FLUID THERAPY IN SHOCK

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Shock is defined as inadequate tissue oxygenation due to poor perfusion. Poor tissue perfusion can be due to hypovolemic shock, cardiogenic shock, or septic shock. The prognosis, regardless of the type of shock, depends on early recognition and intervention.

The goal of treatment for all types of shock is the improvement of tissue perfusion and oxygenation. For hypovolemic and septic shock, expansion of the intravascular volume by intravenous fluid therapy is the mainstay of treatment. Cardiogenic shock poses a different problem because the decreased cardiac output and poor tissue perfusion are primarily due to the heart’s inability to pump blood forward, rather than a primary decrease in intravascular volume. Cardiogenic shock is covered elsewhere in this issue. This article focuses on fluid therapy in hypovolemic and septic shock.

HYPOVOLEMIC SHOCK

Hypovolemic shock occurs when circulating blood volume decreases, which can be secondary to hemorrhage, gastrointestinal losses of fluid or blood, extensive loss of fluids into a third body space such as the peritoneal cavity, or significant external loss of fluid, such as might occur in the burn patient or the patient with extensive soft tissue injury. The decreased blood volume leads to decreased venous return to the heart, which in turn causes decreased cardiac output and activation of a variety of homeostatic mechanisms that act in concert to improve circulating volume and maximize perfusion of vital organs.

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After an animal sustains extensive fluid or blood loss, the decreased effective blood volume leads to inadequate renal perfusion, which activates the renin-angiotensin-aldosterone system. The juxtaglomerular cells in the kidney release renin, which causes the conversion of angiotensinogen to angiotensin I. Angiotensin I is then converted to angiotensin II in the lungs by angiotensin-converting enzyme. Angiotensin II is one of the most powerful known vasoconstrictors, resulting in an increase in blood pressure. Adrenocortical release of aldosterone leads to sodium and water reabsorption in the distal nephron, resulting in partial restoration of intravascular volume. Additionally, increased antidiuretic hormone (ADH) release causes increased water reabsorption by the renal collecting tubule, further restoring intravascular volume toward normal. Catecholamine release from the adrenal medulla, triggered by stress, causes increased heart rate and contractility.

In addition to hormonal modulation, a variety of cardiovascular neurologic reflexes are also stimulated. In particular, decreased volume causes a decreased rate of firing in the baroreceptors or stretch receptors located in the aorta and at the bifurcation of the carotid arteries. Afferent fibers from these receptors travel to the medulla via the vagus nerve, where they connect with the neurons of the vasomotor center. Decreased stimulation of the baroreceptors causes vasoconstriction and increases heart rate.

These compensatory mechanisms help improve blood volume, sustain the blood pressure, and maintain perfusion to the vital organs (heart and brain). Although perfusion can be maintained for a short period of time following mild to moderate volume loss, without intervention the compensatory mechanisms eventually fail. Complications of shock ensue, which most significantly include decreased coronary and cerebral perfusion. With decreased oxygen delivery, the tissues switch to anaerobic metabolism and accumulate an oxygen debt. Arterial lactate concentrations, reflecting the end product of anaerobic metabolism, correlate with the extent of hypoperfusion. The goal of fluid therapy is to increase intravascular volume, thereby improving venous return and cardiac output. The enhanced circulating volume and cardiac output increase perfusion and thus oxygen delivery to the tissues, which helps repay the oxygen debt and allows the tissues to switch back to aerobic metabolism.

The severity of shock is determined by the rate and amount of fluid lost, the age of the patient, and the presence of pre-existing disease. Physical examination findings include pale mucous membranes, prolonged capillary refill time, weak pulses, tachycardia, cool extremities, and depressed mentation. The history and physical examination findings all help determine the cause of the hypovolemic shock.

The initial approach to any animal that presents in shock includes obtaining venous access with a large-bore catheter, using a central or peripheral vein. A data base including a packed cell volume (PCV), total solids (TS), a reagent strip estimation of blood urea nitrogen (Azostix,
Fluid Therapy in Patients with Hemorrhagic Shock

Hemorrhagic shock occurs when a patient loses 30% of its blood volume. It is important to determine and control the source of the hemorrhage as early as possible during the initial stabilization. Common locations include peritoneal hemorrhage due to traumatic lacerations of the liver or spleen or ruptured neoplasms; gastrointestinal tract hemorrhage; blood loss into the retroperitoneal cavity, pleural space, or lungs (pulmonary contusions); intracranial hemorrhage; or blood loss from any external site such as a laceration. Although the basic approach to fluid therapy of patients in hemorrhagic shock remains the same for most situations, special consideration is given to circumstances in which the fluid therapy itself may cause problems. For example, the approach to fluid therapy for an animal with pulmonary contusions is slightly different from that for an animal with a fractured liver.

The emergency data base provides information about whether blood loss is acute or chronic. Dogs with acute blood loss usually have a normal or high PCV due to splenic contraction, and a low TS, reflecting initial redistribution of fluid into the bloodstream from the interstitial space. Over the next few hours, the decreased intravascular volume causes decreased capillary hydrostatic pressure in relation to interstitial hydrostatic pressure, which, in time, leads to fluid movement from the interstitium into the vascular space. Fluid movement from the interstitium, combined with exogenous fluid therapy, causes hemodilution. Packed cell volume and TS obtained hours after the initial blood loss and fluid therapy are therefore the most accurate reflections of the extent of hemorrhage.

The main goal of therapy in hemorrhagic shock is obtaining adequate tissue oxygenation. Because the patient has lost both intravascular volume and oxygen-carrying capacity, cardiac output and hemoglobin content must both be addressed to fully restore oxygen delivery to the tissues. Intravenous fluids, crystalloids, and/or colloids should augment cardiac output, thus increasing tissue perfusion and potential oxygen delivery to the tissues. Blood products may be necessary to improve hemoglobin content and oxygen-carrying capacity.

The advantages and disadvantages of crystalloids and colloids are discussed elsewhere in this issue. The primary advantages of colloids in hypovolemic shock are twofold: (1) they rapidly increase intravascular volume; and (2) owing to their high molecular weight, almost all of the volume administered tends to remain within the vascular space. In contrast, because of the rapid redistribution of 75% of administered crystalloids into the interstitium, four times the amount of crystalloids (compared with colloids) needs to be infused to expand the intravascular space. Thus, in dogs, the shock dose of crystalloids is 60 to 90
mL/kg (45–60 mL/kg in the cat), which equals one blood volume. This can be compared with a canine shock dose of colloids of 15 to 20 mL/kg (10–15 mL/kg in the cat). If both crystalloids and colloids are used together, the crystalloid dose should be reduced by 40% (Table 1).

When treating a patient in hypovolemic shock, a decision should be made whether crystalloids, colloids, or both should be used for initial resuscitation. This decision depends primarily on the TS of the patient at presentation, recognizing that crystalloid fluids cause significant further hemodilution and result in serious decreases in colloid osmotic pressure. If the TS is less than 4 g/dL, most patients benefit from colloids as all or part of the shock bolus. If crystalloids are used, balanced electrolyte replacement solutions or 0.9% saline are the most common choices. Assuming that there is no clinical evidence of serious cardiac or pulmonary disease, a total shock dose of fluids is calculated, about half of this volume is given as a bolus (as fast as possible), and physical examination and blood pressure parameters are then re-evaluated. If signs of hypovolemic shock, such as tachycardia, weak pulses, and pale mucous membranes, are still present, then the rest of the shock bolus can be given.

In an emergency situation, especially when not much time is available for administration of a full shock bolus of crystalloids, hypertonic saline (7.5%) can be administered at a dose of 5 mL/kg. Hypertonic saline acts by rapidly increasing the osmolality of the vascular space, thus drawing water out of the interstitium into the vasculature. In addition, as the hypertonic solution travels through the pulmonary artery, a variety of reflexes are stimulated which result in increased cardiac output and renal perfusion.\(^5\, 9\) However, because of an induced natriuresis and rapid redistribution of sodium molecules, the positive effects of hypertonic saline are short-lived. Shock resuscitation with 7.5% saline must be followed by appropriate fluid therapy as required to maintain normal physiologic parameters. To create a 7.5% solution of sodium chloride, 23.4% hypertonic saline solution is commonly diluted with either dextran or hetastarch in a 1:2.5 ratio, which effectively prolongs the duration of action of this resuscitation fluid.\(^6\, 29\, 49\)

Colloids and hypertonic saline are not without their disadvantages, however. If active hemorrhage exists, these fluids can leak out into the site and cause more fluid to extravasate owing to their oncotic and osmotic pull. This becomes of utmost concern when the hemorrhage is occurring into a closed cavity, such as the intracranial cavity (see later). Serial measurements of the PCV and TS and frequent monitoring of physical examination parameters are extremely important in determining if active hemorrhage is occurring.

Adequate hemoglobin levels are required to maintain oxygen-carrying capacity and to deliver oxygen to the tissues. In addition, plasma is an excellent source of coagulation factors and proteins such as albumin, which are required for drug binding and buffering. In animals with acute blood loss, fresh whole blood or packed red blood cells and fresh frozen plasma should be transfused if the PCV and TS are lower than 25% and 4 mg/dL, respectively. Packed red blood cells are administered
### Table 1. FLUID DOSES FOR UNCOMPLICATED AND COMPLICATED SHOCK

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Initial Bolus (Uncomplicated Shock)</th>
<th>Head Trauma</th>
<th>Pulmonary Contusions</th>
<th>Intra-abdominal Hemorrhage</th>
<th>Fluid Loss</th>
<th>Septic Shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isotonic</td>
<td>60–90 mL/kg (dog)</td>
<td>60–90 mL/kg (dog)</td>
<td>20–30 mL/kg*</td>
<td>60–90 mL/kg (dog)</td>
<td>60–90 mL/kg (dog)</td>
<td>60–90 mL/kg (dog)</td>
</tr>
<tr>
<td>Crystalloids</td>
<td>45–60 mL/kg (cat)</td>
<td>45–60 mL/kg (cat)</td>
<td>45–60 mL/kg (cat)</td>
<td>45–60 mL/kg (cat)</td>
<td>45–60 mL/kg (cat)</td>
<td>45–60 mL/kg (cat)</td>
</tr>
<tr>
<td>Colloids</td>
<td>15–20 mL/kg (dog)</td>
<td>15–20 mL/kg (dog)</td>
<td>4–6 mL/kg*</td>
<td>15–20 mL/kg (dog)</td>
<td>15–20 mL/kg then add or switch to crystalloids</td>
<td>20 mL/kg (dog)</td>
</tr>
<tr>
<td></td>
<td>10–15 mL/kg (cat)</td>
<td>10–15 mL/kg (cat)</td>
<td>10–15 mL/kg (cat)</td>
<td></td>
<td>10–15 mL/kg (cat)</td>
<td></td>
</tr>
<tr>
<td>Hypertonic saline</td>
<td>5 mL/kg</td>
<td>5 mL/kg</td>
<td>2–3 mL/kg*</td>
<td>5 mL/kg</td>
<td>Should not be used</td>
<td>5 mL/kg</td>
</tr>
</tbody>
</table>

Doses are for crystalloids, colloids, or hypertonic saline use. If crystalloids are added to colloid therapy then the crystalloid dose should be decreased by 40–60%.

*At a time (see text).
at doses of 15 to 20 mL/kg, fresh frozen plasma at doses of 10 to 15 mL/kg, and whole blood at doses of 20 to 25 mL/kg. Absolute requirements vary with individual animals and the presence or absence of ongoing blood loss. Ideally, blood transfusions should be administered over a period of 2 to 3 hours to minimize transfusion reactions and volume overload, but in the emergency situation it is sometimes necessary to give blood products as a bolus.

Ideally, a shock bolus of crystalloids and colloids is an excellent starting point to increase intravascular volume, venous return, cardiac output, and tissue perfusion. As these fluids are being infused, fresh whole blood or blood constituents can be obtained to be used for transfusion if deemed necessary.

Following a period of shock, fluid therapy support should not be suddenly withdrawn. It is important to continue to provide some intravascular volume expansion, to ensure adequate ongoing renal perfusion, and to continue to replace any ongoing losses. Once the shock bolus has been completed, most patients therefore require ongoing replacement intravenous fluids at rates of two to three times maintenance (approximately 4 to 12 mL/kg/hr). The fluid rate required and the total duration of intravenous fluid therapy vary greatly among individual patients.

**Management of Patients with Blood Loss into the Abdominal Cavity**

Animals that present with shock due to hemoperitoneum usually have the classic physical examination findings mentioned earlier, with or without abdominal distention. Occasionally, animals with intra-abdominal hemorrhage may also present with bradycardia due to a vagally mediated mechanism. Along with a peripheral venous PCV and TS, an abdominocentesis should be performed, with PCV/TS and cytology studies done on any fluid obtained.

In cases of ongoing active peritoneal hemorrhage, an abdominal pressure bandage can be placed from the xiphoid to the pelvic inlet (Fig. 1). Active hemorrhage may be suspected if there is progressive distention of the abdomen, if the patient appears to be refractory to fluid therapy, or if the PCV and TS continue to decrease. In patients with decreasing PCV, the clinician must take into consideration the expected hemodilution that occurs following fluid therapy. Dogs that have improvement in mucous membrane color, blood pressure, and heart rate are unlikely to be suffering from an ongoing severe hemorrhage, even if the PCV drops slightly following fluid therapy. The major complication of abdominal pressure wrapping is compression of the thorax, leading to increased respiratory effort or even respiratory distress in patients with concurrent pulmonary injury. If respiratory difficulty is recognized after placement of an abdominal wrap, it may be necessary to cut through the cranial part of the wrap to relieve pressure on the chest.

Fluid therapy for animals with peritoneal hemorrhage (without
Figure 1. This dog was hit by a car, and abdominocentesis revealed frank blood. An abdominal pressure bandage from the xiphoid to the pelvic inlet was placed. He received one unit of packed red blood cells and two units of fresh frozen plasma along with isotonic crystalloids. The bandage was gradually removed after 24 hours, and he was discharged 60 hours after presentation to the hospital.

serious intracranial or thoracic injury) should be as described earlier for patients in hemorrhagic shock. Some reports suggest that rapidly increasing the blood pressure can disrupt clot formation and allow active hemorrhage to resume, possibly indicating a more cautious, slower resuscitation in these patients. Because the ongoing hypoperfusion seen with slow fluid resuscitation may lead to acute renal failure and shock gut, the clinician must balance these concerns in individual patients and attempt to find an appropriate rate of resuscitation that maintains perfusion of the vital organs without precipitating further hemorrhage (see subsequent section on monitoring).

Monitoring the patient that has sustained major blood loss is of utmost importance. The PCV and TS should remain stable following transfusion and fluid resuscitation. If intra-abdominal hemorrhage is present and the patient continues to decline despite adequate blood product transfusion and an abdominal pressure bandage, exploratory laparotomy must be considered in an attempt to eliminate the source of the hemorrhage.

Management of Patients with Blood Loss into the Lungs

Most animals that have pulmonary contusions or pulmonary hemorrhage significant enough to cause hypovolemic shock show clinical
evidence of respiratory distress (Fig. 2). These patients are in obvious discomfort, with increased respiratory rate and effort; postural adaptations such as unwillingness to lie down, elbow abduction, and neck extension; pale, white, or cyanotic mucous membranes; and harsh lung sounds or crackles on thoracic auscultation. Because pneumothorax is a common cause of respiratory distress in the trauma patient, diagnostic

Figure 2. Lateral (A) and DV (B) radiographs of a dog with serious pulmonary contusions after sustaining blunt trauma (hit by car). There is also a flail segment on the right. Fluid therapy in this animal should be cautiously started while continuously assessing pulmonary function (see text).
Thoracocentesis should be considered in addition to management for pulmonary contusions.

Oxygen therapy should be started immediately via face mask, nasal cannula, or oxygen cage. If hypoxia is present, oxygen supplementation alone can sometimes produce an improvement in cardiovascular status of these patients. Pulse oximetry determines the percent hemoglobin saturation with oxygen and can be helpful in determining the extent of the respiratory compromise. In shock patients, however, poor perfusion and hypothermia can impair ability to obtain an accurate reading from the pulse oximeter. Arterial blood gas collected from the femoral or dorsal metatarsal artery is ideal in determining the extent of the lung injury. Arterial lactate can also be measured to estimate the extent of hypoperfusion (see monitoring).

The most important consideration in fluid resuscitation of an animal with pulmonary contusions is the potential for increased hemorrhage and thus worsening of the respiratory compromise. Improvement in blood pressure with administration of crystalloids and colloids results in increased capillary hydrostatic pressure and potentially exacerbates fluid movement into the interstitium of the lung. Colloids and/or hypertonic saline can potentially move into the area of hemorrhage and, owing to the increased oncotic or osmotic pressure, pull water along with them. In fact, in any patient that has suffered pulmonary hemorrhage, some degree of concurrent pulmonary edema is expected following fluid resuscitation.

In patients with pulmonary contusions, colloids could be considered advantageous because a lesser volume is required for shock resuscitation than with crystalloids. Crystalloids may have a greater tendency to distribute into the interstitial space, which can worsen pulmonary edema and hemorrhage if the pulmonary lymphatic system is unable to keep up with the volumes produced. In patients with increased microvascular permeability, colloids may also be a better fluid choice because of their large molecular mass. In severe pulmonary capillary leak syndromes, however, colloids may also leak into the interstitium, potentially causing more harm than good. The clinician must use good clinical judgment in deciding whether crystalloids or colloids are appropriate for individual patients with pulmonary contusions. If one is in doubt and the patient has significantly low TS, a small test dose of colloid can be administered and the patient carefully observed for response to therapy. If deterioration in the respiratory status of the patient occurs following the test dose, further administration of colloids should be avoided.

When pulmonary contusions are present, one fourth to one third of the shock bolus of crystalloids or colloids should be administered while continually assessing pulmonary function. When patients in respiratory distress are also exhibiting signs of shock, the determination of the total volume of fluids required for resuscitation can be very challenging. Once again, the clinician is attempting to walk a fine line between improvement of tissue perfusion and worsening of the pulmonary status. Serial
measurements of urine output, urinalysis, arterial blood pressure, arterial lactate concentrations, and arterial blood gases help determine which way the balance is leaning.

Despite judicious use of fluid therapy, in the most severely affected patients pulmonary hemorrhage can continue, interstitial edema fluid can accumulate, and pulmonary function can deteriorate. Following fluid therapy in some of these patients, once adequate intravascular volume expansion has been achieved, small doses of diuretics (furosemide 0.5-1 mg/kg, or 0.1-0.3 mg/kg/hr CRI) can be considered in an attempt to resolve the pulmonary edema component of the respiratory compromise. Diuretics should not be expected to remove erythrocytes from the lung parenchyma and, because the primary mechanism of action of diuretics is to decrease the intravascular volume by inducing diuresis, no rationale exists for diuretic use immediately after presentation. If the $P_aO_2$ remains less than 60 mm Hg, or the $P_aCO_2$ remains greater than 50 mm Hg despite oxygen supplementation with an $F_iO_2$ of 60% or greater, mechanical ventilation should be considered as a means of supporting the patient until the pulmonary contusions resolve.

**Management of Patients with Intracranial Hemorrhage**

The physical examination findings of an animal that has sustained head trauma and intracranial blood loss depend on the extent and site of the hemorrhage. Signs that should alert the clinician include blood in the ears, epistaxis, scleral hemorrhage, hyphema, and skull and/or mandibular fractures. In addition, neurologic signs include anisocoria, depressed mentation, seizures, and/or coma. Patients with head trauma should be thoroughly evaluated to determine the severity of shock and the extent of concurrent soft tissue and orthopedic injuries in the rest of the body.

The most important priority in patients with head trauma is the maintenance of systemic arterial blood pressure to prevent cerebral hypoperfusion. Cerebral perfusion pressure is directly related to arterial blood pressure, and, in the presence of hypovolemic shock and hypoperfusion, ischemic neuronal cell death can occur. These cells then release cytokines and oxygen free radicals, which lead to increased capillary permeability with resultant edema, vasodilation, and increased intracranial pressure. The second priority in patients with head trauma is maintenance of oxygenation and the absolute avoidance of periods of hypoxia. Arterial oxygen content should be carefully monitored using pulse oximetry or arterial blood gas analysis, and if any doubt exists supplemental oxygen at 40% should be administered.

Hypertonic saline (7.5%) is thought to be the fluid of choice in head trauma; indeed, some reports have shown that it may have a cerebral protective effect. By virtue of its osmotic effect, hypertonic saline pulls fluid from the interstitium into the vascular space, thus decreasing edema. Its ability to increase cardiac contractility and decrease systemic vascular resistance via peripheral vasodilation may result in improve-
ment of cerebral perfusion pressure. A shock bolus of hypertonic saline consists of 5 mL/kg, compared with 90 mL/kg of isotonic crystalloids. Thus, owing to the small volume required for resuscitation, the possible cerebral protective effect, and the vascular effects, hypertonic saline is the fluid of choice for head trauma.16, 20 Possible complications include transient hypernatremia, hyperchloremia, and hyperosmolality.

Colloids can also be used for resuscitation of the head trauma patient in shock.20, 51 They are potentially useful in this patient population because of the smaller volumes required for resuscitation and the decreased chance of extravasation into the interstitium. If ongoing intracranial hemorrhage is present, either hypertonic saline or colloids could theoretically move into the area of hemorrhage and pull water with them, worsening the size of the lesion. Owing to the closed and unexpanding nature of the cranium, even a small amount of hemorrhage can lead to a deleterious increase in intracranial pressure, with resultant decrease in cerebral perfusion.

Frequent neurologic examinations are extremely important. If neurologic function worsens or signs of increased intracranial pressure are seen, further treatment should be instituted.5, 16 Treatment modalities to decrease intracranial pressure include the administration of mannitol (0.5–1 g/kg over 20 minutes), head and neck elevation on a board, avoidance of coughing and jugular compression, and maintenance of ventilation at a PaCO₂ between 30 and 35 mm Hg.

Fluid Therapy in Animals with Hypovolemia Secondary to Fluid Losses

Hypovolemia can occur secondary to fluid loss, without concurrent loss of erythrocytes as occurs in hemorrhage. For example, severe vomiting and/or diarrhea can lead to significant fluid loss from the gastrointestinal tract, and obligatory diuresis such as that seen in patients with diabetes insipidus can lead to significant fluid loss via the kidneys. Following the initial loss of fluid from the vasculature, water shifts from the interstitium to the vascular space, maintaining intravascular volume. Interstitial fluid depletion results in the clinical appearance of dehydration, including pink but tacky mucous membranes, sunken eyes, and decreased skin turgor. It is important to recognize that the fluid shift into the vascular space is a protective mechanism that acts to maintain intravascular volume, so in the early stages of dehydration intravascular volume is maintained and shock may not be present. Crystalloids are the fluid of choice for volume replacement in dehydration because of their extensive redistribution into the interstitium.18

If the vomiting, diarrhea, or other source of fluid loss continues without fluid replacement, hypovolemia eventually ensues. The clinical appearance of the animal then includes the classic signs of shock: tachycardia, weak pulses, and pale mucous membranes with prolonged capillary refill time.
Fluid therapy in this patient relies on rapid replacement of the vascular volume and also on correction of the interstitial deficit. If the patient is in shock, crystalloids at 60 to 90 mL/hr or colloids at 15 to 20 mL/hr should be immediately started. In the presence of moderate to severe dehydration, hypertonic saline should not be used in the initial stabilization because it acts to pull fluid from the interstitium, and in this patient the interstitium is already depleted. Administration of hypertonic saline in this patient could result in clinically significant hypernatremia. As with patients with hemorrhagic shock, about half of the calculated shock bolus is administered and the patient re-evaluated to assess its response to therapy. If the mucous membranes, pulses, and heart rate have not improved, the remainder of the bolus should be administered. In most cases, this shock fluid regimen significantly improves the hydration status of the patient and produces volume expansion and improved tissue perfusion as well. Once the clinical parameters have improved, any remaining dehydration should be corrected over 12 to 24 hours. An isotonic balanced electrolyte solution should be infused to replace losses, and electrolytes such as potassium concentrations should be monitored and supplemented as needed. Following correction of shock, the fluid requirement for complete replacement of deficits is calculated as follows:

\[
\text{Total deficit} = [\text{maintenance requirements (2-4 mL/kg/hr)}] + \\
[\text{estimated ongoing losses}] + [\text{percent dehydration (BW}_{kg})]
\]

Once the total deficit has been calculated for a 24-hour period, a fluid rate can be determined that replaces the deficit over the desired period of time.

**SEPTIC SHOCK**

Sepsis syndrome is defined as a generalized inflammatory process (infectious or noninfectious in origin), with evidence of decreased organ perfusion. Both noninfectious and infectious processes can result in the same magnitude of signs. In veterinary medicine we commonly recognize bacterial sepsis or endotoxemia in patients with extensive bacterial infections, such as those with peritonitis or severe bite wounds. A similar pathophysiologic condition can, however, occur in some situations without the presence of an infectious agent. Acute necrotizing pancreatitis and severe ischemic tissue necrosis are examples of clinical syndromes that produce similar generalized inflammatory pathophysiology without necessarily being bacterial in origin. This has led many people to change the term sepsis syndrome to the systemic inflammatory response syndrome (SIRS) and reserve the term sepsis for patients with an identifiable source of infection.\(^2, 13, 30\)

Gram-positive, gram-negative, and anaerobic bacteria, viruses, and fungi can all cause infections that can lead to sepsis syndrome. Gram-negative septicemia/endotoxemia has been well documented, with the
lipopolysaccharide component of the cell wall identified as the inciting factor. Endotoxin, other bacterial/fungal components, or any sterile inflammatory focus activates macrophages and neutrophils, provoking the release of a multitude of inflammatory mediators (Table 2). A cascade of these mediators, activating each other in an avalanche effect, then causes the systemic signs and peripheral vasodilation, endothelial damage and leaky vessels, platelet activation, neutrophil activation, and hypotension. The vasculitis leads to extravasation of fluid and protein into the interstitial space. This is most important in the lungs, where noncardiogenic pulmonary edema and hypoxemia can result. The peripheral vasodilation, increased vascular permeability, and fluid losses or shifts ultimately result in a decreased effective intravascular volume. Ensuing hypotension can then lead to decreased perfusion of the gastrointestinal tract, kidneys, liver, and, in end stage, heart and brain. Platelet activation can lead to microcirculatory clots, sludging of blood in the periphery, and overt disseminated intravascular coagulation or thromboembolic events. Neutrophils become sequestered, resulting in leukopenia. If vasodilation and effective hypovolemia become severe enough, hypotension ensues, and the syndrome is known as septic shock.

Table 2. SOME MAJOR CYTOKINES, THEIR SOURCES, AND ACTIONS IN SEPTIC SHOCK

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Source</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interleukin-1</td>
<td>Activated macrophage/monocytes</td>
<td>Induction of fever; stimulation of T-cell and B-cell differentiation and proliferation; activation of macrophages; increased vascular permeability</td>
</tr>
<tr>
<td>Tumor necrosis factor</td>
<td>Activated macrophage</td>
<td>Activation of phagocytic cells; stimulation of secretion of other cytokines; stimulation of eicosanoid synthesis; cytotoxicity to tumor cells; increased vascular permeability, procoagulant</td>
</tr>
<tr>
<td>Interleukin-6</td>
<td>Macrophage, fibroblasts, vascular endothelial cells, T-cells, mast cells</td>
<td>Induction of acute phase proteins, activation of B-cells and antibody production</td>
</tr>
<tr>
<td>Interleukin-10</td>
<td>Activated T-cells</td>
<td>Suppression of cytokine production by T-cells and macrophages; suppression of production of reactive nitrogen oxides by macrophages</td>
</tr>
<tr>
<td>Platelet activating factor</td>
<td>Leukocytes, endothelial cells, platelets</td>
<td>Stimulation of platelet activation and aggregation, macrophage activation, leukocyte chemotaxis, vasodilatation, coronary and pulmonary vasoconstriction, increased capillary permeability</td>
</tr>
<tr>
<td>IL-8</td>
<td>Activated macrophage</td>
<td>Chemotactically attracts neutrophils, induces the adherence of neutrophils to vascular endothelial cells, aids in migration into the tissue spaces</td>
</tr>
</tbody>
</table>
The sequela of inadequate tissue oxygen delivery is the development of lactic acidosis due to anaerobic metabolism and then multiple organ failure. Respiratory failure is manifested by hypoxemia, decreased PaO$_2$/FiO$_2$, bilateral alveolar infiltrates, and permeability pulmonary edema (acute respiratory distress syndrome). Signs of renal failure include azotemia and anuria or oliguria, and altered mental status may indicate cerebral involvement. Cardiac arrhythmias may occur as a result of myocardial ischemia and electrolyte and acid-base disturbances. Signs of gastrointestinal failure include anorexia, vomiting with or without blood, and bloody diarrhea (shock gut). Intestinal mucosal ischemia can also contribute to bacterial translocation, which can further intensify the septic process. Hepatobiliary failure is manifested by functional cholestasis and icterus, hypoalbuminemia, and elevated serum ammonia levels. Disseminated intravascular coagulation is characterized by thrombocytopenia with petechiae, ecchymoses, prolonged prothrombin time (PT), partial thromboplastin time (PTT), and signs of hemorrhage and/or thromboembolic disease.

The most important goal for the clinician is not only to recognize signs associated with septic shock and SIRS and respond quickly but also to determine which patients are at risk and take steps to monitor these patients carefully and prevent progression to shock.

Septic shock has three stages, and physical examination findings depend on the stage. The first stage is the early compensated or hyperdynamic stage. Compensatory mechanisms such as the renin-angiotensin-aldosterone system, baroreceptor reflexes, and catecholamine release from the adrenals all act to maintain intravascular volume, arterial blood pressure, and perfusion of vital organs (heart and brain). Catecholamines also lead to glycogenolysis, lipolysis, and insulin resistance, which cause elevated serum glucose concentrations. Signs of early hyperdynamic septic shock include brick red mucous membranes with fast capillary refill time, possible bounding pulses, tachycardia, and normal to high body temperature. These animals have high cardiac output due to tachycardia and low systemic vascular resistance and low pulmonary capillary wedge pressure due to arterial and venous dilation.

As the compensatory mechanisms fail and hypovolemia progresses, reserves are exhausted, cardiac output decreases, and the animal enters hypodynamic septic shock. Signs of this stage include pale mucous membranes with prolonged capillary refill time, weak pulses, hypothermia (as the body shifts perfusion to the core) with cold extremities, hypoglycemia due to substrate depletion, increased glucose utilization and decreased hepatic gluconeogenic capacity, tachycardia, and hypotension. These animals have low cardiac output, high systemic vascular resistance, and high pulmonary capillary wedge pressures. Some animals can be converted to the hyperdynamic phase from the hypodynamic phase with very aggressive fluid therapy.

If no treatment is instituted, the animal enters the third stage: refractory shock. In refractory shock the hypotension becomes refractory
to treatment, and vascular damage, vasodilation, and myocardial depression are unresponsive to fluid and inotropic or pressor support.

The clinician should search for a septic focus in any animal that presents with fever or hypothermia, leukocytosis or leukopenia, tachycardia, and tachypnea. Bacterial infections are most commonly associated with the respiratory, gastrointestinal, urogenital, and hepatobiliary systems. Noninfectious causes include heat stroke, pancreatitis, multiple trauma, and neoplasia. Diagnostic tests include complete blood count, chemistry panel, urinalysis, coagulation panel, chest radiography, abdominal radiography, abdominal ultrasonography, and urine, blood, and fecal cultures.

**Fluid Therapy in Patients with Septic Shock**

Once again, the most important facet of treatment is volume expansion by administration of intravenous fluids. The main goal is to increase the effective circulating blood volume, increase venous return to the heart, and thereby improve cardiac output and oxygen delivery to the tissues. Adequate volume replacement can be extremely difficult in septic shock. Owing to the profound capillary and venous vasodilation, blood pools in the large-capacitance vessels and is unavailable as effective circulating volume. Increased microvascular permeability causes protein and water movement into the interstitium, which further decreases the effective circulating blood volume. Additionally, ongoing fluid losses and fluid shifts into third body spaces due to the primary disease process contribute to decreased circulating blood volume. All of these act in concert to make it difficult to increase the circulating vascular volume, and enormous amounts of fluids may be required.4, 22, 28, 44

If inadequate tissue oxygen delivery occurs, cellular respiration switches from aerobic to anaerobic metabolism, and an oxygen debt accumulates. In the face of diminished oxygen supply, the tissues also have an increased oxygen requirement due to an increased metabolic rate. During resuscitation, patients are thought to have a better prognosis if oxygen consumption and delivery are pushed to supranormal levels, thereby repaying the oxygen debt, reversing the ischemia, and meeting the increased demands at a cellular level. Although supranormal levels are controversial, no less than normal levels of oxygen consumption and delivery should be targeted.19, 37, 42, 43

Colloids can be the ideal solution in this situation.17, 22, 24, 26, 32, 38, 40 Crystalloids, with their rapid redistribution, can aggravate an already expanding interstitium. In the presence of vasculitis, depending on the size of the permeability defect, colloid molecules may remain in the vascular space. Colloids therefore provide an option for rapid and sustained expansion of intravascular volume. If the vascular leak syndrome is severe, however, colloid molecules may also leave the vasculature and enter the interstitium, which can result in therapeutic failure. A test bolus of colloid can be given and clinical response assessed. If the patient
shows clinical improvement, colloid therapy should be continued. If there is no apparent clinical response, the clinician should give careful consideration to the possibility that the large molecules could be leaking out into the interstitium. In this situation, crystalloids may be a safer option because they are less likely to institute an osmotic pull, exacerbating interstitial edema. Direct measurement of colloid osmotic pressure using a colloid osmometer (Wescor 4400 Colloid Osmometer, Wescor Inc, Logan, UT) is the only objective way to assess the retention of colloid molecules in the vasculature, providing valuable additional information to monitor colloid fluid therapy.\textsuperscript{12, 23}

A shock bolus of colloids (20 mL/kg) should be given if signs of shock are present. Colloids at a rate of up to 40 mL/kg/day may be needed to maintain intravascular volume and colloid osmotic pressure in the septic patient. Research studies in experimental dogs have demonstrated that hetastarch doses greater than 20 mL/kg can cause a coagulopathy that is primarily dilutional but also due to inactivation of von Willebrand's factor and direct effects on platelets.\textsuperscript{45} Doses of less than 20 mL/kg appear to be safe, and if higher rates are required, we recommend the concurrent administration of fresh frozen plasma (10-15 mL/kg) as a source of clotting factors. If high volumes of hetastarch are combined with plasma, clinically relevant coagulopathies directly attributable to the synthetic colloid appear to be unusual. Fresh frozen plasma also provides an important source of albumin and other factors such as antithrombin III, a modulator of the coagulation cascade. Because the coagulopathy induced by dextrans is more severe than that induced by hetastarch, dextran 70 rates should not exceed 20 mL/kg/day. Crystalloids may be added to either synthetic colloid regimen, decreasing the total dose by 40% to 60%. The clinician must carefully monitor physiologic parameters as described below to determine the ongoing fluid requirements of each individual patient.

If hypotension is present, intravenous fluids should be administered until the central venous pressure (CVP) increases, indicating adequate volume replacement. If the arterial blood pressure is still unacceptable, continuous infusions of catecholamines should be instituted for pressor and/or inotropic support. Dobutamine, a β agonist and a positive inotrope, can be started at 5 μg/kg/min and gradually increased to effect up to 20 μg/kg/min. The limiting factor for dobutamine use is the development of excessive tachycardia or ventricular arrhythmias. An alternative choice is a continuous infusion of dopamine, which can be titrated from 5 to 10 μg/kg/min (primarily effective as a β agonist) to 10 to 15 μg/kg/min or more when it acts as an α agonist. In the most severely refractory cases, continuous infusions of epinephrine may be required to increase blood pressure. If the blood pressure does not increase and perfusion does not improve despite adequate fluid administration and inotropic and pressor therapy, the animal is likely to be in refractory shock, which has a grave prognosis.

If a septic focus is suspected, broad-spectrum antibiotic coverage must be started as soon as possible, using intravenous drugs effective
against gram-positive, gram-negative, and anaerobic bacteria. Ideally, appropriate cultures should first be obtained (i.e., blood, urine, and transtracheal wash cultures). In patients with thrombocytopenia or overt signs of disseminated intravascular coagulation, heparin therapy may also be considered. Heparin is used in an attempt to prevent ongoing consumption of coagulation factors, thereby slowing or preventing the onset of coagulopathies. In septic patients, we routinely evaluate coagulation parameters. If prolongation of PT and PTT are present, we administer heparin at doses of 50 to 100 units/kg subcutaneously every 6 hours. If there is no prolongation of the coagulation times, higher doses of heparin can be considered, up to 150 to 200 units/kg subcutaneously every 6 hours. Heparin should not be administered to patients that may be surgical candidates but can be instituted postoperatively.

**MONITORING FLUID THERAPY IN THE SHOCK PATIENT**

Because the goal of fluid therapy in both forms of shock is to re-establish perfusion of the vital organs, the most important facet of monitoring is the assessment of perfusion and effective vascular volume status. In addition, patients must be monitored carefully for early signs of end-organ failure as a result of poor perfusion.

Clinical assessment of physical examination parameters, and in particular dynamic changes in these parameters over time, plays a vital role in monitoring the shock patient. Cardiovascular status should be studied every few hours, with particular emphasis on mucous membrane color, heart rate, the presence of cardiac arrhythmias, and pulse quality. If these parameters are acceptable, tissue perfusion is probably adequate. In addition to physical examination, several tools are available to improve the sensitivity of patient assessment.

Systemic arterial blood pressure should be frequently measured, and the mean pressure maintained above 60 mm Hg (or systolic pressure greater than 90 mm Hg) to ensure adequate renal and splanchnic perfusion. Direct arterial blood pressure monitoring, using an arterial catheter in the dorsal metatarsal or femoral artery, is the gold standard for blood pressure monitoring. Indirect pressure monitoring devices such as Doppler or oscillometric monitors can also be used but are slightly less accurate, especially in the poorly perfused patient. Even if the systemic arterial pressure appears to be adequate, this may not be synonymous with adequate tissue perfusion, as significant vasoconstriction may be occurring to maintain arterial pressures. In this instance, tissue blood flow and perfusion may still be poor, and further fluid volume may still be required. Clinical parameters such as mucous membrane color and the temperature of the extremities are used to assess the effectiveness of tissue perfusion in this situation.

Central venous pressure (CVP) provides an indication of the adequacy of volume replacement. Central venous pressure reflects right
atrial and right ventricular end-diastolic pressure and therefore is an index of the degree of filling of the great vessels. If the CVP of a shock patient remains low, inadequate volume expansion is likely, and further fluid therapy should be considered if the patient is hypotensive or has poor perfusion. Central venous pressure is measured by connection of a water manometer or direct pressure transducer to a long jugular venous catheter (Fig. 3). Normal values are approximately 0 to 8 cm H₂O, although trends are more important than solitary readings.

Pulmonary capillary wedge pressure (PCWP) is the ideal way to determine whether blood volume has been adequately replaced. The PCWP reflects the left atrial and left ventricular end-diastolic pressure and therefore provides more information about the systemic circulation, compared with CVP, which primarily provides information about filling pressures on the right side of the heart. Measurement of PCWP requires

![Figure 3. Central venous pressure set up. A jugular catheter and water monometer are needed. Central venous pressures are very useful in judging adequate fluid resuscitation or replacement in animals presenting with all forms of shock.](image-url)
the placement of a Swan-Ganz balloon-tipped pulmonary artery catheter and a physiologic monitor, which are not readily available except at large teaching hospitals or referral centers. A pulmonary artery catheter connected to a cardiac output computer also provides the ability to measure oxygen delivery, oxygen consumption, and cardiac output, allowing further fine-tuning of fluid, inotropic, and pressor therapy. Normal PCWP is 6 to 12 mm Hg, and elevations above this indicate vascular overload and the imminent risk of pulmonary edema.

Blood lactate measurement is also helpful in assessing tissue oxygenation. When oxygen delivery is inadequate, cells switch from aerobic to anaerobic metabolism and produce lactate. Normal plasma lactate concentration is 0.5 to 2.5 mmol/L in dogs. Blood lactate concentration has been correlated with survival rates in hemorrhagic and other forms of shock. Successful intravascular volume replacement is usually associated with a decreasing lactate concentration, which may be used to guide volume resuscitation. Persistent or worsening hyperlactatemia (in the face of apparently adequate fluid resuscitation) often indicates a poor prognosis.

Because urine output is an index of renal perfusion and renal function, urine output of the shock patient should also be serially monitored. Minimal urine output is considered to be approximately 1 to 2 mL/kg/hr, but this volume is extremely variable, depending on the volume of fluids being administered and the extent of ongoing fluid losses. Careful monitoring of fluid “ins and outs” may be necessary to fully establish renal function in the shock patient. Placement of a urinary catheter and closed collection system is mandatory if decreased urine output is suspected. Because inadequate renal perfusion can lead to acute tubular necrosis and oliguric or anuric renal failure, serial urinalyses should be performed to detect the presence of renal tubular casts. The presence of casts indicates that the kidneys have sustained damage, and efforts should be made to maximize renal perfusion to prevent further tubular necrosis.

Colloid oncotic pressure (COP) measurements are also very useful if synthetic colloids are being used. Because the refractometer does not measure synthetic colloids, it can be difficult to assess the response to synthetic colloid therapy without direct measurement of COP. Serial measurements of the COP help determine whether the colloids are staying in the vascular space; they also determine the efficacy of therapy. Mean values for COP in whole blood of normal dogs are 19.95 ± 2 mm Hg, and mean values of COP in whole blood of normal cats are 24.7 ± 3.7 mm Hg. The goal of colloid therapy should be to maintain the COP above 15 mm Hg.

Electrolyte and acid-base abnormalities should also be addressed once shock doses of fluids are started. In particular, attention should be paid to changes in serum potassium, phosphorus, and magnesium, and these electrolytes should be supplemented if required. Volume expansion and restoration of tissue perfusion are usually adequate to correct acid-base balance and metabolic acidosis, and the majority of shock patients
do not require supplementation with sodium bicarbonate. Both electrolyte abnormalities and acid-base management are addressed in detail in other articles in this issue.

SUMMARY

The goal of treatment for all types of shock is the improvement of tissue perfusion and oxygenation. The mainstay of therapy for hypovolemic and septic shock is the expansion of the intravascular volume by fluid administration, including crystalloids, colloids, and blood products. Frequent physical examinations and monitoring enable the clinician to determine the adequacy of tissue oxygenation and thus the success of the fluid therapy.

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