Cardiovascular System Support: Protocols for Shock

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Most aspects of the treatment of noncardiogenic shock syndromes can be summarized by the following 10 goals, with a treatment order that depends on individual circumstances:

Treat the underlying disease

Treatment of shock syndrome cannot succeed if the underlying trigger remains uncontrolled. Animals with physical signs of hypovolemia due to hemorrhage should be immediately examined to determine the source of blood loss. Fluid therapy may be useless unless ongoing severe hemorrhage is controlled as rapidly as possible by external tamponade or exploratory surgery when the source is internal. Treatment or removal of any underlying source of inflammation should begin as soon as possible during the course of resuscitation. Likewise, early surgical drainage and administration of appropriate antibiotics is critical when treating septic shock. Trauma victims may require immediate intervention to physically stabilize injury to the thorax, abdominal organs, or spine.

Insure that the arterial pO_2 is > 70 mm Hg or the SaO_2 is > 90%

Oxygen should be administered to any patient with shock syndrome, particularly those with suspected or confirmed arterial hypoxemia. Pulse oximetry provides a quick method (when it works!) to estimate arterial oxygen saturation. If prolonged oxygen administration is likely to be needed, insertion of a nasal cannula is often an ideal delivery method as it is well tolerated and will allow continued administration during patient manipulation. If the lungs or thoracic bellows mechanism are sufficiently damaged to prevent control of hypoxemia even with oxygen administration, intubation and mechanical ventilation is indicated to improve oxygenation.

Insure an adequate arterial oxygen content (at least 10-15 ml/dl of blood)

In addition to optimizing the gas pressure of oxygen in the arterial blood, the functional hemoglobin concentration must be high enough to allow the blood oxygen content to be at least 10 ml/dl of whole blood. Symptomatic anemic animals and animals with ongoing hemorrhage should be treated with either fresh whole blood or packed red blood cells to maintain a hematocrit of around 30-40% (dog; slightly lower for cats may be OK). Because there is some evidence that aged (> 1 week old) stored red blood cells lose their ability to deliver oxygen for many hours after infusion, it may be better to use relatively fresh stored blood products.

Reduce oxygen demand

The unrelieved pain and anxiety invoke behavioral and physiological responses that may increase oxygen demand by muscle and the heart; controlling these complications with analgesics and sedatives may reduce oxygen demand and allow improved concentrations in tissues where it is in short supply. Heat support will reduce the need for endogenous thermogenesis, sparing oxygen from that process. In animals with labored breathing, a large fraction of total oxygen delivery may be required simply to fuel the work of breathing. By taking over the work of breathing, mechanical ventilation will free up oxygen from the muscles of ventilation to other tissues that may have ongoing need.

Insure adequate cardiac end diastolic blood volume, high venous return

Control of hemorrhage and provision of fluid therapy are the cornerstones of therapy for most forms of noncardiogenic shock. Fluid therapy in these patients capitalizes on relationship between cardiac left-ventricular end-diastolic volume (LVEDV) and stroke volume (SV). When LVEDV is increased via improved venous blood volume and blood return to the heart, SV is increased and directly increases cardiac output (CO). Since increasing cardiac output is such an effective method to increase systemic oxygen delivery, fluid therapy is often essential to the successful treatment of animals with shock syndromes due to causes other than heart failure. The clinical goal for fluid therapy in these patients should be to optimize blood volume relative to cardiac performance as rapidly as possible within the technical constraints on administration and within the clinician's limits on monitoring frequency and quality. Fluid therapy is stopped when therapeutic goals are met or the rate of rise in CO relative to the volume of fluid administered falls, whichever comes first. The thick curve in Figure 1 illustrates the relationship between the filling pressure (in this example, left atrial pressure, LAP) driving blood into the left ventricle during diastole and the amount of blood pumped per minute (CO) in a hypothetical large dog.

If the dog is subjected to hemorrhage of ~ 40-50% of its blood volume causing venous return and left atrial pressure to fall, CO may be reduced to very low levels (the segment to the left of point A) and this hypothetical patient will be afflicted with shock syndrome. The rationale of fluid therapy is to rapidly increase left atrial pressure (and LVEDV) to push the CO up into the A-B region. For most patients, clinical signs abate and therapeutic goals are met when CO is increased into this range. If those goals are not met, fluid may be administered until the rate of increase in CO begins to flatten (the beginning of segment B-C). In this range,

continued fluid therapy increases LAP but provides very little increase in CO. At the same time, the increase in LAP is pushing the patient closer to the point where the pulmonary lymphatic system is overwhelmed and lung water increases (point E on the thin curve depicting lung water content).

Figure 1

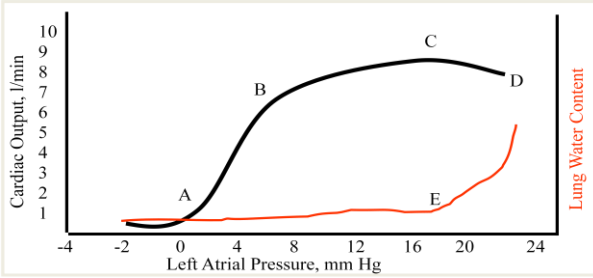
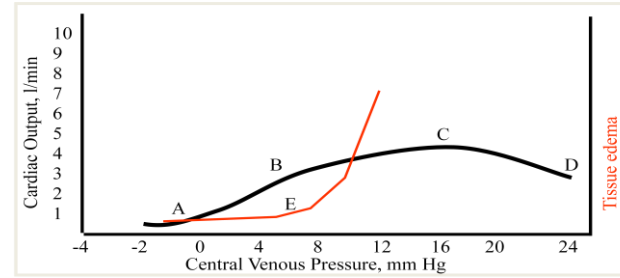


Figure 2



Therefore, fluid therapy is indicated only when animals are symptomatic for impaired cardiac output and the relationship between LAP and CO is to the left of point C; in fact it has the greatest impact in patients whose relationship is farthest to the left. Once point B is reached, further fluid therapy does little to improve CO and eventually puts the patient at risk for pulmonary edema.

The relationship between filling pressure, CO, and edema formation becomes more complicated in shock states with impaired heart function, as is often the case in septic shock and heart failure. In this case, the relationship between filling pressure and CO may be much flatter as depicted by the thick curve in Figure 2, a hypothetical patient with septic shock. In this example, the filling pressure is the central venous pressure (CVP), and instead of pulmonary edema the thin line depicts the formation of tissue edema. Because heart function is compromised, the rate of rise in CO as the CVP is increased is comparatively flat, and the 'steep' portion of the curve (segment A-B) is only slightly steeper than the 'plateau' portion (segment B-C). Thus, for any given amount of increase in filling pressure, the increase in CO is small and the clinical signs of any response may be quite subtle or ambiguous. In addition, tissue edema begins to form relatively early due to increased capillary permeability seen in SIRS and sepsis, a complication that further limits the usefulness of fluids in this setting.

The preferred method of fluid administration for shock is via direct intravenous administration through a short, large diameter catheter. Ideally, the catheter should be rapidly inserted percutaneously into a peripheral vein. The largest IV catheter gauge size possible should be used. A 20 - 18 gauge catheters may suffice for adult cats, but for dogs larger than 10 kg a 10 - 16 gauge catheter is necessary to achieve a satisfactory flow rate.

The standard approach we use for initial fluid therapy is to push in small amounts of fluid very rapidly. The clinician must remain at the animal's side and continuously monitor responses and side effects. A rapidly administered (< 3 minutes) bolus of 10-20 ml/kg of replacement solution or 3- 5 ml/kg of colloid will often provoke significant changes in physical signs that may then be evaluated. Bolus fluid administration may be repeated as necessary to achieve therapeutic goals. Fortunately, many animals with dramatic physical signs of compensated hypovolemic shock will rapidly respond to a relatively small cumulative dose of intravenous fluids (< 30-70 ml/kg of replacement solutions) and this positive response will be readily observed via physical examination. Animals with uncontrolled occult hemorrhage or deranged compensatory mechanisms (e.g. septic shock or near-lethal hypovolemic shock) may not demonstrate unequivocal physical signs of improvement and will require additional monitoring and therapeutic maneuvers. A reasonable general goal is to have completed initial fluid resuscitation within 15 minutes of your decision to administer fluids. Animals that do not respond to 1 or 2 fluid challenges with obvious changes in their physical signs may not need fluids or may have a very flat response curve or may be so severely hypovolemic that they simply need more than what was administered to demonstrate a response. This last possibility is minimized by rapid administration (1-5 minutes).

Fluid therapy options

Currently available fluid types appropriate for use in shock therapy include replacement fluids, colloids, hypertonic saline (HS), and blood products. Although there is little clinical evidence that one fluid type is "better" than another for all cases of shock, there is growing experimental evidence that the high [Cl] in 0.9% saline is detrimental, crystalloid fluids in general are pro-inflammatory, and using plasma better preserves endothelial function.

The most commonly used crystalloid solutions in the US are lactated Ringer's solution (LRS), 0.9% sodium chloride, and commercial products that include buffer precursors such as the proprietary product Normasol-R. The products are inexpensive and have low viscosity allowing rapid administration. All replacement-type crystalloids distribute into the entire extracellular fluid compartment within minutes of administration; thus only about 200 ml of every liter administered remain in the plasma compartment. There are some side effects that are significant in certain patients. All of the products dilute plasma protein and clotting factors. The high chloride concentration of .9% NaCl produces a metabolic acidosis and may predispose to coagulopathy. The low sodium

concentration of LRS predisposes to hyponatremia. The acetate present in proprietary products may cause hypotension when administered rapidly to patients at the edge of decompensation.

On an equal mEq basis, hypertonic sodium chloride solution provides at least as much resuscitative power as isotonic replacement fluids; that is, administration of 300 mEq of sodium as a 7.5% solution yields an effect that is comparable to administration of 300 mEq of sodium in the form of 0.9% saline, despite the fact that it is diluted in a much smaller volume. One advantage of this is that the smaller volume requirement allows more rapid delivery of a resuscitative dose of fluid; this advantage may be significant in large patients (especially humans and horses). Another is that since less water needs to be administered this product contributes less to edema formation. It should be administered just once, at the onset of resuscitation, at a dose of 4 (cat) to 6 (dog) ml/kg over a few minutes.

Blood products are ideal in some settings, such as fresh whole blood to treat hemorrhagic shock or plasma to treat certain coagulopathies. Packed red blood cells are an effective way to increase both the oxygen carrying capacity and the blood volume in an animal prone to hypovolemia from increased capillary permeability. Although expensive, these products are increasingly available in the US. Albumin solutions used in dogs include 25% and 5% human albumin, and just recently, commercially available canine albumin. The primary limitations of human albumin are the expense (which fluctuates considerably) and the risk of both immediate and delayed immune reactions.

Commercially available synthetic colloid solutions in the US are all based on starch polymers, and hetastarch products predominate. Although the most widely used product is hetastarch, newer products that use a different substitution ratio may reduce the impact on coagulation and products that use a lower chloride concentration than the usual .9% saline vehicle may improve tissue perfusion at the capillary level (e.g., Hextend™). Clinical confirmation that any synthetic colloid improves long-term survival when compared to other fluid therapy remains elusive.

Insure adequate heart pumping action

Arrhythmias should be controlled aggressively in animals that appear hemodynamically unstable. The most common arrhythmias encountered in shock states include relative sinus bradycardia in sick cats (especially those with severe sepsis) and idioventricular rhythm (HR 100-160) or ventricular tachycardia (HR > 160) in dogs. Cats should be treated with warming to a normal body temperature and atropine 0.04 mg/kg IV as needed. Cats that fail to respond to atropine and warming are usually administered epinephrine at 0.1 – 2 mcg/kg/min, adjusted to achieve a heart rate of > 160 BPM and a systolic BP > 140 mm Hg. Ventricular arrhythmias in dogs often require no therapy other than correction of predisposing causes such as hypoxemia or electrolyte abnormalities. When treatment is necessary the initial treatment is usually lidocaine (2 mg/kg IV up to 4 times at 3 minute intervals, then 1.8-5 mg/kg/hour). Ventricular arrhythmias are in cats are generally not treated unless associated with severe (> 300 BPM) tachycardia, a relatively rare finding.

Administration of positive inotrope drugs may follow appropriate and adequate fluid resuscitation if there is evidence of persistently low cardiac output in the absence of arrhythmia (dog) or in the presence of an inappropriately low heart rate (<160 BPM in a sick cat). Therapeutic endpoints include improved clinical signs, optimal heart rate, improved arterial blood pressure without induction of tachycardia, reduced plasma lactate concentration, increased mixed or central venous blood oxygen content or saturation, and if measured, increased cardiac output. Dobutamine is administered to dogs at an initial dose of 5 mcg/kg/min and titrated up in increments of 2.5 – 5 mcg/kg/min to a maximum of around 15 mcg/kg/min. The drug is not often used in cats because a) it induces generalized seizures in some and b) cats requiring inotropic support often have profound hypotension that benefits more from either epinephrine or dopamine administration.

Insure that vascular tone and distribution is well matched to cardiac output

Animals with straightforward hypovolemic shock from hemorrhage, isotonic dehydration, or trauma generally do not have persistent problems with hypotension following control of hemorrhage and administration of adequate amounts of fluid. A patient that has persistent hypotension soon after trauma likely has ongoing unidentified hemorrhage or has serious cardiopulmonary impairment due to tamponade, arrhythmia, or pneumothorax. That animal generally requires emergent localization of the problem and surgical correction. In contrast, animals with septic shock or severe SIRS from other causes reliably have arterial hypotension that is unresponsive to fluid therapy alone. These patients often require pressor therapy to survive, and must be cared for in a facility capable of blood pressure monitoring. Pressor therapy is universally administered as constant-rate intravenous infusions of drugs with short biological half-lives.

Dogs with persistent hypotension after optimal fluid therapy are initially treated with norepinephrine (0.1 -2 µg/kg/min) or, if norepinephrine is not available, dopamine at 5-20 mcg/kg/min. With either drug, the infusion is begun at the low end of the range and titrated up as needed in response to blood pressure.

Our goal for blood pressure in animals with septic shock or severe SIRS is to raise the diastolic pressure to 70-90 mm Hg, which is usually associated with a mean pressure of 110-140 mm Hg and a systolic of 140-180 mm Hg. If we fail to reach this by the time the norepinephrine dose has reached between .5 and 1 mcg/kg/min we routinely add an infusion of vasopressin 1-4 milliunits/kg/min. As with the catecholamines, this infusion is begun at the low end of the range and titrated upwards in response to need. Vasopressin is

used to take advantage of its permissive effects on vascular response to catecholamines. As septic shock progresses, a significant number of patients experience depletion of endogenous vasopressin, blunt their response to administered catecholamines. Supplementation with a low dose of vasopressin restores this responsiveness and improves the hemodynamic response to therapy with catecholamines.

Cats with refractory hypotension are treated with epinephrine unless the heart rate is > 180 BPM, in that case norepinephrine 0.1 – 2 µg/kg/min) is used. Although epinephrine is detrimental to dogs in septic shock, in our experience cats appear to have less problems with the adverse effects of the hormone and benefit from its stimulatory effect on heart rate and pressor effect on the vasculature. Because we often rely on indirect arterial blood pressure measurements in cats, pressor therapy is usually titrated to achieve an indirect systolic pressure of > 140 mm Hg.

Corticosteroids do not appear to confer any benefit in trauma or other causes of hypovolemia, and their use is not recommended, particularly if one plans to use a NSAID for analgesia following trauma. High dosages of corticosteroids increase mortality in most animal models and human clinical studies of septic shock, but low doses may be beneficial. In humans with septic shock, doses comparable to 1-2 mg/kg of hydrocortisone/day modify the stress response, reduce dependency on vasopressors, and improve survival to discharge in some studies. Meta-analysis of data from experimentally-induced septic shock in several species of animals (dog, cat, rodents, rabbits, and chimpanzees) demonstrates a similar pattern: high doses of steroid increases mortality, but low doses (equivalent to around 0.01 – 0.02 mg/kg/hour dexamethasone) improve survival.

Prevent excessive coagulation or hemorrhage

Microvasculature thrombosis occurs during shock states and is one cause of organ failure, and in experimental models of hypovolemic or septic shock low dosages of heparin administered during or before initial resuscitation maintain tissue perfusion better than placebo. Heparin may be administered as an intravenous bolus of 10-100 units/kg and followed immediately by subcutaneous administration of 50 - 100 units/kg every 6-8 hours, or a continuous infusion of heparin diluted in IV fluids administered at a rate of 300 IU/kg/day. In animals that are more prone to thrombosis, as evidenced by thromboelastography (TEG^{TM}) or spontaneous venous thrombosis at catheter sites, more aggressive anticoagulation is performed to limit the risk of injury from pulmonary embolism. Dogs are treated with heparin at an initial dose of 900 IU/kg/day and cats at an initial dose of 600 IU/kg/day, with the dose continuously adjusted to maintain a modestly hypocoagulable state as determined by TEG^{TM} or prolongation of the aPTT. Fractionated heparin (e.g., dalteparin [Fragmin^{TM}] at 1-200 IU/kg SQ q 8-12 hours) may be used as an alternative to heparin. Although the efficacy of fractionated heparin in companion animals with coagulopathy is unknown, these agents have the potential to achieve significant antithrombotic action with a lower likelihood of hemorrhage.

Maintain glycemic control

Both hypo- and hyperglycemia are detrimental to critically ill patients, and derangement of glucose metabolism is routinely observed in shock syndromes. Common disorders include the hyperglycemia of the stress response to critical illness or injury and hypoglycemia seen during progressive severe sepsis and septic shock. Our goal for glycemic control is to maintain the blood glucose concentration between 80 and 160 mg/dl.

Maintain normal electrolyte balance of potassium, magnesium, and ionized calcium

Electrolyte concentrations are frequently abnormal in patients with shock syndromes and will further impair cardiovascular function. Common abnormalities include hypokalemia, hyperkalemia, and ionized hypocalcemia. Life-threatening abnormalities are treated within minutes of recognition, followed by longer-term measures aimed at correction. The following suggestions are a general guide for animals with marked abnormalities attended by clinical signs. These are all performed with the clinician continuously monitoring the patient ECG and clinical signs:

Serum [K] < 2 mEq/l: Administer diluted KCl into a central catheter at an initial dose of 0.1-0.2 mEq/kg lean body weight over 2-4 minutes, followed by an infusion of .3 – 1 mEq/kg/hour until normalized.

Serum [K] > 6 mEq/l: Options to reduce serum [K] include sodium bicarbonate 1 mEq/kg IV over several minutes and regular insulin 0.1 units/kg IV followed immediately with an infusion of dextrose 3 grams/kg IV over the next hour. To counteract the effect of hyperkalemia on the heart, calcium gluconate may be administered at a dose of 1 ml/kg IV of the 10% solution over 1-2 minutes.

Serum ionized [Ca] < .8 mEq/l: Calcium gluconate 1 ml/kg IV of the 10% solution over several minutes, repeated to effect.

Electrolytes, glucose, analgesics, and other medications are routinely administered as fluid additives. Our practice is to provide every animal that requires IV fluids with a dedicated line containing a low-sodium fluid (usually 0.45% saline, or a commercial maintenance solution like Normasol-M) at a rate calculated to replace normal daily ongoing losses as estimated by the equations $97*Wt_{kg}^{0.655}$ for sick or quiet animals or $140*Wt_{kg}^{0.73}$. The rate of this fluid never changes, allowing us to add constant rate infusions of other agents to the solution. Other fluids, for example fluid administered to replace ongoing gastrointestinal fluid loss, is administered from a separate bag and administration set.

References are available upon request