For Veterinarians only

PET POD

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Fluid Resuscitation in Companion Animals

Fluid therapy is replenishing body fluid loss in any pathological condition. In 1832, Thomas Latta described the first intravenous administration of salt-based solutions for cholera patients. Since then, intravenous fluid therapy has become the ubiquitous symptomatic treatment for human and Veterinary practices. It has become the most common therapeutic protocol and is a gateway to the care of companion animals with abnormal fluid disturbances.

Fluid Physiology

Body is considered a closed system, any fluid lost must come from extracellular or intracellular space. To comprehend fluid therapy and its uses, fluid and water circulation through the body must first be understood. Total body water (TBW) is responsible for ~60-70% of body weight (BW) and is the primary component of all body fluids. The two main body fluid compartments are the intracellular fluid (ICF) and extracellular fluid (ECF). Approximately two-third (≈40%) of TBW is intracellular fluid (ICF) and one-third (≈20%) extracellular fluid (ECF). The ECF is comprised of four sub-compartments, the intravascular fluid volume (*i.e.,* blood volume: BV; 6-8% BW; plasma volume: PV; 4-5% BW), the fluid that surrounds cells (*i.e.,* interstitial fluid volume: IFV; ≈15-18% BW), lymph, and fluids contained within epithelial lined spaces (transcellular fluids) [Fig. 1].

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Dear Vets,

Fluid therapy is the most common therapeutic approach and a gateway to the care of companion animals with abnormal fluid disturbances. It is a supportive measure to underlying disease process that lead to aberrations in water, electrolyte and acid-base status. Principally fluid therapy is provide for correcting life-threatening hypovolemia, restoring accumulated deficits of fluids, correcting electrolyte and acid-base disturbances, and providing sufficient fluids, electrolytes to meet continuing losses each day and meeting normal daily requirements. Common fluids include crystalloids, such as normal saline and lactated Ringer solution, and colloids such as albumin and hydroxyethyl starch. The choice of fluid depends on patient-specific factors, including electrolyte levels, acid-base status, and clinical response.

A comprehensive examination of fluid therapy in Veterinary medicine is necessary for those looking to provide the best possible care to their patients. Fluid management/ resuscitation is a critical aspect of animal care, as each patient has unique needs based on their medical condition, fluid losses, and ability to maintain fluid intake. The primary goals to replace fluid deficits is to maintain normal physiological balance. Veterinarians need to differentiate between the maintenance therapy, which replenishes daily fluid losses, replacement therapy, which corrects fluid deficits caused by illness, injury, or third-space shifts; and resuscitative fluids, which are required in cases of hypovolemia or shock.

We believe that this information will support the therapeutic approach to manage fluid loss in companion animals. To share your valuable experiences, feedback, and suggestions, please scan the QR code below. Alternatively, feel free to reach out to us *via* email at petpod@intaspharma.com.

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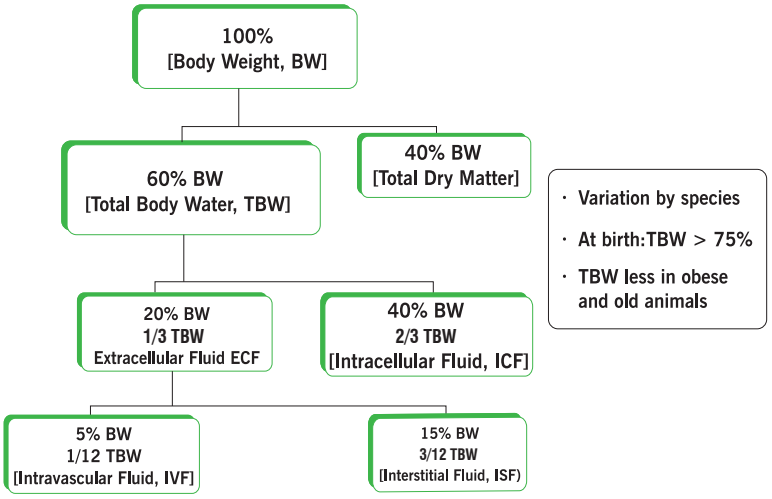
Distribution of Body Fluids



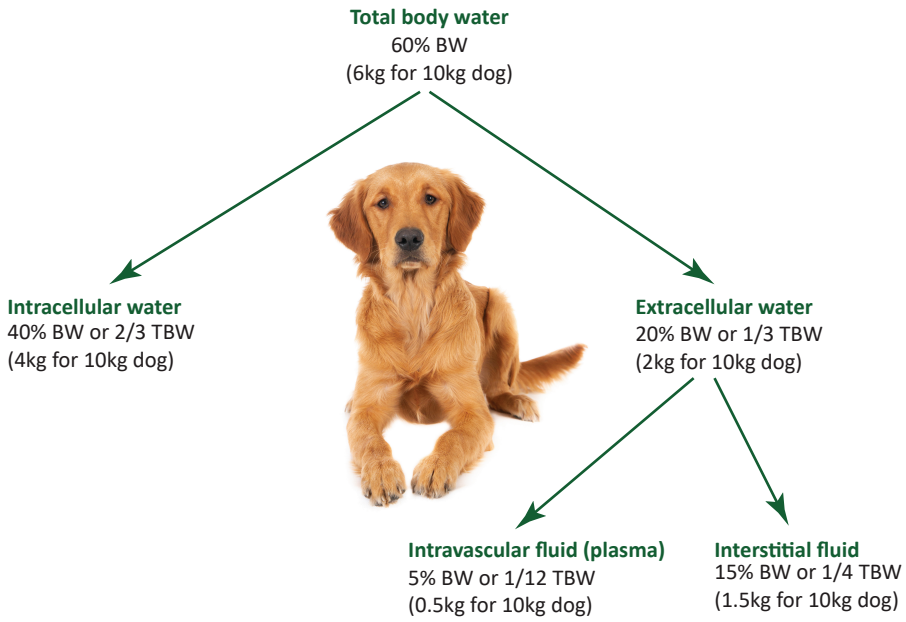


Fig. 1: Diagrammatic representation of fluid in different compartments of body

Fluid Balance

Water intake and output is governed by a variety of neural and neuroendocrine high-gain homeostatic feedback mechanisms that include, osmoreceptors, osmotically stimulated thirst receptors, hormones [e.g., renin-angiotensinaldosterone system (RAAS), angiotensin-converting enzyme-2 (ACE2)/ angiotensin 1-7 (Ang 1-7), vasopressin (antidiuretic hormone: ADH), erythropoietin (EPO), atrial natriuretic peptide (ANP)] and membrane water channels (*i.e.,* aquaporins), especially those located in renal tubules. Kidney is responsible for regulating fluid, electrolyte balance and blood volume, and also produces and secrets erythropoietin (e.g., low Hb, PaO2, flow) signaling bone marrow to produce more red blood cells. Activated atrial stretch receptors secrete ANP producing vasodilation and increases in glomerular filtration, salt and water excretion, and vascular permeability, thereby regulating PV and lowering arterial blood pressure (ABP). Therefore, kidney is regarded as a key determinant of both PV and BV. Negatively charged glycosaminoglycans (GAGs) located in interstitial spaces and lymphatics of skin also function as non-renal regulators of sodium ion concentration and ECF volume serving as indirect controllers of arterial blood pressure (ABP) by shifting fluid from the interstitial to the intravascular space.

In response to osmotic forces, fluids freely passes cell membranes, through interstitium, into and out of cell. The amount of fluid that moves across capillary membrane depends on a number of factors, including capillary colloid oncotic pressure (COP), hydrostatic pressure, and permeability, which is dictated by factors such as the endothelial glycocalyx layer (EGL) and pore sizes between the cells. Fluid moves into interstitial space when intravascular hydrostatic pressure is increased over COP, when membrane pore size increases, EGL is disrupted, or when intravascular COP becomes lower than interstitial COP. The EGL is known to play an important role in controlling fluid and other molecule (e.g., albumin) transport across capillary layer, and oncotic pressure of glycocalyx plays a larger role than oncotic pressure of interstitium. To preserve cell size and for normal function, body retains osmolality within a tight range. Any fluid loss from any compartment must be replaced by fluid from other above compartment. Osmolality is controlled primarily by water intake, *i.e.,* thirst or retention or excretion of water by kidney.

Fluid Loss

Fluid loss disturbances warranting fluid therapy encompass changes in volume, alterations in content, and shifts in distribution within body as below;

1. **Change in fluid volume (dehydration from any cause, blood loss, heart disease):** Dehydration is a state of excessive fluid loss in the interstitial and intracellular compartments of a living organism, whereas hypovolemia explains intravascular fluid shortages. Hypovolemia can occur with or without dehydration and usually induced by extreme dehydration, the rapid loss of fluid (gastrointestinal loss, blood, polyuria), and vasodilatation. Dehydration can be isotonic, hypotonic, or hypertonic in canine and feline.
   - **Isotonic/ isonatremic dehydration:** Water and salt loss together. Vomiting and diarrhoea usually result in isotonic fluid loss, serum sodium concentration, chloride concentration, and osmolality within the usual reference range. It is characterized by tiredness, no thirst, a ring around eyes, wrinkles in skin, weak and fast pulse and frequent kidney failure.
   - **Hypertonic/ hypernatremic dehydration:** Extracellular fluid loss is more than salt loss. Diabetes, pulmonary losses due to hyperventilation and temperature, and diarrhoea result in hypotonic fluid loss. It is characterized by severe thirst, mucous membrane and tongue dryness, neurological symptoms, generalized impairment and fever.
   - **Hypotonic/ hyponatremic dehydration:** Extracellular fluid loss is less than salt loss, which is uncommon. However, it can be seen in hypoadrenocorticism, secretory diarrhoea, vomiting, and third space (such as peritoneal and pleural) fluid loss and diuretic administration. It is characterized by nausea, loss of appetite, convulsion, moist tongue and third sensation loss.
2. **Change in fluid content:** The variation include electrolyte abnormalities, blood glucose variation, anaemia and polycythemia. Specific electrolyte imbalances in cats and dogs include hypo- and hyperkalemia, hypo- and hypernatremia, hypoproteinemia/hypoalbuminemia, and hypo- and hyperglycemia.
3. **Change in fluid distribution:** It include different edema types (interstitial, peripheral, and pulmonary and patients with effusion (skin burn, pleural and abdominal). The primary causes for both these conditions are loss of vascular integrity and decreased intravascular oncotic pressure.

Determination of Fluid Deficit

Assessment of dehydration is necessary for determination of fluid deficit in body. Loss of fluid volume from intravascular fluid compartment is manifested by poor perfusion (shock) and inadequate tissue oxygenation. This volume deficit results in a lower vessel wall tension. Decreased wall tension in aortic arch and carotid arteries results in decreased stimulation of the baroreceptors. Stimulation of the sympathetic nervous system is manifested by clinical changes in heart rate, pulse intensity, blood pressure, capillary refill time, mucous membrane color, level of consciousness, and rectal temperature. These physical perfusion parameters, combined with blood pressure, are used clinically to detect intravascular volume deficits.

Fluid deficit in interstitial and intracellular spaces causes clinical signs of dehydration. Physical findings are used to estimate the percentage of dehydration. Semidry oral mucous membranes, normal skin turgor, and eyes maintaining normal moisture indicate 4-5% dehydration. Dry oral mucous membranes, mild loss of skin turgor, and eyes still moist indicate 6-7% dehydration. As dehydration becomes more severe, significant quantities of fluid shift from the intravascular space

into interstitium, causing concurrent perfusion deficits with dehydration. Dry mucous membranes, considerable loss of skin turgor, retracted eyes, acute weight loss, and weak rapid pulses (concurrent intravascular deficit) indicate 8-10% dehydration. Very dry oral mucous membranes, complete loss of skin turgor, severe retraction of eyes, dull eyes, possible alteration of consciousness, acute weight loss, and weak pulses indicate ≥12% dehydration.

Fluid Requirement

In the emergency phase of Veterinary care, determining the fluid requirement is crucial, especially considering factors like body weight and percentage of dehydration. The formula for calculating the volume required to correct dehydration is body weight (kg) multiplied by the percentage of dehydration. Maintenance fluid rates, follow thumb rules for cats (80 x body weight $(kg)^{0.75}$ per 24 hours) and dogs (132 x body weight $(kg)^{0.75}$ per 24 hours), with recommended hourly rates of 2-3 mL/kg/hr for cats and 2-6 mL/kg/hr for dogs. Considering insensitive fluid loss and assuming standard urine output, the maintenance fluid requirement for pets is typically 50 to 60 mL/kg/day. When correcting dehydration, it is important to consider existing and current fluid losses along with maintenance volumes. Current deficits should be replaced within 2-3 hours, while existing volume losses may be replaced over a more extended duration. The standard goal is to rectify dehydration within 24 hours, though certain conditions, such as cardiac disease. Monitoring frequency, typically ranging from 15 to 60 minutes, depends on the extent of resuscitation delivered. Regular assessment of euhydration is essential to avoid fluid overload. Additionally, caution is advised against using maintenance solutions low in Na to replace extracellular deficiencies, as these solutions may contribute to hyponatremia and hyperkalemia when administered in significant volumes.

Fluid Therapy

It is one of the most important aspects of animal's management and it is the act of replenishing animal with adequate fluids. However, important to realize that fluid therapy is a supportive measure to underlying disease process that lead to aberrations in water, electrolyte and acid-base status. Principally fluid therapy is provide for correcting life-threatening hypovolemia, restoring accumulated deficits of fluids, correcting electrolyte and acid-base disturbances, and providing sufficient fluids, electrolytes to meet continuing losses each day and meeting normal daily requirements.

The goal of fluid therapy is to expand intravascular volume, restore circulatory function, and ultimately deliver oxygen to tissues. Although in most situations the importance of fluid therapy is quite clear, there are different opinions regarding the type of fluid, volume of fluid, and rate of fluid to be administered.

Depending upon requirement of animals, fluid can be divided into following phases:

- **Resuscitation** - correcting perfusion abnormalities
- **Rehydration** - correcting hydration abnormalities
- **Optimisation** - ongoing administration of replacement fluids that are working to optimizecirculation
- **Stabilisation** - is a recovery stage in which the patient is hemodynamically stable and the infusion therapy moves toward optimizing electrolyte balance and replacing ongoing losses
- **Evacuation** - cessation of assisted fluid therapy, as self-sufficiency via oral intake is adequate

Types of Fluids

There are three different types of fluids that can be used:

a) Fluids containing isotonic, hypotonic and hhpetonic crystalloids, mimic osmotic pressure

b) Colloids, create oncotic pressure, found in both natural and synthetic forms

a) Crystalloids: These are solutions containing electrolytes dissolved in water, commonly used for fluid resuscitation, medication delivery, and maintenance of fluid balance. They distribute rapidly throughout extracellular fluid space and are classified by their tonicity as isotonic, hypotonic and hypertonic. The small molecular weight particles in crystalloids are primarily electrolytes and buffers. Crystalloids are considered buffered when they contain molecules (such as acetate, gluconate, and lactate) that are converted to bicarbonate in liver, equilibrating the pH of fluid to normal blood pH (7.4). Crystalloids are considered balanced when they contain electrolytes in addition to Na and Cl (such as K, Mg, Ca), making them similar to plasma. Lactated Ringer's is an example of a balanced solution; normal saline is not balanced.

It is available as isotonic, hypotonic and hypertonic fluid.

- **Isotonic fluid:** It has the effective osmolality as the extracellular fluid (approximately 270 to 310 mOsm/L). It has a sodium concentration similar to that of extracellular fluid, having little effect on intracellular volume. These solutions have an advantage over other solutions for maintenance as they can be administered through all the routes except oral. Isotonic fluid is commonly used to treat hypovolemia and intestinal dehydration since fluid losses are mostly isotonic or hypotonic. Solutions like, 0.9% normal saline or physiological saline, Ringer's, lactated Ringer's, acetated Ringer's, and 2.5% dextrose in 0.45% saline are commonly used.
- **Hypotonic solution:** This solution has a lower concentration of sodium ions (Na+) and chloride ions (Cl-). It has less effective osmolality than ECF and plasma. This re-distributes all fluid compartments, with most going into intracellular space. This enables water replenishment and maintenance. As they are ineffective at increasing intravascular volume and may result in cerebral edema from intracellular fluid shifting, hypotonic solutions are inappropriate for bolus therapy. When administered directly, hypotonic solutions cause haemolysis by moving water into erythrocytes. Solutions like 5%, 2.5% dextrose in water and 0.45% sodium chloride solution.
- **Hypertonic solution:** It is important to note that hypertonic saline solutions have a greater osmolality than plasma and extracellular fluid. It helps to maintain fluid balance in fully rehydrated patients, it should be administered slowly through an IV and never used in dehydrated animals. In well-hydrated, hyponatremic patients, it can provide energy and sodium supplementation. Commonly used solution is dextrose 5% in 0.9% saline, which has an osmolality of 560 mOsm/L.

b) Colloids: These are solutions containing large, water-soluble molecules, particularly proteins, which remain in bloodstream longer than crystalloid fluids. These molecules increase oncotic pressure, drawing water from interstitial space into bloodstream, thus expanding plasma volume. This makes them useful for fluid resuscitation in cases of hypovolemic shock, severe bleeding and burns. These are available as natural colloid (e.g., plasma, albumin and whole blood) and synthetic colloid (e.g., Dextran, Hydroxyethyl Starch (HES) and lyophilized albumin).

- **Dextrans** are polysaccharides composed of linear glucose residues. They are produced by the enzyme dextran sucrase during growth of various strains of Leuconostoc sp. in media

containing sucrose. Dextrans are isotonic and can be stored at room temperature. Dextran is broken down completely to CO_2 and H_2O by dextranase present in spleen, liver, lung, kidney, brain, and muscle @ approaching 70 mg/kg every 24 hours. In normal dogs, dextran 70 increases plasma volume 1.38 times (138%) the volume infused.

- **Lyophilized canine albumin** is available as a 5% lypophilized solution that can be reconstituted. It has been administered to dogs with septic peritonitis and hypoalbuminemia and has been demonstrated to increase oncotic pressure, measured albumin levels, and Doppler-measured blood pressure, with increased albumin levels persisting for as long as 24 hours.
- **Hydroxyethyl starch (HES):** HES is parent name of a group of synthetic polymers that are most frequently used as plasma expanders. The molecule is made from a waxy species of either corn or potatoes and is composed primarily of amylopectin (98%). HES molecules vary in size from ten thousand to several million daltons (average 70-670 thousand daltons). It is composed of 6 percent hydroxyethyl starch 130/0.4 in 0.9 percent sodium chloride (PlasmUp Pet). It is a synthetic colloid, synthesized from amylopectin, which is hydroxylated to prevent rapid degradation by circulating amylase. The low molar substitution (0.4) of it is the main pharmacological determinant for beneficial effects on pharmacokinetics, intravascular volume and hemodilution. A colloid is a large hydrophilic molecule in solution that does not pass freely through a semipermeable membrane. The primary use of HES solution is to increase intravascular volume during hypovolemic shock and to boost intravascular colloid osmotic pressure (COP) during hypoalbuminemic states.

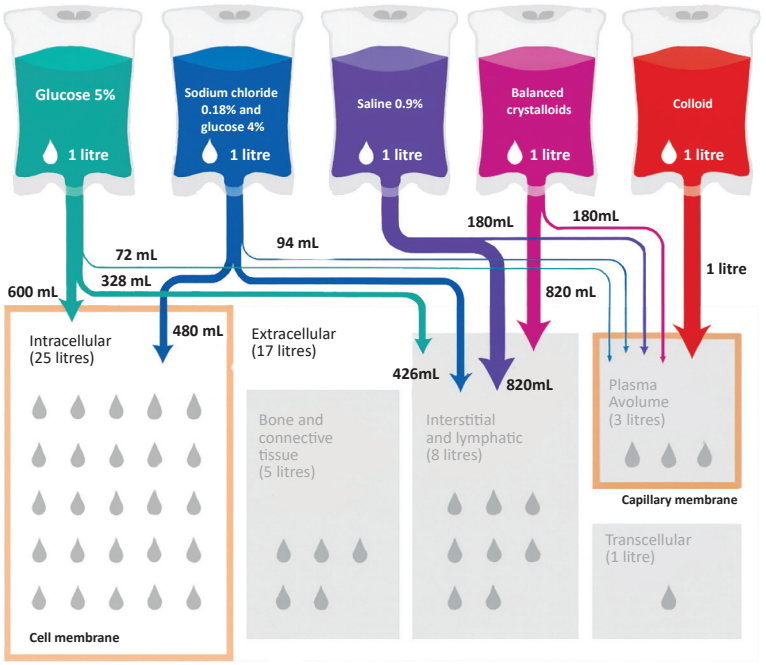


Fig. 2: Theoretical distribution of intravenous fluids on infusion

HES favor retention of intravascular fluid and prevent washout of interstitial proteins. In hypo-oncotic situations, HES infusion has a great advantage over other colloids because the larger molecules remain intravascular, limiting pulmonary fluid flux. It is nontoxic and non-allergenic in dosages as high as 100 mL/kg in dogs. Following intravenous administration 75 percent of peak concentration is recorded within 30 minutes post-infusion and decrease to 14 percent at 6 hours post-infusion. Plasma levels returns to baseline levels around 24

hours following infusion. Approximately 62 percent is excreted as hydroxyethyl starch molecules in urine within 72 hours. Pharmacokinetics remains similar following single or multiple dose administration. HES is primarily used as a plasma volume expander in intravenous therapy for volume resuscitation, COP support, hypoalbuminemia, increasing capillary permeability and sepsis support. When administered intravenously, HES mimics the action of albumin protein present in actual blood and inhibits outward flow of fluid by generating oncotic pressure due to its high molecular weight. So it doesn't get out of blood vessel and fluid remains in blood capillaries for 12-48 hours.

Assessment of Resuscitation

The ability to create an effective fluid resuscitation plan depends on an understanding of the different body fluid compartments and the dynamics of fluid movement and distribution between fluid compartments. Once the fluid therapy plan is underway, ongoing assessment is critical. If adequate fluids have been administered and reasonable resuscitation endpoints have not been reached, several causes should be considered; these variables should be rapidly assessed and corrected:

- Inadequate volume administration
- Ongoing fluid losses from hemorrhage
- Heart disease or pericardial fluid accumulation
- Severe vasodilation or vasoconstriction
- Organ ischemia
- Hypoglycemia
- Hypokalemia
- Hypocalcemia
- Arrhythmias
- Severe acidemia or alkalemia
- Anemia or hypoxemia
- Decreased venous return
- Hypothermia
- Intracranial disease
- Critical illness

An adequate fluid resuscitation plan is necessary to optimize survival. The fluid resuscitation plan should include the following steps:

1. Determine where the fluid deficit lies
2. Select fluid(s) specific for the patient
3. Determine resuscitation endpoints
4. Determine the resuscitation technique to be used

Interstitial and intracellular volume deficits (dehydration) are replaced by the administration of crystalloids. Intravascular volume (perfusion) deficits can also be replaced with crystalloids alone. However, when large quantities of isotonic crystalloids are rapidly administered intravenously, there is an immediate increase in intravascular hydrostatic pressure, a decrease in intravascular

COP, and extravasation of large fluid quantities into the interstitial spaces. By administering colloids in conjunction with crystalloids during fluid resuscitation of perfusion deficits, less total fluid volume is required (crystalloids reduced by 40-60%), there is less tendency toward fluid overload, and resuscitation times are shorter.

A comprehensive examination of fluid therapy in Veterinary medicine is necessary for those looking to provide the best possible care to their patients. This includes a thorough understanding of the various types of fluids available, indications for their use, and the potential complications that can arise.

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