

Perfusion Versus Hydration: Impact on the Fluid Therapy Plan

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Abstract: *Creating a fluid therapy plan that is adequate to meet an individual patient's needs depends on identifying whether the animal has poor perfusion, is dehydrated, or both. This article reviews the body's fluid compartments, fluid dynamics, and the clinical parameters used to differentiate perfusion from hydration and create a fluid therapy plan.*

Water is the most important nutrient. It defines cell size and shape and provides necessary support for fibrin, collagen, and cells in tissue. In addition, it is the medium on which transport of nutrients, proteins, electrolytes, and cells throughout the body depends. The function of water is dynamic: it shifts from transport to support to intracellular metabolism, depending on the fluid compartment. When the body loses or redistributes water, the transportation, tissue support, and cellular processes can become impaired. The degree of impairment is typically proportional to the amount and rate of water loss.

Fluid therapy is the principal method for correcting water deficits and blunting the effects of water imbalance. Inappropriate or inadequate fluid therapy can have a major effect on recovery and survival. Therefore, recognizing whether a fluid deficit is affecting transport of blood to the tissues (perfusion), tissue support and intracellular processes (hydration), or both is critical to implementing an effective fluid therapy plan for the patient.

Knowledge of the normal composition and distribution of body water and the physiologic responses of the body to fluid deficits is essential to successful fluid therapy. This information is used to calculate the volume of fluid required, the rate of fluid administration, and the type of fluid needed.

Body Water Composition and Distribution

Water makes up 60% of the body weight of mammals.¹ Total body water is mainly

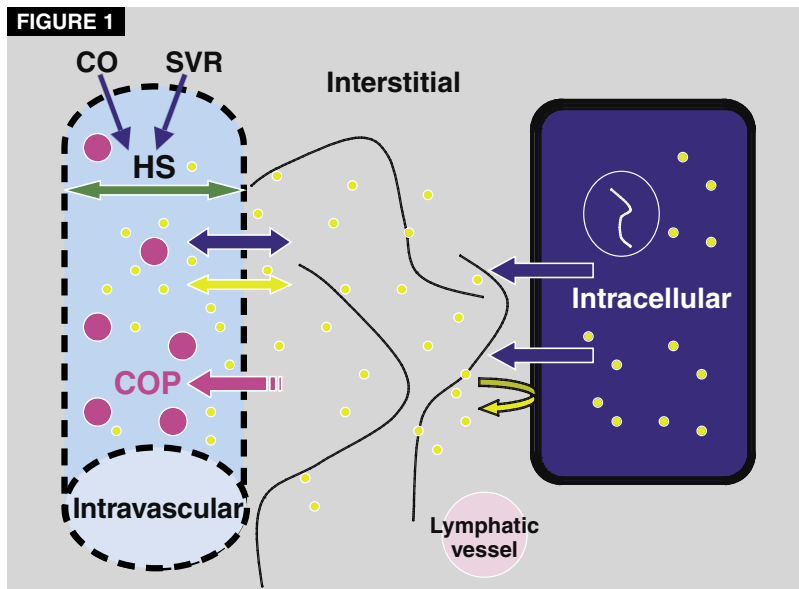
distributed between the intracellular and extracellular body compartments. The intracellular compartment contains 66% of the total body water, while the extracellular space contains 33%. The extracellular compartment is further divided into the interstitial and intravascular spaces. Of the total body water within the extracellular space, 75% is in the interstitium and 25% is in the intravascular compartment. The remaining 1% of total body fluid is transcellular, located in the synovial, peritoneal, pericardial, and intraocular spaces.²

The intracellular and extracellular fluid compartments are separated by cell membranes. The vascular membrane, which separates the interstitial and intravascular spaces within the extracellular compartment, is composed of a thin layer of endothelial cells resting on a bed of collagen, fibrin, and sometimes smooth muscle, depending on the type of vessel. Most extracellular movement of water and solutes occurs at the capillary level.²

The interstitial space comprises a macromolecular complex that contains water, collagenous molecules, glycoproteins, elastin, proteoglycans, and glycosaminoglycans. This matrix supports the capillaries and separates them from the cells, facilitates the transport or diffusion of oxygen and solutes between cells, and houses the lymphatic vessels (**FIGURE 1**). The interstitial environment gives organs their form.³

Because the barriers separating the fluid compartments do not restrict water movement, additional forces must hold

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Relationship of forces governing water movement between the fluid compartments in a normal capillary. The cell membrane is freely permeable to solute-free water (blue arrows), which moves in and out of the cell as a result of osmolar gradients established between the intracellular and interstitial fluid compartments.

Starling's forces dictate water movement and retention in the extracellular space. The capillary hydrostatic pressure (HS; green arrow) is a consequence of the cardiac output (CO) and systemic vascular resistance (SVR). The intravascular colloid osmotic pressure (COP; pink arrow) opposes the HS, retaining water in the vessel. The COP is maintained by the presence of large molecules, primarily proteins (pink dots), which have a negative charge that attracts sodium. This increase in sodium exerts an osmotic effect (Donnan effect; yellow arrows), promoting water retention within the capillary. The vascular membrane prevents the proteins from leaving the capillary, thereby maintaining a higher concentration of proteins in the blood vessel than in the interstitial space (black lines). The lymphatic vessels within the interstitial matrix carry excess fluid, proteins, and solutes (yellow dots) from the interstitium back to the circulation.

water within a compartment. Water moves across the vascular membrane as a result of the interaction of the physical forces represented in Starling's equation⁴:

$$V = kf \times [(HS_c - HS_{is}) - \Sigma[COP_c - COP_{is}] - Q$$

V = filtered volume, *kf* = filtration coefficient, *HS* = hydrostatic pressure, *c* = capillary, *is* = interstitial fluid, Σ = membrane pore size, *COP* = colloid osmotic pressure, *Q* = lymph flow

The characteristics of the vascular membrane, including the size of the interendothelial gaps (Σ) and the electrostatic charge of the gaps (filtration coefficient), also play a role in the movement of fluid and solutes between the capillaries and the interstitium. These traits become important in disease states because they can support or oppose the passage of large solutes across the vascular membrane.²

Physiologic Responses to Fluid Deficits

The volume and rate of fluid loss, as well as the composition of the fluid being lost, determine the severity of clinical signs associated with a deficit in any fluid compartment. Clinical signs can change as the equilibration shifts between body compartments. Small, slow isotonic volume losses, as with chronic, once-a-day vomiting, typically cause subtle clinical signs. Moderate or rapid isotonic volume losses, as with vomiting secondary to parvovirus or with hemorrhage, commonly manifest as obvious clinical signs reflecting the compartment(s) affected. Regardless of the rate of loss, large isotonic volume losses can be expected to lead to significant clinical signs.

Intravascular Water Deficits

A reduction in intravascular fluid volume (hypovolemia) can be a serious complication of a number of disease processes (TABLE 1). Hypovolemia manifests as abnormalities in perfusion, the process of nutrient and oxygen delivery by arterial blood to capillary beds in tissue. Changes in physical perfusion parameters include altered heart rate, capillary refill time (CRT), mucous membrane color, and pulse quality (TABLE 2). The loss of whole blood or plasma water results in reduced intravascular hydrostatic pressure and decreased baroreceptor stretch. The sympathetic system becomes the dominating force as vagal activity is decreased, leading to increased heart rate and contractility, together with peripheral vasoconstriction, in dogs.⁵

In dogs with mild to moderate volume loss, clinical signs include red mucous membranes, rapid CRT (<1 second), and bounding pulses (i.e., compensatory shock, TABLE 2). When this response fails to improve oxygen delivery or there is a large volume loss, the sympathetic response intensifies, causing selective peripheral vasoconstriction with shunting of blood flow and tachycardia with increased cardiac contractility. Clinical signs associated with early decompensatory shock include tachycardia, weak/absent peripheral pulses, pale to white mucous membranes, and a CRT of <2 seconds. Late decompensatory shock manifests as organ malfunction (e.g., loss of tachycardic response, altered mentation, oliguria/anuria, hypothermia).⁶

In contrast to dogs, cats with hypovolemic

TABLE 1 Mechanisms and Conditions Resulting in Initial Fluid Loss From Specific Fluid Compartments^a

Compartment	Common Mechanisms	Conditions
Intravascular	<ul style="list-style-type: none"> ▶ Hemorrhage ▶ Vasculitis 	<ul style="list-style-type: none"> ▶ Trauma ▶ Surgery ▶ Coagulopathy ▶ Bleeding tumor ▶ Systemic inflammatory response syndrome ▶ Pancreatitis ▶ Pneumonia ▶ Peritonitis ▶ Infection ▶ Allergic reaction ▶ Gastroenteritis
Interstitial	Loss of hypotonic fluids (third-space fluid loss, ^b hyperthermia, polyuria)	<ul style="list-style-type: none"> ▶ Heatstroke ▶ Fever ▶ Diabetes mellitus ▶ Renal insufficiency ▶ Gastroenteritis ▶ Pyometra ▶ Burns ▶ Diarrhea
Intracellular	<ul style="list-style-type: none"> ▶ Gain of impermeant solute (i.e., hyperglycemia) ▶ Loss of solute-free water (i.e., hyperthermia) ▶ Iatrogenic hyperosmolar conditions 	<ul style="list-style-type: none"> ▶ Heatstroke ▶ Diabetes insipidus ▶ Chronic lung disease ▶ Hyperosmolar nonketotic diabetes mellitus ▶ Mannitol administration ▶ Ethylene glycol toxicosis

^aThese categories are not absolute and are only examples of conditions encountered in practice. Multiple compartments can be affected at one time.
^bThird-space fluid loss is fluid loss into spaces “outside” the body (e.g., gastrointestinal tract, pleural/peritoneal space, environment).

QuickNotes

Physical findings used to monitor perfusion include mucous membrane color, capillary refill time, heart rate, pulse quality, and blood pressure.

shock often present with bradycardia and hypothermia. Cats with underlying conditions such as significant pain, hyperthermia, tachyarrhythmia, or hyperthyroidism may present with tachycardia or normal body temperature (TABLE 2). It is postulated that hypothermia results in a reduced response of adrenergic receptors to catecholamines, playing an important role in fluid resuscitation techniques for cats.⁷ Rapidly infusing large volumes of fluid can result in signs of fluid intolerance after the body temperature returns to normal (BOX 1). Therefore, we recommend actively warming

BOX 1

Clinical Signs of Fluid Intolerance³⁰

- ▶ Shivering
- ▶ Restlessness
- ▶ Serous nasal discharge
- ▶ Peripheral edema
- ▶ Chemosis
- ▶ Hock swelling
- ▶ Submandibular swelling
- ▶ Respiratory changes
- ▶ Tachypnea
- ▶ Moist lung sounds
- ▶ Moist cough
- ▶ Respiratory failure
- ▶ Tachycardia or bradycardia
- ▶ Pleural or peritoneal effusion
- ▶ Decreased level of consciousness

TABLE 2 Changes in Perfusion Parameters During Stages of Hypovolemic Shock

Parameter	Normal	Compensatory Shock	Early Decompensatory Shock	Late Decompensatory Shock	Comments
Heart rate (bpm)	Dog: 60–120 Cat: 170–200	Dog: ↑ Cat: ↑	Dog: ↑ Cat: ↓↑	Normal or ↓	
Mucous membrane color	Pink	Red	Pale pink	Gray or white	
Capillary refill time (sec)	1–2	<1	>2	>2	
Respiratory rate (breaths/min)	12–36	↑↑	↑	Normal or ↓↓	
Body temperature (°F)	99.5–102.5	Normal or ↑	Normal or ↓	↓	Significant hypothermia will make resuscitation efforts more difficult
Mentation	Alert	Alert	Depressed	Depressed or obtunded	
Mean arterial blood pressure (mm Hg)	80–100	Normal or ↑	Normal or ↓	↓	
Urine output (mL/kg/h)	1–2	Normal or ↑	↓	↓	
Lactate (mmol/dL)	<2.0	Normal or ↑	Normal or ↑	↑	
Central venous pressure (cm H ₂ O)	0–2	Normal or ↑	↓	↓	Goal: 5–8 in critical patient

QuickNotes

Physical findings used to monitor hydration include mucous membrane dryness, skin tenting, eye position in the orbit, and body weight.

hypothermic cats after initiating fluid resuscitation. This practice minimizes the volume of fluid necessary for reaching perfusion end points.

When plasma water loss causes an increase in the concentration of plasma solutes, an osmotic gradient develops between the plasma and interstitium (FIGURE 2). Water mobilizes from the interstitial space and redistributes into the plasma space. While correcting the osmotic gradient, this fluid shift can also cause an interstitial water deficit.

Interstitial Water Deficits

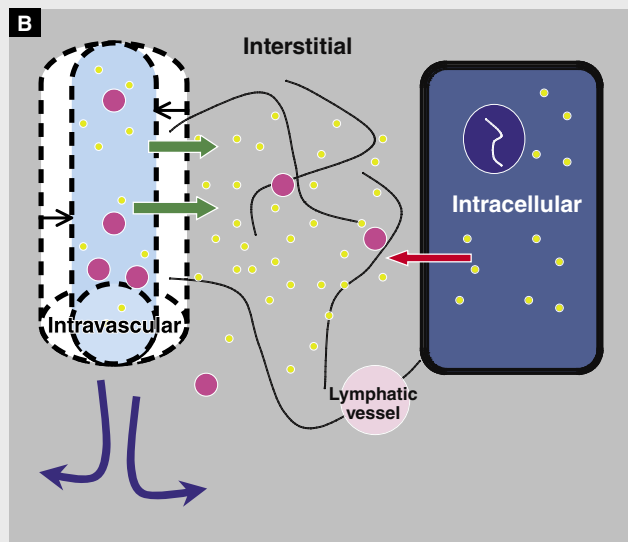
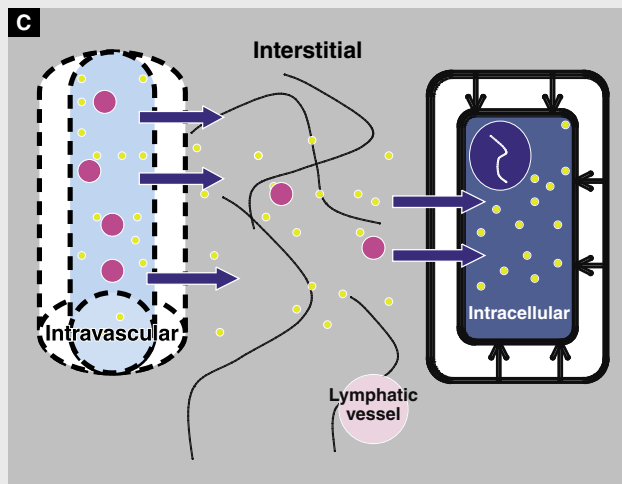
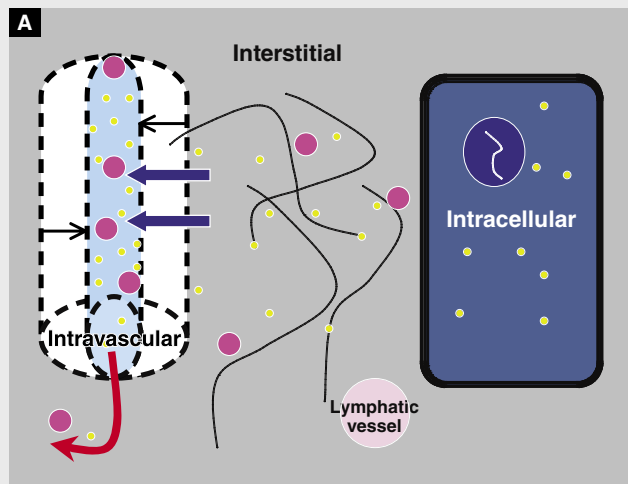
Interstitial water content is responsible for signs of tissue hydration and dehydration.

Examples of disease processes complicated by interstitial dehydration are listed in TABLE 1. Fluid loss from the interstitium raises the interstitial colloid osmotic pressure (COP) and electrolyte concentration and lowers the interstitial hydrostatic pressure. This favors the movement of fluid from intravascular and intracellular spaces into the interstitium (FIGURE 2).

Clinical manifestations of interstitial dehydration are listed in TABLE 3. Perfusion deficits do not typically result from mild to moderate interstitial dehydration. Acute interstitial fluid loss may not allow time for physical changes in interstitial compliance and shape. Ongoing interstitial water deficits reduce the support

FIGURE 2

Effects of fluid deficits on water distribution and function.



A. Hypovolemia. Loss of intravascular volume through hemorrhage (red arrow) or plasma water and protein loss results in reduced blood flow through the capillary. Over time, the loss of plasma water (e.g., severe gastroenteritis) will result in an increased intravascular solute (yellow dots) concentration, promoting water movement (blue arrows) from the interstitial space (black lines) into the intravascular space by osmosis. (pink dots = proteins)

B. Interstitial dehydration. If loss of intravascular water (blue arrows) exceeds the loss of solutes (yellow dots), water will move primarily from the intravascular space into the interstitium (green arrows) by osmosis, resulting in hemoconcentration. If dehydration is significant, water will also pass out of the intracellular space into the interstitium (red arrow). (pink dots = proteins)

C. Intracellular dehydration. Loss of intracellular water leads to an increase in the intracellular concentration of solutes (yellow dots). Solute-free water moves from the extracellular compartment into the intracellular compartment (blue arrows) by osmosis. (pink dots = proteins)

medium and alter the elasticity and shape of the tissues, causing them to become less compliant. This results in tenting of the skin when stretched and dryness of the mucous membranes and corneas.

As fluids shift from the intravascular to the interstitial space, dehydration can also be associated with increasing packed cell volume (PCV) and total protein (TP). Plasma sodium and chloride concentrations can increase with the loss of hypotonic fluids or solute-free water. When extracellular water loss causes an increased concentration of interstitial solutes that cannot permeate the cell membrane, intracellular water moves into the extracellular

spaces, leaving an intracellular water deficit (FIGURE 2).

Intracellular Water Deficits

Intracellular water deficits (intracellular dehydration) cannot be measured directly or determined by physical parameters. Intracellular fluid loss of any magnitude is associated with diseases that result in intravascular or interstitial hypernatremia due to loss of solute-free water or a dramatic increase in impermeable solutes. Clinical signs of altered mentation and seizures occur when brain cell function has been altered by cellular fluid shifts. Diseases that can result in intracellular dehydration

TABLE 3 Clinical Parameters Used to Evaluate Interstitial Dehydration

Estimated % Dehydration	Clinical Signs
4–6	Dry mucous membranes
6–8	Loss of skin moisture Dry mucous membranes ↑ PCV/TP
8–10	Loss of skin moisture Dry mucous membranes ↑ PCV/TP Retracted globes within orbits
10–12	Persistent skin tenting due to complete loss of skin elasticity Dry mucous membranes ↑ PCV/TP Retracted globes within orbits Dull corneas
>12	Persistent skin tenting due to complete loss of skin elasticity Dry mucous membranes ↑ PCV/TP Retracted globes within orbits Dull corneas Signs of perfusion deficits

PCV = packed cell volume; TP = total protein.

QuickNotes

Perfusion deficits suggest intravascular volume deficits, for which rapid fluid resuscitation with IV isotonic crystalloids with or without colloids is recommended.

with or without hyponatremia are listed in **TABLE 1**.

Clinical Signs Without Fluid Deficits

There are several clinical situations in which changes in perfusion and physical parameters of hydration do not accurately reflect fluid balance in the intravascular or interstitial spaces. Adequate intravascular volume or hypervolemia may be present. Cardiac dysfunction, hypoxia, brain injury, and profound pain can result in signs typical of poor perfusion in the absence of an intravascular fluid deficit. The contributions of the heart, lungs, brain, and pain response to the cardiovascular system must be determined before initiating aggres-

sive fluid resuscitation to avoid volume overload. Monitoring the central venous pressure or administering a small “test” fluid bolus can aid in determining whether hypovolemia is playing a role in the initiation and maintenance of poor perfusion (see Restoration of Perfusion Deficits).

Chronic weight loss without dehydration can cause the loss of skin elasticity and metabolism in the fat pad around the eye, leading to skin tenting and retraction of the eyes within the sockets. However, mucous membrane and corneal moisture should remain normal, with any changes in the PCV and TP reflecting the underlying disease process rather than hemoconcentration.

The Fluid Therapy Plan

When the fluid compartments have been assessed and a fluid deficit has been identified, a fluid therapy plan is constructed by (1) selecting the appropriate fluids (crystalloids, colloids, or both) to administer; (2) determining patient-specific resuscitation end points or goals; (3) assigning the route and rate of infusion; (4) determining the time frame over which replacement is needed; and (5) employing appropriate monitoring techniques. Perfusion deficits are more life-threatening than dehydration; therefore, perfusion deficits must be corrected first. The decision regarding the rate and volume of fluids to administer is guided by monitoring physical parameters to achieve the desired clinical goals. This is called *early goal-driven, goal-oriented, or end-point resuscitation*.^{8,9} **BOX 2** presents four case examples of fluid therapy plans and goals.

Fluid Selection

Crystalloids, natural colloids, and/or synthetic colloids can be used to replace fluid volume, depending on which fluid compartments have deficits and the rate of volume replacement required (**FIGURES 3 AND 4**). Crystalloids are water-based solutions with small particles that permeate freely across the capillary membrane. A colloid solution is a crystalloid-based fluid that also contains molecules that are too large to pass through the endothelial gaps of the capillary membrane.

Crystalloids

The cornerstone of fluid resuscitation is the infusion of isotonic replacement crystalloids.

Box 2. Case Examples

The following cases demonstrate clinical examples of fluid deficits affecting perfusion, hydration, or both. Readers are challenged to create a fluid therapy and monitoring plan for each. Suggestions for fluid therapy and the monitored parameters are provided in **TABLE A**.

Case 1

A 3-month-old, 15-kg male rottweiler presents with a primary complaint of vomiting and bloody diarrhea for 24 hours. On physical examination, the mucous membranes are gray and the capillary refill time (CRT) is prolonged (3 seconds). A femoral pulse is not palpable. The rectal body temperature is 98.5°F, heart rate is 190 bpm, and respiratory rate is 40 breaths/min. The dog is recumbent and weak and has skin tenting, dry mucous membranes, dull corneas, and eyes that are slightly sunken.

Case 2

A 12-year-old, 5-kg spayed Siamese cat presents with lethargy and a history of hiding for 2 days. The cat began vomiting white foam with traces of blood during the past 24 hours. The cat has been drinking and using the litterbox with increased frequency for the past 2 months. On physical examination, the cat has ad-

equated femoral pulses, pink mucous membranes, and a CRT of 1 to 2 seconds. The corneas and mucous membranes are dry, the eyes are retracted, and when the skin is pulled upward over the shoulders, skin tenting is marked. The rectal temperature is 99°F, heart rate is 200 bpm, and respiratory rate is 24 breaths/min.

Case 3

A 3-year-old German shepherd presents after being hit by a snow plow. The pet is ambulatory, with a heart rate of 180 bpm, weak peripheral pulses, pale mucous membranes, and a CRT of 3 seconds. The skin turgor is normal, and the mucous membranes and corneas appear moist. The abdomen is painful on palpation, with bruising of the skin on the ventral aspect.

Case 4

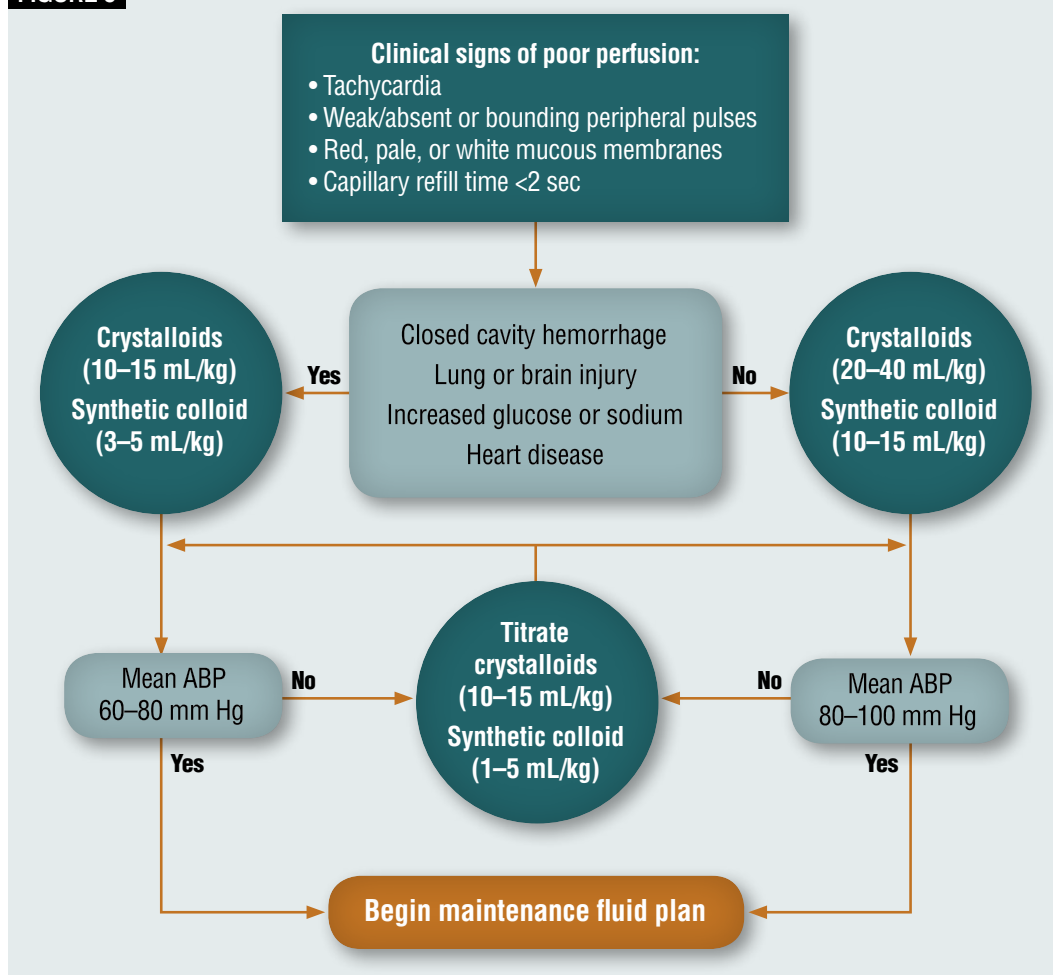
A 6-year-old castrated cat weighing 4 kg presents with difficulty breathing. A 3/6 systolic heart murmur is auscultated, and prominent lung sounds are heard throughout the thorax. The cat has a heart rate of 120 bpm, a rectal temperature of 97.5°F, absent femoral pulses, gray mucous membranes, and a CRT of 3 seconds. Pink liquid is issuing from both nostrils. The skin elasticity is normal, and the mucous membranes and corneas are moist.

TABLE A Suggestions for Fluid Therapy and Monitored Parameters

Case Number and Diagnosis	Location of Deficit	Fluid Treatment	Goals of Fluid Therapy
1: Severe gastroenteritis	Intravascular	<ul style="list-style-type: none"> ▶ Isotonic replacement crystalloid (20–40 mL/kg IV) + HES (10 mL/kg IV) bolus infusions ▶ Can be repeated to achieve desired end points ▶ Administer while actively warming 	Normal perfusion parameters
	Interstitial	<ul style="list-style-type: none"> ▶ Calculate hydration deficit: $0.06 \times 15 \text{ kg} = 900 \text{ mL}$ isotonic replacement crystalloid Presumably an acute loss; administer IV over 1–4 h ▶ Add maintenance fluid rate to rehydration rate ▶ Add fluids based on ongoing fluid losses (e.g., vomiting, diarrhea) 	<ul style="list-style-type: none"> ▶ Normal skin turgor ▶ Moist mucous membranes ▶ Bright, moist corneas
2: Diabetic ketoacidosis	Interstitial	<ul style="list-style-type: none"> ▶ Calculate % dehydration: $0.08 \times 5.0 \text{ kg} = 400 \text{ mL}$ isotonic replacement crystalloid Presumably chronic loss; administer IV over 4–6 h ▶ Add maintenance fluid rate to rehydration rate 	<ul style="list-style-type: none"> ▶ Normal skin turgor ▶ Moist mucous membranes ▶ Bright, moist corneas
3: Trauma	Intravascular	Isotonic replacement crystalloid (10–20 mL/kg IV) + HES (5 mL/kg IV) bolus infusions	<ul style="list-style-type: none"> ▶ Normal perfusion parameters ▶ Monitor serial PCV/TP to evaluate for ongoing hemorrhage
4: Congestive heart failure	None; poor perfusion is not related to hypovolemia	No fluids, or (if needed) isotonic replacement crystalloid or half-strength saline at a maintenance rate if using aggressive diuretic therapy or if additional organ dysfunction exists	To maintain some blood flow to the kidneys and other compromised organs

HES = hetastarch; PCV = packed cell volume; TP = total protein.

FIGURE 3



QuickNotes

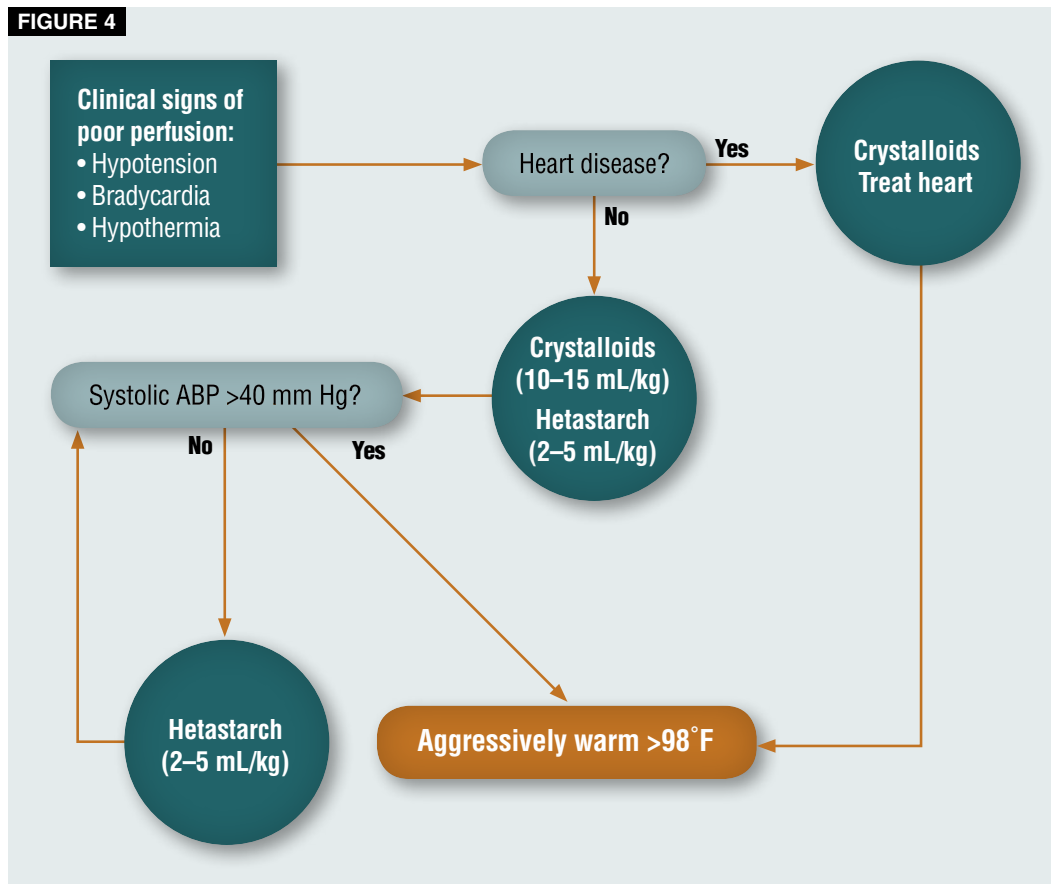
Interstitial dehydration is treated with isotonic crystalloids over 6 to 12 hours for acute changes and over 12 to 24 hours for more chronic fluid losses.

Resuscitation algorithm for hypovolemia in dogs. Before correction of intravascular water deficits is initiated, dogs with signs of hypovolemia must be assessed for closed-cavity hemorrhage, lung or brain injury, increased glucose or sodium concentration, and heart disease. These patients may not tolerate rapid, large-volume infusions; therefore, lower initial fluid volumes must be used and resuscitation end points may include a low-normal mean arterial blood pressure (ABP). Replacement isotonic crystalloids are administered with synthetic colloid (hetastarch or dextran 70) boluses. Bolus infusions of crystalloids and colloids are titrated in succession, and clinical parameters (TABLE 3) are assessed between boluses until end point parameters are achieved.

“Isotonic” implies that the solutes (primarily sodium) are in concentrations similar to those of normal plasma and will not cause an osmolar water shift from blood cells to the plasma. “Replacement” implies that the fluid has sodium and chloride concentrations similar to those of the extracellular space. Buffer-containing crystalloids (e.g., Plasmalyte-A, Normosol-R, lactated Ringer’s solution) contain gluconate and acetate, or lactate for metabolism to bicarbonate, and may restore the acid–base balance more rapidly than buffer-free isotonic crystalloids (e.g., 0.9% sodium chloride). Buffered replacement crystalloids are a reasonable

choice when fluid therapy is first initiated and until an emergency laboratory database (e.g., PCV, TP, blood urea nitrogen, glucose, venous blood gases, electrolyte panel, lactate) can be obtained. Metabolic alkalosis, hyperkalemia, hyponatremia and hypernatremia, hypochloremia, and hypercalcemia may be better treated with 0.9% sodium chloride. Compared with other isotonic solutions, 0.9% sodium chloride causes less of an osmotic shift when treating animals with hypernatremia. In addition, the higher chloride concentration can rapidly correct hypochloremic metabolic alkalosis. Normal saline does not contain supplemental

FIGURE 4



Resuscitation algorithm for hypovolemia in cats. In contrast to dogs, clinical signs of poor perfusion in cats include bradycardia, hypotension, and hypothermia. Signs of poor perfusion call for evaluation for certain conditions (e.g., heart disease). Evidence of heart disease (e.g., heart murmur, increased lung sounds and respiratory rate, gallop arrhythmia) warrants the judicious use of crystalloids to prevent significant dehydration and hypovolemia while treating for heart disease and aggressively warming the cat to normal body temperature. Exceeding normal body temperature may cause peripheral vasodilation, making resuscitation difficult. If signs of heart disease are not present, then a combination of isotonic replacement crystalloids and hetastarch is used to improve systolic arterial blood pressure (ABP). When the systolic ABP is >40 mm Hg, the patient is aggressively warmed to a temperature of 98°F. If 20–40 mL/kg hetastarch has been used and/or the blood pressure remains <70 mm Hg after body temperature has returned to normal, vasopressors and positive inotropes may need to be considered.

electrolytes that can exacerbate hyperkalemic and hypercalcemic conditions.

Intravenous hypertonic crystalloids such as 7% hypertonic saline produce an osmotic gradient that promotes water movement into the intravascular space from the interstitium and intracellular space. The use of hypertonic crystalloids can cause profound and immediate intravascular volume expansion that dissipates at the same rate as expansion produced by isotonic crystalloids. If the interstitium or intracellular compartments are dehydrated, the use of hypertonic crystalloids is not recommended.

The infusion of crystalloids immediately

increases intravascular hydrostatic pressure and lowers the intravascular COP (through dilution), favoring movement of fluid through the capillary membrane into the interstitium. In normal vessels, 75% or more of infused crystalloids redistribute into the interstitial space within 1 hour.¹⁰ This property makes isotonic crystalloids ideal for interstitial volume replacement and maintenance.

Colloids

Colloid fluids augment intravascular fluid and increase intravascular volume.^{11,12} A colloid that contains molecules large enough to

remain within the vessel and increase the vascular COP over the anticipated increase in hydrostatic pressure from fluid infusion can be beneficial in critical illnesses associated with endothelial cell dysfunction.¹³ The ideal colloid would contain molecules larger than the gaps between the endothelial cells and be readily available, affordable, hypoallergenic, and free of adverse effects. No single colloid fulfills all these criteria; however, available natural and synthetic colloids fulfill some.

Natural colloids increase the COP mainly through albumin. Albumin infusion using species-specific plasma products (5% albumin) can be cost prohibitive and carries a risk for transfusion reaction. In addition, these fluids pass into the interstitium when the endothelial gap size is larger than the albumin molecule, and large volumes are required to effectively increase the COP.¹⁴ Plasma products are useful as adjuncts to other colloids to provide albumin, coagulation proteins, and antithrombin.¹⁵ Although its use in veterinary medicine has been limited, concentrated human albumin (25% albumin; 0.1 to 0.25 mL/kg IV) can be an effective colloid in dogs and cats.^{16,17} The strong COP effect (200 mm Hg) can initially cause interstitial fluid depletion when the product is given without crystalloids.¹⁸ Human albumin has also been associated with a risk of type III hypersensitivity in dogs.¹⁹

Synthetic colloids such as dextran 70 and 6% hetastarch (HES) are readily available, require no preparation, are less expensive than blood products, and rarely cause immunologic reactions. When vasculitis and hypoalbuminemia are prominent features of the disease process (e.g., systemic inflammatory response syndrome [SIRS]), the colloid molecular size must be larger than albumin (62,000 to 69,000 Da).²⁰ Dextran 70 (average molecular weight: 70,000 Da) might extravasate in this situation.²¹ HES contains a large proportion of high-molecular-weight colloid molecules (average 450,000 Da) as well as smaller colloid molecules. The larger molecules can sustain intravascular COP when the gaps between the endothelial cells increase.²⁰

The use of synthetic colloids has been associated with adverse effects in patients with hemostatic abnormalities (e.g., von Willebrand's disease). In patients with coagulation abnormalities, large doses of these fluids can interfere with platelet function and prolong clotting times.²² In cases of increased vascular perme-

ability, plasma proteins and small synthetic colloid molecules leak into the interstitium, raising the interstitial COP. It is important to maintain the intravascular COP above the interstitial COP to avoid the movement of intravascular fluid into the interstitial space.

The use of colloid therapy in situations of increased lung permeability is hotly debated in human medicine. Recent recommendations concerning fluid management in sepsis-related acute lung injury and respiratory distress syndrome have stressed the need for judicious fluid support to maintain organ perfusion, and the use of colloids in hypoproteinemic patients is now considered an acceptable adjunct to therapy.²³

The administration of high-molecular-weight synthetic colloids results in the intravascular retention of large colloid molecules, an elevation in intravascular COP, and a fluid shift from the interstitium into the intravascular space. The intravascular volume increases by more than the volume of synthetic colloid administered. This allows the estimated necessary crystalloid volume to be decreased by 40% to 60%.²⁴ When multiple colloid fluids are needed, they should be administered consecutively rather than simultaneously to avoid sudden, dramatic elevations in hydrostatic pressure.

Hemoglobin-Based Oxygen-Carrying Solutions

Hemoglobin-based oxygen-carrying solutions such as Oxyglobin (Biopure, Cambridge, MA; average molecular weight: 150,000 Da) have a colloid osmotic effect and transport hemoglobin-bound oxygen into tissue beds where the flow of erythrocytes may have been obstructed.^{25,26} Veterinarians who have access to Oxyglobin should consider its use for volume expansion and oxygen transport in patients with circulatory shock, anemia, or maldistribution of blood flow (e.g., trauma, SIRS). Oxyglobin can also cause mild vasoconstriction, which may be of benefit in hypovolemic and distributive shock. It has universal compatibility and is unlikely to transmit hematogenous diseases. Erythrocyte replacement may still be required if significant anemia is present, and the red color of the solution can interfere with enzyme chemistry analyses. Adverse effects may include pulmonary edema, vomiting, and diarrhea; associated hypertension can be minimized by slow administration, titrated to effect.

Restoration of Perfusion Deficits

Clinical signs of perfusion abnormalities (**TABLE 2**) reflect an intravascular volume deficit in the absence of cardiac dysfunction, hypoxia, brain injury, and profound pain. Adequate perfusion of peripheral tissue depends on sufficient intravascular volume. Perfusion parameters must be monitored to evaluate the effectiveness of the fluid therapy plan. Intravascular volume loss through hemorrhage reduces intravascular hydrostatic pressure. Intravascular plasma protein and water loss through increased capillary permeability (e.g., SIRS) reduces intravascular COP and hydrostatic pressure. Losses of fluid into a third body fluid compartment (not the interstitium) cause fluid to translocate from the interstitial compartment into the vascular compartment, resulting in concurrent interstitial fluid deficit and dehydration.

Pain management with analgesics is an important part of the initial resuscitation and monitoring plan. When present, severe hypoxia, cardiac arrhythmias, and central nervous system disease must be treated early in the course of resuscitation. If hypovolemia is suspected in a dog with cardiac or neurologic dysfunction or hypoxia, we recommend a fluid challenge. This involves a “test” intravenous bolus infusion of 10 to 15 mL/kg of isotonic replacement crystalloids and 3 to 5 mL/kg of HES to see whether perfusion parameters improve. If the fluid challenge is effective and the parameters improve, careful fluid resuscitation is continued (**FIGURE 3**).

A combination of synthetic colloids and crystalloids can provide prolonged and rapid intravascular volume replacement, which can lead to resolution of interstitial dehydration (**FIGURES 3 AND 4**). To avoid fluid overload, the minimum volume of each fluid necessary to reach the desired end points should be used. If hypertonic (7%) saline solution is used for rapid intravascular volume replacement, a 4-mL/kg dose can be combined with a colloid to improve intravascular volume expansion.²⁷

If hypotension persists despite adequate volume replacement and return of body temperature to normal, vasopressors and/or positive inotropes should be considered. We have successfully used infusion of small volumes of Oxyglobin, based on its colloidal and vasoconstrictive properties, to augment arterial blood pressure and oxygen delivery in persistently

hypotensive dogs and cats. In dogs, Oxyglobin can be titrated in 3- to 5-mL/kg increments to desired end points, up to a total of 30 mL/kg; in cats, 1- to 3-mL/kg increments can be administered slowly to effect, up to 10 mL/kg. As with any colloid therapy, careful monitoring is necessary to identify early signs of fluid intolerance.

Once the desired end points of resuscitation have been reached, we use a constant-rate infusion of HES (20 mL/kg/d) or Oxyglobin (10 mL/kg/d in cats; 30 mL/kg/d in dogs) in conjunction with crystalloids as part of the intravascular fluid maintenance program until recovery is certain.^{28,29} The crystalloid infusion rate is reduced when the end points are met to the minimum amount required to provide rehydration, maintenance fluid needs, and replacement of ongoing losses.

Rehydration

Interstitial Dehydration

Common clinical parameters used to estimate interstitial dehydration include mucous membrane moisture, skin turgor, eye position within the orbit, changes in body weight, and emergency laboratory database results, including the PCV/TP (**TABLE 3**). Isotonic replacement crystalloids are used to replenish interstitial fluid deficits. The ideal route for rapid rehydration is intravenous or intraosseous administration, but the subcutaneous route can be used when the fluid deficit is minimal. The volume of isotonic replacement crystalloid fluids necessary to rehydrate the interstitial space is estimated using the following calculation:

$$\% \text{ dehydration} \times \text{body weight (kg)} = \text{L of fluid required for replacement}$$

The volume of fluid is divided by the number of hours needed to replenish the interstitial fluid. Acute losses can be corrected over 6 to 12 hours, whereas more chronic conditions causing dehydration should be corrected over 12 to 48 hours.¹³ When interstitial dehydration occurs in a patient with cardiac and renal disease, careful administration of fluids is warranted, with repeated evaluation for signs of volume overload (**BOX 1**).³⁰ Low urine output and heart failure or polyuric renal failure with hypertension may require less fluid to be administered over a longer period of time. Some experts advocate the use of low-sodium fluids (e.g.,

0.45% saline solution + 2.5% dextrose) to rehydrate patients with cardiac disease.³¹

Intracellular Dehydration

Treatment of intracellular dehydration requires the administration of intravenous fluids that will primarily move into the intracellular compartment, such as solute-free water. To prevent hemolysis from intravenous infusion of solute-free water, 5% dextrose (D5W) is added to create an osmotic gradient sufficient to prevent movement of water into the circulating blood cells. As the dextrose is metabolized, 66% of the water moves into the interstitium and then the intracellular compartment. Other solutions with solutes that are metabolized (e.g., partial parenteral nutrition fluids) can be used to provide more water than solutes. Half-strength crystalloid solutions (e.g., 0.45% saline solution or 50%-strength lactated Ringer's solution) can also be used to slowly restore water in the intracellular space without causing cell lysis.

Perfusion and hydration must be restored before the volume of water needed to replace intracellular losses is determined. The serum sodium level reflects the concentration of solute-free water, with hypernatremia in a normally perfused and interstitially hydrated patient indicating a deficit of solute-free water. The volume of solute-free water necessary to restore the cellular water balance is calculated by determining the amount of sodium excess and the volume of water distribution³²:

$$\text{Water deficit (L)} = \text{Weight (kg)} \times \left(\frac{\text{Na [measured]}}{\text{Na [desired]}} - 1 \right)$$

Na = sodium

This calculated deficit should be replaced very slowly (over 24 to 48 hours) with D5W or half-strength solutions to avoid cellular swelling and lysis. A general rule of thumb is to decrease sodium levels by 0.5 mEq/L/h.³³ If hypernatremia occurs in conjunction with congestive heart failure or oliguric renal failure, loop diuretic administration may also be indicated.³¹

Monitoring Perfusion

Bedside methods of monitoring perfusion parameters can be invasive or noninvasive, continuous or intermittent, physical, and biochemical (TABLE 2). Heart rate can be checked using cardiac auscultation, continuous electro-

cardiography, or Doppler monitoring. Pulse rate is compared with heart rate to identify dysrhythmias. A "bounding" or weak pulse may indicate increased systemic vascular resistance, decreased stroke volume, or decreased cardiac performance.³⁴

Arterial blood pressure, urine output, lactate levels, and central venous pressure can be tracked in patients that need more extensive monitoring. Arterial blood pressure should always be assessed in conjunction with heart rate. A normal arterial blood pressure does not signify normal perfusion when the heart rate is elevated. When the heart rate is normal, the optimal arterial blood pressure is approximately 120/60 mm Hg, with a targeted mean arterial pressure of approximately 80 mm Hg. Indirect blood pressure measurements can be obtained with Doppler or oscillometric monitors. Patients that are subject to rapid decompensation require intensive monitoring and may benefit from direct arterial catheterization to track blood pressure.

Urine output provides an indirect estimate of renal perfusion when renal function is adequate. Normal urine production depends on a mean arterial pressure >60 mm Hg. Lower mean arterial pressures result in oliguria, which can progress to acute renal failure. Target urine output in critical patients is 1 to 2 mL/kg/h, depending on the patient's urine concentrating ability. This volume increases if fluid diuresis is prescribed or polyuric renal disease is present. Patients with decreased urine output must be evaluated for oliguric/anuric renal failure, hypotension, hypovolemia, and urinary tract obstruction.

The plasma lactate concentration has been used in human and veterinary medicine as a marker of global tissue perfusion.^{35,36} Hyperlactatemia in a critically ill animal is usually associated with conditions causing inadequate tissue perfusion, hypoxemia, increased tissue oxygen demands, decreased hemoglobin concentration, or a combination of these factors. The lactate level can also increase with severe hepatic dysfunction and intense muscle activity. A goal of resuscitation is to return the blood lactate value to normal; however, a normal serum lactate concentration does not guarantee adequate regional tissue perfusion.

Central venous pressure (CVP) measurement can provide information for estimating

intravascular volume. Placement of a central venous catheter early in resuscitation can help guide fluid therapy. In the absence of cardiac disease, hypovolemia causes low CVP (<1 to 2 cm H₂O). Elevated CVP (>8 to 10 cm H₂O) can indicate volume overload, pleural space disease, right heart dysfunction, or pulmonary artery obstruction. The ideal CVP after fluid resuscitation is 5 to 8 cm H₂O. When the CVP is normal or elevated and clinical signs of poor perfusion persist, causes of nonresponsive shock should be evaluated and vasoactive or inotropic agents administered to further promote perfusion.

Hydration

Interstitial hydration status is monitored by evaluating changes in mucous membrane and corneal moisture, skin turgor, body weight, respiratory rate and effort, and PCV and TP levels. Signs of interstitial fluid overload are listed in **BOX 1**.

Intracellular hydration is monitored by obtaining serial serum sodium values. The serum

sodium concentration is monitored frequently to prevent rapid changes. Consequences of correcting serum sodium concentrations too quickly include mental dullness, seizures, coma, and death.³⁷ Chronic need (>48 hours) for crystalloid infusion to maintain hydration may necessitate a change to maintenance fluid therapy using Normosol-M or partial parenteral nutrition, which contain less sodium and potassium.

Conclusion

Perfusion and hydration parameters are used to assess the intravascular, interstitial, and intracellular body water compartments. Perfusion deficits related to hypovolemia must be corrected before rehydration of the interstitial and intracellular compartments. Isotonic crystalloids are used during fluid replacement, and colloids can be added for intravascular volume replacement. When end-point parameters have been achieved, close monitoring is necessary to identify early signs of decompensation or fluid intolerance. **C**

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3 CE
CREDITS

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- Perfusion deficits indicate a fluid deficiency in which compartment?
 - interstitial
 - intravascular
 - intracellular
 - third-space
- A crystalloid is best described as
 - a water-based solution containing only small molecules that freely cross the capillary membrane.
 - a water-based solution containing large molecules that cannot freely cross the capillary membrane.
 - a hemoglobin-based oxygen-carrying solution.
 - solute-free water.
- Which statement regarding colloids is true?
 - Colloids cannot be used for fluid resuscitation.
 - Colloids contain only small molecules and particles that readily cross the capillary membrane into the interstitium.
 - Colloids can increase COP, thereby minimizing redistribution of fluid from the intravascular space to the interstitial space.
 - Synthetic colloids have no adverse effects.
- Which is not a clinical sign of decompensatory shock in cats?
 - hyperthermia
 - hypotension
 - hypothermia
 - bradycardia
- Which clinical parameter does not reflect perfusion status?
 - mucous membrane moisture
 - mucous membrane color
 - capillary refill time
 - blood pressure
- When 5% dextrose (D5W) is used to replace a free water deficit in an interstitially hydrated, hypernatremic patient,
 - it should be given as a bolus because hyponatremia is a life-threatening condition.
 - the amount should be calculated carefully, but overdosing or underdosing is not a problem.
 - the plasma sodium levels should be measured only after the infusion is complete.
 - it should be given at a rate calculated to decrease the sodium levels by 0.5 mEq/L/h.
- Which type of fluid is used to treat interstitial dehydration?
 - HES
 - D5W
 - crystalloid
 - 0.45% saline solution
- Which clinical sign is used to assess interstitial dehydration?
 - poor pulse quality
 - prolonged capillary refill time
 - skin tenting
 - tachycardia
- Which of the following statements is true?
 - Crystalloids are the only fluids used for resuscitation from hypovolemia.
 - CVP measurements can be used to estimate hydration status.
 - A normal plasma sodium concentration indicates adequate fluid resuscitation and tissue perfusion.
 - The addition of a synthetic colloid to crystalloid therapy can decrease the total volume of fluid used to achieve end-point resuscitation.
- A dog in compensatory or decompensatory shock without evidence of closed-cavity hemorrhage should be resuscitated with a crystalloid dose of _____ and a colloid dose of _____ to reach end points of resuscitation.
 - 20 to 40 mL/kg, 10 to 15 mL/kg
 - 10 to 20 mL/kg, 5 to 10 mL/kg
 - 20 to 40 mL/kg, 1 to 5 mL/kg
 - 10 to 20 mL/kg, 20 to 40 mL/kg