Resuscitative Fluid Therapy for Circulatory Shock

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Resuscitative fluid therapy commonly refers to the treatment of circulatory shock and utilizes intravenous fluids to help restore circulating blood volume.[1,2]

Shock is best defined as inadequate cellular energy production.[3] When oxygen delivery (DO_2) to the tissues is insufficient relative to tissue oxygen consumption (VO_2), an energy deficit occurs. The **Figure** illustrates contributors to DO_2 and portrays how inadequacy of any of these factors can lead to shock.

Classifying Shock

In 1972, Hinshaw and Cox proposed a classification scheme for shock.[4] The main categories were:

- **Hypovolemic**: Inadequate circulating volume (eg, hemorrhage)
- **Obstructive**: Extracardiac obstruction of blood flow (eg, cardiac tamponade)
- **Distributive**: Maldistribution of blood flow and volume (eg, sepsis)
- **Cardiogenic**: Primary cardiac pump failure.

Newer shock classifications have been proposed but all of these can be included in 1 or more of the previous 4 categories and have yet to be universally accepted:

- **Metabolic** (eg, hypoglycemia, mitochondrial dysfunction)
- **Endocrine** (eg, hypoadrenocorticism, hypothyroidism, hyperthyroidism)
- **Hypoxemic** (eg, severe anemia)
- **Neurogenic** (eg, spinal cord transection)
- **Anaphylactic**.

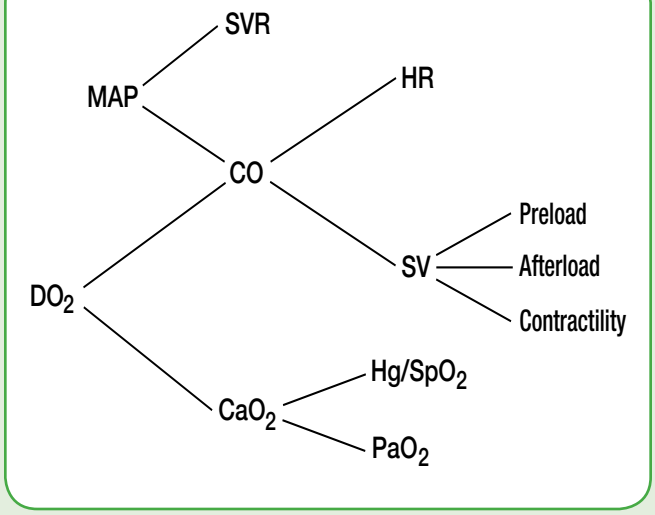

Figure. Contributors to Oxygen Delivery
CaO_2 = *arterial oxygen content;* **CO** = *cardiac output;* **DO_2** = *oxygen delivery;* **Hg** = *hemoglobin;* **HR** = *heart rate;* **MAP** = *mean arterial pressure;* **PaO_2** = *arterial partial pressure of oxygen;* **SaO_2** = *saturation of hemoglobin with oxygen;* **SV** = *stroke volume;* **SVR** = *systemic vascular residence*

Consequences of Shock

Rapid progression of shock can be lethal due to major organ failure (eg, heart, brain). A more insidious progression causes cellular membrane dysregulation, which leads to:

- Exposure of subendothelial collagen
- Activation of platelets, clotting cascade, fibrinolytic, and kinin systems
- Bacterial translocation from the intestinal tract.

Subsequently, systemic inflammatory response, sepsis, and multiple organ dysfunctions often result. Despite adequate shock reversal, they may persist and can result in death.

Fluid Therapy Indications

To optimize the chance of a successful outcome, rapid, aggressive therapy and appropriate monitoring is warranted as soon as a state of shock is identified. While contraindicated for treatment of cardiogenic shock, intravenous fluid therapy is the cornerstone of treatment for hypovolemic and distributive shock.

Depending on the location of the obstruction, responsiveness to fluid therapy varies with obstructive forms of shock. Resuscitative fluid therapy can be attempted, but treatment of the underlying disorder is ultimately essential (ie, pericardiocentesis for pericardial effusion causing tamponade).

Types of Fluid Therapy

The arsenal of fluid types available for the treatment of shock comprises:

- Isotonic and hypertonic crystalloids
- Synthetic colloids
- Hemoglobin-based oxygen-carrying solutions
- Blood products.

The patient's clinical condition and type of shock dictates which fluid type to employ and is further discussed in the following sections.

Crystalloid Fluids

Description

Crystalloid fluids primarily consist of water combined with sodium, chloride, and/or glucose. Depending on the type of fluid, it may also contain other electrolytes, such as potassium and calcium, and buffers, such as lactate, acetate, and gluconate.

Based on the tonicity (effective osmolality) when compared to the extracellular fluid compartment, crystalloids are further subdivided into:

- Isotonic
- Hypotonic
- Hypertonic.

Isotonic Crystalloids

Isotonic crystalloids contain simple electrolytes (sodium and chloride) in proportions similar to that of plasma. Hence, they are also called replacement fluids. Examples include:

911 NOTES: RESUSCITATIVE FLUID THERAPY

- Fluid resuscitation is essential for the treatment of noncardiogenic circulatory shock and should be tailored to the patient's clinical needs.
- A myriad of fluid types are available and can be used together to maximize their potential benefits.
- However, each fluid type also carries possible undesirable side effects that can lead to worsening of a patient's well-being.
- Judicious fluid type and dosage choice along with close cardiovascular monitoring is key for safe fluid resuscitation.

- 0.9% sodium chloride
- Lactated Ringer's solution; contains potassium, calcium, and lactate as buffers
- Normosol-R (hospira.com) and Plasma-Lyte-A (baxter.com); both contain potassium, magnesium, acetate, and gluconate as buffers.

Indications

Isotonic crystalloids are the least expensive resuscitative fluids and are commonly used as the initial resuscitative fluid for the treatment of patients in fluid-responsive shock.

Dosing

The empirical shock dosage is the equivalent of the patient's blood volume: 90 mL/kg in the dog and 50 mL/kg in the cat.[5] A common dosing approach consists of administering ¼ to ⅓ of the shock dose; then reassessing the patient's cardiovascular parameters prior to further administration.

Considerations & Precautions

These fluids rapidly redistribute into the extracellular compartment following administration and approximately 25% of the delivered volume remains in the vascular space 30 minutes postinfusion.[6] While this is beneficial in dehydrated patients, overzealous use should be avoided to prevent volume overload and interstitial, pulmonary, or cerebral edema.

Furthermore, large volumes of isotonic crystalloids cause hemodilution of blood constituents and may lead to cardiac and pulmonary complications, gastrointestinal dysmotility, coagulation disturbances, and immunological and inflammatory mediator dysfunction.[7]

Hypotonic Crystalloids

Because rapid intravasacular infusion of hypotonic fluids does not lead to a sustained intravascular volume increase but does lead to potentially dangerous changes in cellular osmolality, they are contraindicated as resuscitative fluids.

DOSING DETAILS: FLUID THERAPY

Shock dosage refers to the amount of fluid type required to reverse clinical manifestations of shock. The **Table** below offers a quick reference of total shock dosages for each of the commonly used fluid types. However, the dosage of fluid required to improve the cardiovascular status of each patient is variable and depends on the nature and severity of shock.

A prudent common clinical practice consists of:

1. Administration of aliquots of the total empirical dose
2. Rapid reassessment of cardiovascular parameters, such as:
   - Heart rate & pulse quality
   - Blood pressure
   - Mucous membrane color
   - Capillary refill time
   - Mentation
   - Urine output
   - Blood lactate level.
3. Administration of additional aliquots as needed until desired effect is reached.

Fluid Type	Total Shock Dosage (mL/kg)	
	Canine	**Feline**
Isotonic Crystalloids	90	50
Hypertonic Saline (7%–7.5%)	4–7	3–4
Hetastarch	20	10
Packed Red Blood Cells	10–15	10–15
Fresh Frozen Plasma	10–15	10–15
Whole Blood	20–25	20–25

**It is recommended that fluids are titrated to effect, often requiring less than the maximum doses listed.*

Hypertonic Crystalloids

Hypertonic saline is a sodium chloride solution with an osmolality greater than the patient's plasma osmolality. The usual concentration used for fluid resuscitation is approximately 7.5%, which has an osmolality of 2400 mOsm/L.

After rapid infusion, an osmotic gradient is created that draws water from the intracellular and interstitial space into the intravascular space. Therefore, the vascular volume expansion is greater than the infused volume (approximately 3 times greater).[8,9]

Indications

Hypertonic saline presents a good option for patients with traumatic brain injury or when rapid

intravascular volume expansion is required. Additional benefits include increased cardiac contractility, mild peripheral arteriolar vasodilation and immunomodulatory effects.

Its use, however, is contraindicated in patients that are dehydrated, hyperosmolar, or hypokalemic and it is controversial in patients that have uncontrolled hemorrhage (eg, intracranial or intra-abdominal).[10]

Dosing

The usual shock dosage of hypertonic saline is 4 to 7 mL/kg in dogs and 3 to 4 mL/kg in cats, administered over approximately 10 minutes. Infusion rates greater than 1 mL/kg/min may cause a vagally mediated bradycardia, vasodilation, and bronchoconstriction.

To prolong the intravascular volume expansion effect, a hypertonic saline/synthetic colloid mixture can be administered:

- 1:2.5 ratio of 23.4% sodium chloride:hetastarch = approximately 7.5% saline mixture (44 mL of 23.4% sodium chloride in 106 mL hydroxyethyl starch)
- It should be administered in small volumes (up to 5 mL/kg) over 5 to 10 minutes.

Considerations & Precautions

As with isotonic crystalloid solutions, the infused sodium chloride solution will ultimately equilibrate between the intravascular and interstitial space. In addition, the transient hyperosmolality will cause an osmotic diuresis.

The volume expanding effect lasts approximately 30 minutes[8] and subsequent isotonic crystalloid infusion is required (see **Dosing**). As discussed above, concurrent colloid administration prolongs the volume effect and may be beneficial.

Synthetic Colloids

Description

Synthetic colloids are large molecules (molecular weight > 20 kilodaltons [kDa]) that do not readily escape across the capillary membrane if normal permeability is present. Synthetic colloids are suspended in isotonic crystalloid-base solutions. When infused IV, the macromolecules increase the oncotic pressure, resulting in fluid movement from the extravascular into the intravascular space.

Commercialized synthetic colloids include:

- Glucose polymers (dextran)
- Gelatins
- Hemoglobin-based oxygen carriers (HBOC)
- Hydroxyethyl starches.

Glucose Polymers & Gelatins

Historically, the most commonly used and studied glucose polymer was Dextran 70; however, it is no longer commercially available. Gelatin solutions, a chemical modification of bovine collagen, have limited use due to their short duration of action and numerous side effects.

Hemoglobin-Based Oxygen Carriers

Indications

HBOC solutions may be beneficial in animals with

CRYSTALLOIDS & COLLOIDS: THEIR RAPPORT

Synthetic Colloids versus Hypertonic Saline

- With synthetic colloid administration, intravascular volume expansion is greater than the infused volume, which is similar to hypertonic saline.
- However, contrary to hypertonic saline administration, mobilized fluid volume remains in the vascular space due to sustained increase in oncotic pressure.

Crystalloids & Colloids in Unison

- Both synthetic colloids and hypertonic saline achieve a rapid increase in intravascular volume and are often combined to prolong the benefit of hypertonic saline.[11]
- Additionally, synthetic colloids are often used in conjunction with isotonic crystalloids to help retain the infused volume in the intravascular space, reducing the crystalloid volume required for resuscitation.

severe anemia because they increase oxygen delivery to the tissues. HBOC may also increase perfusion of capillary beds with microvascular thrombosis due to the small size of free hemoglobin.

Considerations & Precautions

Despite the aforementioned potential benefits of HBOC and its long shelf life, it is not widely used due to inconsistent supply, undesirable side effects, and lack of clear benefit over natural blood products.

Hydroxyethyl Starches

Hydroxyethyl starches are composed of amylopectin polymers with specific chemical modifications that dictate their pharmacokinetics and elimination.

Commercially available hydroxyethyl starch products differ by their concentration, average molecular weight, and degree of substitution (see **The Finer Features of Hydroxyethyl Starches**) and include:

- Hetastarch
- Pentastarch
- Tetrastarch.

Indications

Although the use of hydroxyethyl starches alone have no proven benefit over the use of crystalloid solutions alone for the treatment of fluid responsive shock, they remain a good adjunct treatment, especially in patients with low colloid osmotic pressure or increased vascular permeability.

Dosing

The recommended shock dose of hetastarch is up to 20 mL/kg in dogs and up to 10 mL/kg in cats. A common practice consists of administering increments of ¼ to ½ of the total shock dose, followed by reassessment of cardiovascular parameters.

Considerations & Precautions

Use of hydroxyethyl starches may lead to:

- Fluid overload and hemodilution (associated with large infused volumes)
- Coagulation abnormalities due to decreased coagulation factors VIII and von Willebrand, thrombocytopathia, and increased fibrin clot fragility.[12]

Although not contraindicated in patients with coagulopathies, caution should be exercised. Renal impairment and allergic reactions have been reported in people, but not small animals.[13,14,15]

THE FINER FEATURES OF HYDROXYETHYL STARCHES

Concentration: Most hydroxyethyl starch solutions have a concentration of 6%.

Molecular Weight: The weight average molecular weight is categorized into:

- Low molecular weight (70 kDa)
- Medium molecular weight (130–270 kDa)
- High molecular weight (450 kDa).

Degree of Substitution: The degree of substitution refers to the number of hydroxyethyl groups per molecule. A higher degree of substitution confers a longer half-life.

Immunomodulatory Properties

- Historically, it was suggested that molecules of less than 200 kDa, with a degree of substitution less than 0.4, may plug capillary endothelial pores, subsequently decreasing their permeability.
- However, more recent data suggest that hydroxyethyl starches may down regulate adhesion molecule expression, inhibit neutrophil recruitment, and minimize pro-inflammatory cytokine production.[12]

Blood Products

Fresh whole blood contains all the elements of blood:

- Red blood cells
- White blood cells
- Platelets
- Coagulation factors
- Immunoglobulins
- Albumin.

The separation of red blood cells and plasma provides various blood component products that allows for longer preservation of the units and more specific therapy. The product type should be tailored to the patient's needs.

Packed Red Blood Cells

Indications

Packed red blood cell transfusion is indicated in patients with acute anemia (hematocrit < 25%) and persistent clinical cardiovascular instability.[16]

Dosing

Packed red blood cells can be administered at a dose of 10 to 15 mL/kg to raise the hematocrit by 10%.

Fresh Frozen Plasma

Indications

Fresh frozen plasma is indicated to replenish coagulation factors in patients with prolonged coagulation times. However, despite being a source of albumin, its colloidal effect is limited due to its relatively low concentration compared to synthetic colloids.

Dosing

Fresh frozen plasma can be administered at a dose of 10 to 15 mL/kg.

Fresh Whole Blood

Indications

Fresh whole blood provides the benefits of both previously mentioned products (packed red blood cells and fresh frozen plasma) but is also a source of platelets, which is beneficial in patients with:

- Severe thrombocytopenia or thrombocytopathia-induced bleeding
- Massive blood loss
- Severely thrombocytopenic patient in need of surgery.

Dosing

Fresh whole blood is administered at a dose of 20 to 25 mL/kg. Ideally, blood-typing and cross-matching are performed before any blood product transfusion.

In addition, when time allows, any blood product should be infused over 1 to 4 hours to allow for adverse reaction monitoring. However, faster administration may be warranted in patients with severe ongoing hemorrhage until hemostasis can be achieved.

Considerations & Precautions

Potential adverse events associated with transfusion therapy include:

- Acute or delayed immunologic reactions
- Electrolyte imbalances (ie, hypocalcemia, hypomagnesemia, hyperkalemia)
- Transmission of infectious agents.

Another major disadvantage of blood products is their associated cost and limited availability as compared to other types of resuscitative fluids.

Overview of Therapy

An **Overview of Resuscitative Fluid Therapy** table is available on page 60. It is also available at **todaysveterinarypractice.com** as a PDF that you can download for use in your clinic. ■

DO_2 = oxygen delivery;
HBOC = hemoglobin-based oxygen carriers;
kDa = kilodalton; VO_2 = oxygen consumption

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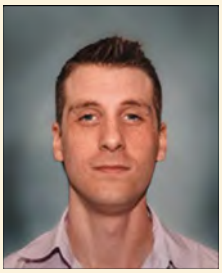

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OVERVIEW OF RESUSCITATIVE FLUID THERAPY

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Fluid Type	Indications	Dosage		Notes
		Dog	Cat	
CRYSTALLOID FLUIDS				
Isotonic crystalloids	Patients with fluid-responsive shock; commonly used as initial fluid therapy	**90 mL/kg** Administer 1/4 to 1/3 of dose; then reassess CV parameters prior to further administration	**50 mL/kg**	• Examples: 0.9% sodium chloride, lactated Ringer's solution, Normosol-R,* & Plasma-Lyte-A§ • Avoid overzealous use to prevent volume overload and hemodilution of blood constituents
Hypertonic saline	Patients with traumatic brain injury or when rapid intravascular volume expansion is needed	**4–7 mL/kg** Administer over ≈ 10 min	**3–4 mL/kg**	• To prolong effect, a hypertonic saline/synthetic colloid mixture can be administered • Contraindicated in patients that are dehydrated, hyperosmolar, or hypokalemic
SYNTHETIC COLLOIDS				
Hydroxyethyl starches	Patients with low colloidal osmotic pressure, increased vascular permeability, or when rapid intravascular volume expansion is needed	**20 mL/kg** Administer 1/4 to 1/3 of dose; then reassess CV parameters prior to further administration	**10 mL/kg**	• Of the synthetic colloids available, hydroxyethyl starches are the ones most commonly used in veterinary patients • Use may lead to fluid overload, hemodilution, and coagulation abnormalities
BLOOD PRODUCTS				
Packed red blood cells	Patients with acute anemia & persistent CV instability	**10–15 mL/kg** Infused over 1–4 H to monitor for adverse reactions (if possible)		**All blood products:** • Blood-typing should be performed before any blood product transfusion. A cross match is recommended if animal has previously received transfusion. • Adverse events include immunologic reactions, electrolyte imbalances, & transmission of disease **Fresh frozen plasma:** • Replenishes coagulation factors • Despite being a source of albumin, its colloidal effect is limited due to its relatively low oncotic pressure compared to synthetic colloids **Fresh whole blood:** • Same benefits as those of packed red blood cells and fresh frozen plasma combined, but also a source of active platelets
Fresh frozen plasma	Patients with prolonged coagulation times	**10–15 mL/kg** Infused over 1–4 H to monitor for adverse reactions (if possible)		
Fresh whole blood	Patients with TCPE, TCPA-induced bleeding, or massive blood loss/surgical candidates with severe TCPE	**20–25 mL/kg** Infused over 1–4 H to monitor for adverse reactions (if possible)		

CV = cardiovascular; TCPA = thrombocytopathia; TCPE = thrombocytopenia
* hospira.com
§ baxter.com

*This table can be downloaded at **todaysveterinarypractice.com** and printed for use in your clinic.*