) may represent impaired tissue oxygen extraction and use. Therefore, if the $S_{CV}O_2$ is low, the patient should be checked for hypotension and hypovolemia. All macrovascular parameters (BP, heart rate, CVP) should be normalized. If the $S_{CV}O_2$ is still low, anemia, hypoxemia, decreased cardiac output, or inappropriate vasodilation may be causing the issue. Supplemental oxygen should be administered if the partial pressure of oxygen, arterial, (Pao_2) is <60 mm Hg on room air. Anemia resulting in a low $S_{CV}O_2$ may require a blood transfusion. If increasing the hematocrit does not improve the $S_{CV}O_2$ to >70%, inotropic therapy with dobutamine should be considered.

Base excess—another indicator of microvascular circulation[16]—is a marker of metabolic acidosis. Lactic acidosis and other unmeasured acids can result in tissue hypoxia. Base excess is being evaluated as a possible prognostic indicator in patients with sepsis and SIRS.

Since 2001, development of early goal-directed therapy (EGDT) for SIRS and sepsis has been a focus in human medicine.[12] EGDT has dramatically decreased the mortality rate of SIRS and sepsis patients. While the guidelines for EGDT can be followed loosely in veterinary medicine, more veterinary studies must be done to definitively determine an effective EGDT for dogs and cats.

Critical Illness–Related Corticosteroid Insufficiency

Critical illness–related corticosteroid insufficiency (CIRCI), formerly called *relative adrenal insufficiency*, may occur in SIRS and sepsis patients.[17] Some critically ill patients have an inadequate adrenal gland response to stimulation of exogenous corticotropin. This results in a lack of cortisol production despite an increased demand for it. Clinical signs of CIRCI are vague and nonspecific but may include depression, weakness, fever, vomiting, diarrhea, and abdominal pain. A "red flag" for a potential CIRCI patient with SIRS is hypotension that remains refractory to fluid resuscitation and requires vasopressor or inotrope therapy. CIRCI patients may not respond adequately to vasopressor or inotrope therapy. These patients should be given a corticotropin stimulation test to confirm the presence of CIRCI. CIRCI is usually transient, and normal adrenal-pituitary axis function returns after resolution of SIRS or the underlying disease. CIRCI should be considered in patients that are critically ill and require vasopressor therapy. Once CIRCI is confirmed, treatment with corticosteroids should

be initiated. A detailed discussion of the adrenal response system is beyond the scope of this article.

Summary

Identification, treatment, and monitoring of SIRS and sepsis patients are challenging. Maintaining a high index of suspicion for SIRS in all ill patients can help technicians identify the clinical signs early. In addition, remembering the diagnostic criteria for SIRS and sepsis can help identify affected patients. Diligent nursing care is vital to producing positive outcomes for these patients. Culture samples should be obtained early so that treatment with antibiotics is not delayed. SICs should be closely monitored for fluid overload, especially several days into treatment. With diligence and care, technicians can play a part in decreasing the mortality rate of SIRS and sepsis patients.

References

1. Sharp CR. Sepsis: what it means to you and your patients. *Proc IVECCS* 2011:613-615.
2. de Laforcade AM. Systemic inflammatory response syndrome. In: Silverstein DC, Hopper K, eds. *Small Animal Emergency and Critical Care Medicine*. St. Louis, MO: Saunders Elsevier; 2009:46-49.
3. Otto CM. Sepsis. In: Wingfield W, Raffe M, eds. *The Veterinary ICU Book*. Jackson Hole, Wyoming: Teton NewMedia; 2002:695-706.
4. DeClue AE. Immunologic & clinical aspects of feline sepsis. *Proc ACVIM* 2010:430-432.
5. Nakamura RK. Myocardial dysfunction in sepsis. *Proc IVECCS* 2009:461-462.
6. Sander M, Chavoshan B, Victor R. A large blood pressure–raising effect of nitric oxide synthase inhibition in humans. *Hypertension* 1999;33:937-942.
7. Rozanski E. Systemic inflammatory cat. *Proc IVECCS* 2009:111-113.
8. Rivera AM. Severe sepsis: new recommendations from human medicine. *Proc IVECCS* 2009:647-649.
9. Sharp CR. Top 10 tips for a successful outcome in sepsis. *Proc IVECCS* 2011:489-491.
10. DeClue AE. Biomarkers for sepsis in dogs. *Proc ACVIM* 2010:420-423.
11. Boller EM, Otto CM. Sepsis. In Silverstein DC, Hopper K, eds. *Small Animal Emergency and Critical Care Medicine*. St. Louis, MO: Saunders Elsevier; 2009:454-458.
12. Sharp CR. Sepsis in the 21st century: what do we know and where are we going. *Proc IVECCS* 2011:477-480.
13. Ragetly GR, Bennett RA, Ragetly CA. Septic peritonitis: etiology, pathophysiology, and diagnosis. *Compend Contin Educ Vet* 2011;33(10):E1-E7.
14. Ragetly GR, Bennett RA, Ragetly CA. Septic peritonitis: treatment and prognosis. *Compend Contin Educ Vet* 2011;33(10):E1-E6.
15. Wingfield W. Fluid and electrolyte therapy. *The Veterinary ICU Book*. Jackson Hole, WY: Teton New Media; 2002:177.
16. Butler AL. Goal-directed therapy in small animal critical illness. *Vet Clin North Am Small Anim Pract* 2011:817-838.
17. Martin LG. Critical illness-related corticosteroid insufficiency in small animals. *Vet Clin North Am Small Anim Pract* 2011:767-782.

CE
1 CE Credit

*The article you have read qualifies for 1.0 credit hour. To receive credit from Alfred State College, choose the best answer to each of the following questions. CE tests must be taken online at **Vetlearn.com**; test results and CE certificates are available immediately.*

1. **Which of the following meets the criteria for SIRS in a dog?**
   - **a.** 103°F, 140 bpm, 32 breaths/min, 28,000 WBCs
   - **b.** 103°F, 80 bpm, 16 breaths/min, 15,000 WBCs
   - **c.** 102.9°F, 120 bpm, 20 breaths/min, 12,000 WBCs
   - **d.** 102.4°F, 112 bpm, 32 breaths/min, 6000 WBCs

2. **The five primary signs of inflammation are**
   - **a.** heat, reduced sensation, redness, pitting edema, and anorexia.
   - **b.** heat, pain, redness, swelling, and loss of function.
   - **c.** coolness, pain, fever, lethargy, and anorexia.
   - **d.** injected mucous membranes, increased CRT, depression, polyuria, and polydipsia.

3. **Noninfectious insults that can predispose a patient to developing SIRS include all of the following except**
   - **a.** burns.
   - **b.** heatstroke.
   - **c.** trauma.
   - **d.** Lyme disease.

4. **Which of the following biomarkers is not being investigated as a potential diagnostic aid for SIRS and sepsis?**
   - **a.** CRP
   - **b.** calcitonin precursor
   - **c.** interferon-γ
   - **d.** All of the above are being investigated.

5. **Which of the following is mostly likely to be a "second hit"?**
   - **a.** surgery
   - **b.** trauma
   - **c.** pancreatitis
   - **d.** burns

6. **The consequences of SIRS do not include**
   - **a.** loss of vascular tone.
   - **b.** increased hepatic consumption of lactate.
   - **c.** disruption of the endothelial permeability barrier.
   - **d.** stimulation of coagulation.

7. **Which of the following is not a common reason why anemia is often seen in SICs?**
   - **a.** Cats have a small intravascular volume.
   - **b.** Feline hemoglobin is prone to oxidative stress.
   - **c.** Cats have smaller red blood cells than dogs.
   - **d.** SICs undergo a lot of blood sampling.

8. **Which of the following parameters can be used to monitor microcirculation?**
   - **a.** BP
   - **b.** CVP
   - **c.** heart rate
   - **d.** lactate

9. **Sepsis patients may develop _____ hyperlactatemia.**
   - **a.** type A
   - **b.** type B
   - **c.** both type A and type B
   - **d.** none of the above

10. **A normal $S_{cv}O_2$ is**
    - **a.** 60%.
    - **b.** 70%.
    - **c.** 80%.
    - **d.** 90%