

## **FLUID THERAPY: IT'S MORE THAN JUST LACTATED RINGERS**

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Total body water constitutes approximately 60% of a patient's body weight in normal individuals, although this value can vary slightly with age, gender, and obesity. Approximately 67% of total body water is located intracellularly. The remaining 33% of total body water is located extracellularly, in the intravascular and interstitial extravascular spaces. A very small amount of fluid, known as transcellular fluid, is located within the compartments of the gastrointestinal tract, within synovial fluid of joints, and the cerebrospinal tract. Within the body, all fluid is in a constant state of flux in between compartments. The movement of fluids from space to space is largely governed by the concentration of electrolytes, proteins, and other osmotically active particles relative to the amount of fluid within each compartment.

The balance of fluids and electrolytes are necessary for normal body functioning and cellular processes. Normally, fluid intake is in the form of drink and foodstuffs. Water is also produced during the oxidation of food materials. Fluid can be lost during excessive panting, vomiting, diarrhea, and urination. Sensible fluid losses in the form of urine, vomit, and feces can be measured, and constitute approximately 2/3 of the body's daily maintenance fluid requirements. Insensible fluid loss is largely estimated from evaporation from the respiratory tract. Insensible losses can be excessive in situations of excessive panting, salivation, or from evaporation or hemorrhage from surgical sites.

In normal individuals, fluid intake and excretion are kept in balance by the activity of sodium and chloride and serum osmolality. Osmoreceptors in the hypothalamus sense sodium and chloride concentration in the vascular space. As serum sodium rises due to increased sodium intake or fluid loss in excess of solute, serum osmolality rises. An increase in serum osmolality stimulates the release of arginine vasopressin (antidiuretic hormone) to be released from the hypothalamus. Antidiuretic hormone stimulates the opening of water channels in the collecting duct of the renal tubules, and thus stimulates water reabsorption. Once water is retained in the vascular space, sodium, urea, and glucose, the major contributors of serum osmolality, are diluted, and serum osmolality decreases. Hypothalamic excretion of ADH ceases once serum osmolality returns to normal.

During a state of equilibrium, a patient's daily water intake equals water loss, creating no net loss or gain of fluid under normal conditions. Daily fluid requirements are based on the metabolic water requirements of a patient in a state of equilibrium. For each kilocalorie of energy metabolized, 1 ml of water is consumed. Metabolic energy requirements are calculated based on the linear formula:  $\text{Kcal/day} = [(30 \times \text{body weight}_{\text{kg}}) + 70]$   
By substituting Kcal for 1 mL H<sub>2</sub>O, the following formula can be used to estimate a patient's daily metabolic water requirements:  $\text{ml/day} = [(30 \times \text{body weight}_{\text{kg}}) + 70]$

Recent studies have indicated that metabolic energy requirements rarely increase during states of critical illness except in cases of sepsis. Because our patients frequently pant and may have excessive evaporative losses or sensible fluid losses in the form of vomiting, diarrhea, wound exudates, body cavity effusions, daily fluid requirements may be greater than that calculated above. The formula should be used as a guideline, and careful assessment and measurement of ongoing losses should be added to the patient's daily fluid therapy as needed, to prevent further dehydration.

## **Dehydration vs. Hypovolemia**

The degree of interstitial dehydration can subjectively be estimated based on a patient's body weight, mucous membrane dryness, skin turgor, degree of sunkeness of the eyes, and mentation. Subjectively, if a patient has a history of fluid loss in the form of vomiting or diarrhea, but no external evidence of mucous membrane dryness or skin tenting, dehydration estimate is less than 5%. A patient is said to be 5% dehydrated when mild skin tenting, and mucous membrane dryness is present. Clinically, 7% dehydration is manifested as increased skin tenting, dry oral mucous membranes, and mild tachycardia with normal pulse quality. A patient is 10% dehydrated with increased skin tenting, dry oral mucous membranes, tachycardia, and decreased pulse pressure is present. Finally, a patient is said to be 12% dehydrated when skin tenting, and mucous membrane dryness is markedly increased, the eyes appear dry and sunken, and alteration of consciousness is observed. The parameters are largely subjective, because they can also be affected by loss of body fat and increased age.

The later stages of dehydration are also accompanied by parameters consistent with hypovolemic shock. Other factors, including hemorrhage and third spacing of body fluids can also result in a decrease in intravascular circulating volume, resulting in signs of hypovolemia. With severe hypovolemia of more than 15% of circulating volume, transcompartmental fluid shift from the interstitial to intravascular compartments occurs within one hour of fluid loss. When fluid loss is so severe that intravascular fluid volume is affected, hypovolemia can result in clinical signs of tachycardia, prolonged capillary refill time, decreased urine output, and hypotension. The vascular space is very sensitive to changes in the amount of circulating volume. During states of normovolemia, the degree of wall tension is sensed by baroreceptors in the carotid body and aortic arch, sending a pulsatile continuous feedback via vagal afferent stimuli to decrease heart rate. In the early stages of hypovolemic shock, a decrease in vascular wall stretch or tension is sensed by baroreceptors in the carotid body and aortic arch, causing blunting of tonic vagal stimulation, and allows sympathetic tone to increase heart rate and contractility to normalize cardiac output in the face of decreased circulating volume. Later, decreased blood flow and delivery of sodium to receptors in the juxtaglomerular apparatus of the kidneys cause activation of the renin-angiotensin-aldosterone axis, stimulating sodium and fluid retention to replenish intravascular volume.

## **Fluid replacement with hypovolemia versus dehydration**

When clinical signs of hypovolemic shock are present, intravascular fluids must be replaced in an emergency phase of fluid resuscitation. Calculated shock volumes of fluids are 90 ml/kg/hour for dogs, and 44 ml/kg/hour for cats. A simple guideline to follow is to replace  $\frac{1}{4}$  of the calculated intravascular fluid deficit, or the "shock volume" as rapidly as possible, then reassess perfusion parameters- heart rate, blood pressure, capillary refill time, and urine output. In dogs, a simple method to calculate  $\frac{1}{4}$  shock volume is to take the animal's weight in pounds and add a zero, giving you the amount of fluid in milliliters to administer as a bolus as quickly as possible. Approximately 80% of the crystalloid volume fluid infused will re-equilibrate and leave the intravascular space within 1 hour of its administration. A constant rate infusion of crystalloid is recommended to provide continuous fluid support in patients that are dehydrated and have ongoing losses. In some cases, the fluid required to restore intravascular and interstitial volume can cause hemodilution and dilution of oncologically active plasma proteins, resulting in interstitial edema formation. In such cases, a combination of a crystalloid fluid along with a colloid containing fluid can help restore colloid oncotic pressure and prevent interstitial edema.

Once immediate life-threatening intravascular fluid deficits are replaced, additional fluid is provided based on the estimated percent interstitial dehydration and maintenance needs. Dehydration estimates can be calculated based on the fact that 1 milliliter of water weighs approximately 1 gram. Dehydration estimates in liters can then be calculated by the formula:

Body weight in kg x estimated percent dehydration x 1000 ml/liter. This provides you with the number of liters deficit. A frequent mistake when replenishing fluid deficits is to arbitrarily multiply a patient's daily water requirement by a factor of 2 or 3 to replenish intravascular and interstitial deficits. This practice frequently underestimates the patient's actual fluid needs, and does little to treat intravascular volume depletion and interstitial dehydration. Instead, it is better to perform the calculation and add this to daily maintenance fluid requirements and ongoing losses, to maintain hydration in your hospitalized patients. Eighty per cent of the calculated fluid deficit can be replaced in the first 24 hours. After successful treatment of hypovolemic shock and replacement of estimated dehydration volumes, maintenance fluids can be supplemented, provided that no signs of dehydration or ongoing fluid loss are present. An objective way of assessing whether fluids volume is adequate is to assess body weight in a regular basis throughout the day. Acute losses in body weight are commonly associated with fluid losses, and can be used to determine whether the patient is at risk of once again becoming dehydrated.

### **Isotonic Fluids, Hypotonic Fluids, and Hypertonic Fluids**

There is a wide variety of fluids available for use by the veterinary practitioner. A crystalloid fluid contains crystals or salts that are dissolved in solution. Specific crystalloid fluids are indicated in certain disease states, and may be contraindicated in others. Therefore, whenever a crystalloid fluid is used, one must carefully consider it to be another drug in the armamentarium, and justify its use or potential disuse in each patient.

Basic categories of crystalloid fluids include isotonic, hypotonic, and hypertonic solutions, depending on the concentration and type of solute present relative to normal body plasma. Isotonic fluids have tonicity, or solute relative to water, similar to that of plasma. Examples of isotonic fluids include 0.9% (normal) saline, Lactated Ringer's solution, Normosol-R, and Plasmalyte-A. Isotonic fluids are indicated to restore fluid deficits, correct electrolyte abnormalities, and provide maintenance fluid requirements.

Hypotonic solutions are fluids whose tonicity is less than that of serum. Examples of hypotonic fluid solutions include 0.45% saline, 0.45%NaCl + 2.5% dextrose, and 5% dextrose in water (D5W). Hypotonic fluids are indicated when treating a patient with diseases processes that cause sodium and water retention, namely, congestive heart failure and hepatic disease. Infusion of hypotonic fluids is also indicated when severe hyponatremia exists, and you need to slowly correct a free water deficit. To calculate a patient's free water deficit, use the following formula:  $\text{Free water deficit} = 0.4 \times \text{lean body weight} \times [\text{patient serum Na}/140 - 1]$  The free water deficit should be corrected slowly, to not cause iatrogenic cerebral edema. Ideally, the patient's sodium should not decrease by more than 15 mEq/L during a 24-hour period.

Hypertonic solutions act to draw fluid from the interstitial fluid compartment into the intravascular space to correct hypovolemia. Their use is absolutely contraindicated if interstitial dehydration is present. Hypertonic solutions such as 3% or 7% saline have solute in excess of fluid relative to plasma. Hypertonic saline should be administered in bolus increments of 3 – 7 ml/kg as a rapid infusion. Because the net effect of hypertonic saline solution lasts only approximately 20

minutes, hypertonic saline must always be infused along with a crystalloid solution to prevent further interstitial dehydration.

**Electrolyte Composition (mEq/L) of Commonly Used Isotonic and Hypotonic Crystalloid Fluids**

	0.9% Saline	0.45% NaCl	Lactated Ringer's	Normosol-R
Sodium	154	77	130	140
Chloride	154	77	109	98
Potassium	0	0	4	5
Calcium	0	0	3	0
Magnesium	0	0	0	3
pH	7.386	5.7	6.7	7.4
Buffer	none	none	lactate 28	acetate 27 gluconate 23

**Colloids**

A colloid solution contains negatively charged large molecular weight particles that are osmotically active, drawing sodium around their core structures. Wherever sodium is, water follows. By drawing sodium around the particle, water is thus held within the vascular space. Colloids replace intravascular fluid deficits only. Therefore, colloids are always administered along with crystalloids, to restore both intravascular and interstitial fluid volume. Examples of artificial colloids include Hetastarch, Vetstarch, Pentastarch, and Voluven. Whenever a colloid is administered along with a crystalloid, calculated crystalloid fluid requirements should be decreased by 25% - 50%, to avoid intravascular volume overload.

Natural colloid solutions include whole blood, packed red blood cells, and plasma. Fresh whole blood is indicated when loss of both red blood cells and plasma has occurred. The Rule of Ones states that one ml of fresh blood infused per one-pound body weight will increase the patient's packed cell volume by one per cent, provided that no ongoing losses are present. Packed red blood cells can be administered when anemia is present in sufficient quantity to cause clinical signs of anemia, including lethargy, inappetance, tachycardia and tachypnea. Fresh frozen plasma can be administered at 10 – 20 ml/kg/day to replenish clotting factors and provide antiprotease activity during inflammatory conditions. Fresh frozen plasma can be used to replace small amounts of albumin, in cases of hypoalbuminemia, however, is not efficient as administering purified concentrated canine-specific (when available) or 25% human albumin. Frozen or fresh frozen plasma (20 ml/kg IV) needs to be infused for every 0.5 g/dL increase in plasma albumin, provided that no ongoing losses are present. The goal of albumin administration is to raise the patient's serum albumin to 2.0 g/dL, then provide the remainder of colloidal support with synthetic colloids.

Hydroxyethyl starch is a polymer of amylopectin suspended in a lactated ringer's solution. The average molecular weight of Hetastarch is 69,000 Daltons. Larger particles are broken down by

serum amylase, and last in circulation for approximately 36 hours. Because Hetastarch can bind with von Willebrand's factor, mild prolongation of a patient's APTT and ACT may be observed, but do not contribute to or cause clinical bleeding. Hetastarch should be administered in incremental boluses of 5 – 10 ml/kg in dogs, and 5 ml/kg in cats. Because rapid administration of hetastarch can cause histamine release and vomiting in cats, the bolus should be administered slowly over a period of 15 – 20 minutes. Some authors recommend that the total daily dose of hetastarch should not exceed 20 – 30 ml/kg/day. Following the administration of hetastarch boluses, it should be administered as a constant rate infusion (20 – 30 ml/kg/day IV) until the patient is able to maintain its albumin and colloidal support on its own.

Concentrated human albumin and concentrated canine albumin solutions are now available for use in veterinary patients. Both immediate and delayed rare Type 3 hypersensitivity reactions have been documented in healthy and hypoalbuminemic dogs following administration of concentrated human albumin. Reactions that occurred that include fever, vomiting, acute anaphylaxis, urticaria, angioneurotic edema, and delayed vasculitis, polyarthropathies, glomerulonephritis and death in both healthy and critically ill animals.

Although there are studies which have demonstrated adverse reactions and the development of anti-human albumin antibodies after concentrated human albumin infusion in dogs, there also have been studies which have documented improved clinical outcome when concentrated human albumin was infused into critically ill animals that were refractory to other more mainstream therapies, including pressors, synthetic colloids, and fresh frozen plasma transfusions. Concentrated 25% human (2 ml/kg IV in dogs over 4 hours; pre-treat with 1 mg/kg diphenhydramine IV). should be considered in any patient with refractory hypoalbuminemia (< 2.0 g/dL) or hypotension unresponsive to other synthetic colloids, pressors, and inotropes. The perceived benefits of albumin infusion and risks of not infusing albumin must be weighed against the potential risks of its administration. Clients must be aware of the potential risks of complications.