CHAPTER 1

Introduction to Acid-Base and Electrolytes

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Understanding of acid-base and electrolyte chemistry and physiology is both an important and valuable knowledge base for all veterinary technicians, and especially those in emergency and critical care or specialty practice. These very topics, however, are frequently thought of as boring at best or utterly confusing at worst. In actuality neither is true. These topics are often approached in a piecemeal or qualitative way, which lends itself to confusion. It is the goal of this text to provide a useful, easy-to-learn, and practical approach to the concepts regarding acid-base and electrolytes.

Introduction to acid-base

Assessment of acid-base status provides insight into three physiologic processes: alveolar ventilation, acid-base status, and oxygenation. Evaluating acid-base status has become an integral part of the emergent/critical care patient workup and should be performed as a baseline on all emergent patients. Deviation from normal acid-base balances is indicative of clinical disease processes and can aid the clinician in identifying underlying causes of illness in the patient. Venous samples can provide most of the information needed regarding acid-base status and even alveolar ventilation. Arterial samples are required, however, in order to provide oxygenation status (Sorrell-Raschi 2009). It is ever more important for the emergency and critical care (ECC) technician to be familiar in his/her understanding of acid-base values and what they mean.

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What is acidity?

In the simplest of terms, the acidity or alkalinity of a solution is based on how many hydrogen (H^+) ions, or molecules of carbon dioxide (CO_2), are present. Hydrogen ions are produced daily as a normal part of metabolism of protein and phospholipids, and are considered a fixed, non-volatile acid. Carbon dioxide is a byproduct of the metabolism of fat and carbohydrates in the body, and is considered a volatile acid (volatile = readily vaporized). Gaseous CO_2 is soluble in water. CO_2 is considered an acid because it readily combines with H_2O in the presence of carbonic anhydrase (enzyme/catalyst) to form carbonic acid (H_2CO_3). Without the catalyst, this change occurs very slowly. CO_2 is continually removed by ventilation and thereby kept at a stable partial pressure (pCO_2) in the body. The change in dissolved CO_2 in body fluids is proportional to pCO_2 in the gas phase. Elimination of these acids is dependent on the function of the lung, kidney, and liver.

Bronsted and Lowry state an acid is a proton donor (H^+) and a base is a proton acceptor (A^-) (DiBartola 2006: 229). The H^+ concentration ($[H^+]$) of body fluids must be kept at a constant level to prevent detrimental changes in enzyme function and cellular structure. Levels compatible with life are between 16 and 160 nEq/L. Excessive hydrogen ions in the blood result in acidemia. Decreased hydrogen ions in the blood result in alkalemia (Kovacic 2009). Hydrogen ions are not typically measured or tested in clinical practice. Therefore, Sorenson developed pH notation in order to provide simpler notation of the wide range of $[H^+]$ (DiBartola 2006: 229). There is an inverse relationship between pH and $[H^+]$ (Ex: $\uparrow[H^+] \rightarrow \downarrow pH$). Normal pH ranges between 7.35 and 7.45, approximately. The processes which lead to changes in production, retention, or excretion of acids or bases, which may or may not result in a change in pH, are called acidosis or alkalosis.

Buffering systems

The body contains several mechanisms in order to maintain the desired “normal” pH level, which is called buffering. A buffer is a compound that can accept or donate protons (H^+) and minimize a change in pH. Buffers consist of a weak acid and its conjugate salt (Sorrell-Raschi 2009). If a strong acid is added to a buffer, the protons from the acid dissociate to the salt of the buffer and the change of pH is therefore minimized. With these buffers the body is continually converting CO_2, H_2O, H^+, and HCO_3^- to maintain pH within normal ranges. The following equation represents this constant interaction:

$$CO_2 + H_2O \leftrightarrow H^+ + HCO_3^-$$

There are several compounds that serve as buffers in the body. The primary buffer of extracellular fluid (ECF) is bicarbonate (HCO_3^-). Non-bicarbonate buffers consist of proteins and inorganic and organic phosphates, which are primarily intracellular fluid (ICF) buffers. Bone is a prominent source of buffer (calcium carbonate and calcium phosphate). Up to 40% of buffering can be done from resources found in bone. Upon treatment/administration of sodium bicarbonate ($NaHCO_3^-$), carbonate that has been released to buffer can then be deposited back into the bone. In the blood, proteins, including hemoglobin and plasma, serve as buffers. Hemoglobin constitutes 80% of the buffering capacity of blood, whereas plasma proteins only account for 20% of buffering in the blood.

The body's buffering system is considered an open buffering system, with both bicarbonate and carbonic acid systems. In a closed system the exchanges would have to occur in a reciprocal manner. Since the body eliminates the majority of CO_2 through ventilation, keeping pCO_2 constant, a reciprocal reaction does not have to occur, which allows the body's buffering systems to be considered open. Both hydrogen ion excretion and bicarbonate regeneration are regulated by the kidneys.

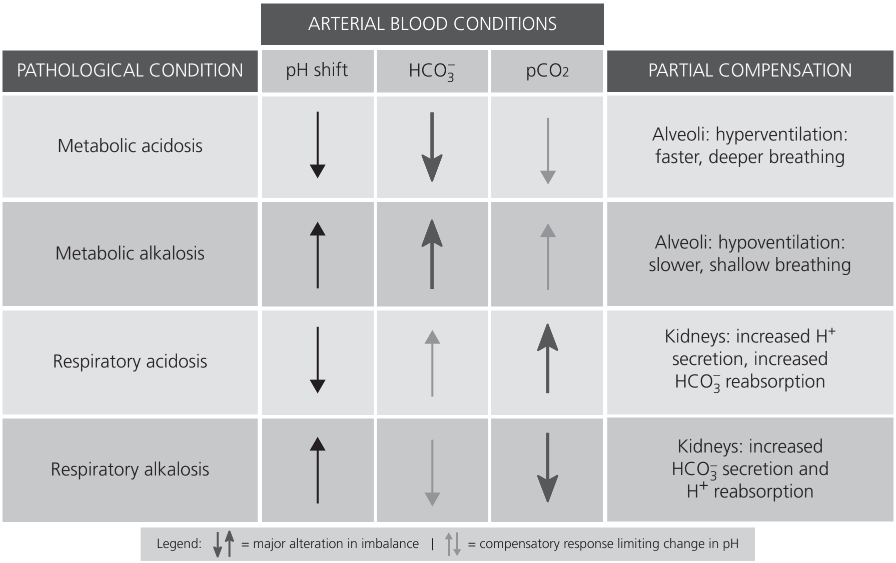
Physiologic response system

The balance of acid-base in the body is regulated by metabolic, respiratory, and renal pathways. In terms of acid-base discussion, generally either a metabolic or a respiratory derangement occurs with the renal or respiratory system compensating for either/both.

When an excess of H^+ ions occurs, this causes a decrease in pH. Within minutes of this imbalance, the hydrogen ions begin to titrate with bicarbonate ions in ECF and then titrate with ICF buffers in order to minimize changes in pH. Next, alveolar ventilation is stimulated in order to decrease CO_2 until levels are below normal, thereby raising the pH back up to near normal. Within hours (2–3 days peak effect), the renal system begins to regenerate HCO_3^-. As HCO_3^- is increased, the body's pH is increased. Alveolar ventilation no longer needs to be increased, so returns to normal rates, restoring pCO_2 levels to normal.

CO_2 concentrations are a balance of mitochondrial production and alveolar removal by ventilation. An excess of CO_2 (in excess of ventilatory regulation) cannot be buffered directly by HCO_3^-. CO_2 is converted to carbonic acid by the mechanisms described above, which then allows H^+ from carbonic acid to titrate with intracellular buffers (proteins/phosphates). The renal system also adapts by increasing HCO_3^- reabsorption (2–5 days peak effect).

There is a variety of terms that can be used to describe acid-base imbalances, including: acidosis, alkalosis, acidemia, and alkalemia. While it may seem overly technical, knowing the differences between the terminologies can be important. The terms acidosis/alkalosis refer to the pathophysiologic processes that cause the net accumulation of acid or alkali in the body. The terms acidemia/alkalemia refer to the actual change in pH of ECF. In cases of acidemia, the pH is lower than normal, or <7.35 ($\uparrow[H^+]$). With alkalemia, the pH is higher than normal, or >7.45 ($\downarrow[H^+]$). For example: a patient with chronic respiratory acidosis may have normal pH due to renal compensation. The patient has acidosis, but not acidemia. Mixed acid-base disorders may also have an overall normal pH, due to one counter-balancing the other (Murtaugh 2002). These concepts will be covered in more detail in subsequent chapters.



	ARTERIAL BLOOD CONDITIONS			
PATHOLOGICAL CONDITION	pH shift	HCO_3^-	pCO_2	PARTIAL COMPENSATION
Metabolic acidosis	↓	↓	↓	Alveoli: hyperventilation: faster, deeper breathing
Metabolic alkalosis	↑	↑	↑	Alveoli: hypoventilation: slower, shallow breathing
Respiratory acidosis	↓	↑	↑	Kidneys: increased H^+ secretion, increased HCO_3^- reabsorption
Respiratory alkalosis	↑	↓	↓	Kidneys: increased HCO_3^- secretion and H^+ reabsorption

Legend: ↓↑ = major alteration in imbalance | ↑↓ = compensatory response limiting change in pH

Figure 1.1 Arterial blood gases chart.

Primary acid-base disturbances

There are four primary acid-base disturbances that may occur in the body: metabolic acidosis, metabolic alkalosis, respiratory acidosis, and respiratory alkalosis. When evaluating a patient's acid-base status, the following parameters are primarily needed: pH, HCO_3^- (or TCO_2), and pCO_2 (Figure 1.1). If blood gases, or oxygenation, are being evaluated on an arterial blood sample, then PaO_2 values are also provided. Simple acid-base analysis may be done on either venous or arterial blood samples. Arterial samples are mandatory if one is attempting to assess the oxygenation status of a patient.

These imbalances will be discussed in greater detail throughout the chapters of this text, as well as practical approaches and applications for day-to-day practice.

Introduction to electrolytes

Just as fluid imbalances can affect the patient's electrolyte balance, electrolyte imbalances can, in turn, result in fluid imbalances, as well as a host of other problems. Imbalances involving sodium, potassium, chloride, calcium, phosphorus, and magnesium can all result in potentially life-threatening problems for animals. It is imperative for technicians to understand the role of electrolytes in the body and recognize the signs of imbalances in these electrolytes in order to aid in the quick recognition, diagnosis, and treatment of these problems. In this section we will introduce electrolyte physiology and regulation in the body, and specific and greater detail on each is covered in its respective chapter.

General electrolyte physiology (Table 1.1)

Electrolytes are substances that ionize when dissolved in ionizing solvents, such as water. An example would include salt, or sodium chloride (NaCl), which when dissolved in water ionizes to form Na^+ and Cl^- ions. A positively charged ion is called a cation (example Na^+) and a negatively charged ion is called an anion (example Cl^-). Electrolytes, in their ionic form, are extremely important in the body as they promote cardiac and neurologic impulse transmissions, regulate water balance, assist in skeletal muscle contraction, regulate acid-base balance, maintain oncotic balance (albumin), and provide concentration gradients for glomerular filtration in the kidney, among many other functions (Table 1.2).

Typically the body's electrolytes are distributed intra- and extracellularly, and it is important to understand in which compartment they mostly reside. Sodium, the body's primary and most abundant cation, resides extracellularly. In addition, sodium's counterpart, chloride, and bicarbonate reside mainly

Table 1.1 Common electrolytes and their charges

Name	Chemical symbol	Charge	Anion/Cation	Role in the body
Sodium	Na^+	1^+	Cation	Nervous/cardiac impulse transmission Water balance
Chloride	Cl^-	1^-	Anion	Water balance Acid-base balance
Potassium	K^+	1^+	Cation	Nervous/cardiac impulse transmission
Magnesium	Mg^{2+}	2^+	Cation	Co-factor in enzymatic processes
Phosphorus/ Phosphate	PO_4^{3-}	3^-	Anion	Acid-base buffer Biochemical reactions
Bicarbonate	HCO_3^-	1^-	Anion	Acid-base buffer
Calcium	Ca^{2+}	2^+	Cation	Skeletal/cardiac muscle contraction
Lactate	CH_3CHCO_2H	1^-	Anion	Byproduct of anaerobic metabolism

Table 1.2 Average intracellular/extracellular electrolyte concentrations

Electrolyte	Average serum concentration (mEq/L)	Average intracellular concentration (mEq/L)
Sodium	142	12
Potassium	4.3	140
Chloride	104	4
Bicarbonate	24	12
Magnesium	1.1	34
Phosphate	2.0	40
Calcium	2.5	4

extracellularly. The abundant intracellular electrolytes include: potassium, calcium, magnesium, and phosphorus/phosphate.

Units of measure

Electrolytes are typically measured in mEq/L, or milliequivalent weight per liter, but can also be expressed as mg/dL or milligrams per deciliter. The milliequivalent weight (or mEq/L) represents the atomic, molecular, or formula weight of a substance divided by its valence. The valence number of a substance refers to the net number of charges it accumulates when it ionizes. For example, calcium, as Ca^{2+}, would have a valence of 2; chloride, as Cl^-, would have a valence of 1. Using sodium as an example, since it has a 1^+ charge its valence number is 1. That means each millimole of sodium provides 1 mEq of sodium, because we are dividing the ionic weight by 1. Atomic, molecular, and formula weights and other units of measure are summarized in Table 1.3. In the case of magnesium, because its valence number is 2, each millimole would contribute in reality 0.5 mEq because we would divide by a valence of 2. This simply provides a reasonable unit of measure when dealing with substances that exist in very large quantities in the body. As some electrolytes are typically measured or reported in concentrations

Table 1.3 Units of measurement of electrolytes

Unit of measure	Definition
Atomic mass Example: $^{12}C = 12.000$	Unitless measure of weight which is an average of all the isotopic weights of a substance. It is typically reported in the periodic table of the elements. For example, C is typically reported as ^{12}C and weighs 12.000
Molecular mass Example: $H_{2O} = 18$	The weight of a molecule (combination of atoms) represented by the addition of their combined atomic weights. For example: H_2O has a molecular mass of 18 because O has an atomic mass of 16 and H has an atomic mass of 1 (which is doubled by the presence of two H molecules)
Formula weight Example: $CaCl_2 = 111$	This is similar to molecular mass but typically is discussed in the case of ions. Since ions dissociate in a solvent, this term is used. Example: calcium chloride is $CaCl_2$ and has a formula weight of 111. This comes from calcium's weight of 40 + 2× chloride's weight of 35.5
Mole	A unit of measure for a large number of particles. 6.02×10^{23} particles of a substance = 1 mole of that substance
Molar mass	This term refers to the weight in grams of 1 mole of a substance. For example, 1 mole of sodium (which is 6.02×10^{23} sodium ions) weighs 23 grams
Millimole/milligram	This represents one-thousandth (10^{-3}) of a mole or a gram
Valence Example: Ca^{2+} = valence of 2	A number representing the number of charges an ion has. Example: Ca^{2+} has a valence of 2; Cl^- has a valence of 1
Milliequivalent (mEq)	This is a measure of an ion's millimolecular weight divided by its valence

(such as mg/dL) these units can be converted back and forth. Phosphorus has an approximately normal plasma concentration of 4 mg/dL. Its average valence, because it exists in several forms, is 1.8. The molecular weight of phosphorus is 31. The equation to convert mg/dL to mEq/L is:

$$\frac{mEq}{L} = \frac{\frac{mg}{dL} \times 10}{molecular\ weight} \times valence$$

So our equation becomes:

$$\frac{mEq}{L} = \frac{4 \times 10}{31} \times 1.8 = 2.3\,mEq\ /\ L$$

Although not terribly important to commit to memory, a basic understanding of the units used to report electrolytes is essential in forming a foundation for interpreting them clinically.

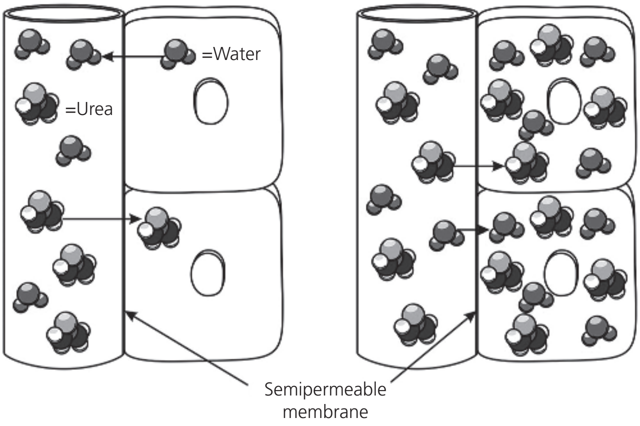
Osmolality and osmolarity

A fundamental concept in electrolyte physiology is understanding how electrolytes affect fluid movement across membranes (tissue, cellular, etc.). This is described in the concept of osmolality. Osmolality describes the number of osmoles per kilogram of solvent, and osmolarity represents the number of osmoles per liter of solvent. An osmole is a measure of the solutes in a solution that exert an osmotic effect and typically is represented as 1 Osm is equal to 1 gram of molecular weight, which also indicates 6.02×10^{23} particles from the definition of a mol. This would be the case of a molecule that does not dissociate in the solution. In the case of NaCl, which dissociates into Na^+ and Cl^-, a millimole of NaCl would contribute 2 mOsm (milliosmole) (1 mOsm of Na^+ and 1 mOsm of Cl^-). In biologic fluids osmolarity and osmolality are used interchangeably and for the sake of uniformity osmolality will be used going forward in this chapter.

The total osmolarity of a solution represents the number of osmoles present in a solution. This can be measured in serum in a clinical patient and is typically between 300 and 310 mOsm/kg in the dog and cat. Hyper- and hypo-osmolar conditions can arise and are beyond the scope of this chapter but will be discussed in future chapters in this textbook.

Since osmoles exert an osmotic effect, they can affect fluid balance and movement in a solution with a membrane. Osmosis is defined as a spontaneous movement of a solvent (fluid) across a semi-permeable membrane from a region of lower solute concentration (solid) to a region of higher solute concentration. This movement will cause an equilibrium in the concentrations of solutes on either side. For example, imagine a beaker with a thin membrane dividing it into two halves. One each side there is a solvent (liquid) of equal volume, and one adds sodium chloride (salt) to the right side. Now on the right

Ineffective osmole



Effective osmole

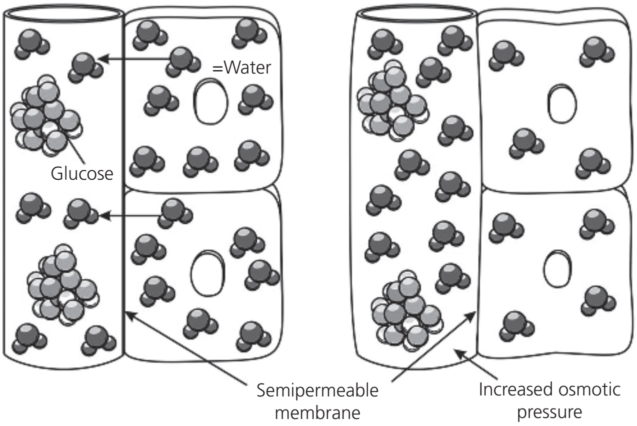


Figure 1.2 Effective and ineffective osmoles.

side there is much solute compared to the left side and this means it is highly concentrated on the right and dilute (low concentration) on the left. Thus, the water will move from the diluted left side (with more solvent than solute) to the more concentrated right side (with more solute than solvent) creating an equilibrium of solute:solvent on each side. This is depicted in the upper portion of Figure 1.2.

This concept is extremely important in physiology, as the body has several of these membranes. Of note are the cellular membrane and the capillary membrane. For a thorough discussion of the anatomy of these, the reader is directed to a physiology textbook, but water and fluid must remain outside of a cell, inside of a cell, outside of a capillary (in tissue) and inside a capillary (blood volume) in appropriate proportions or disease ensues.

Also, not all osmoles are created equal. Some, although called osmoles, can traverse a physiologic membrane and thus do not exert an osmotic effect. These are called ineffective osmoles and lie in contrast to effective osmoles that will pull the solvent across the membrane. An example of an ineffective osmoles is urea: where urea could exert an osmotic effect in the laboratory, in the body urea can pass through the pores of a semi-permeable cellular membrane thereby creating an equilibrium of solute, causing no net movement of solvent across the membrane. This is demonstrated in the lower portion of Figure 1.2. Effective osmoles have a special name for their measure in bodily fluids. This is referred to as the tonicity. The tonicity of a solution is the measure of the effective osmolarity. So in a solution with tonicity fluid will move across the semi-permeable membrane when an effective osmole is added. One such example is sodium. Sodium is an effective osmole in the body, and solutions where there is more sodium relative to the concentration of solvent are referred to as hypertonic, and solutions where the solute (sodium) concentration is less than the solvent are called hypotonic. When solvent:solute concentrations are equal that is called an isotonic solution.

Fluid movement across bodily compartments/membranes

In order to fully understand disorders of sodium and chloride, the veterinary technician needs to comprehend the idea of fluid movement across membranes that reside in the body. Fluid is maintained in several different compartments, including the ICF compartment and the ECF compartment. The ECF compartment is then divided into interstitial fluid (ISF) and intravascular fluid (IVF) compartments. The cell membrane divides the ICF and the ECF compartments and the capillary membrane divides the IVF from the ISF compartments. Osmotically active particles will largely determine the fluid balance across the cell membrane which maintains the balance between the ICF and ECF compartments. In this case, these effective osmoles are not easily or at all permeable to the cell membrane and thus exert the concentration effect drawing fluid either in or out of the cell across the membrane. Sodium, potassium, chloride, bicarbonate, glucose, and to some extent urea can all affect osmolality and fluid balance. Gain or loss of these osmoles from the extracellular or intracellular space, or gain or loss of fluid on either side, will create a ripple effect, causing net movement of fluid in or out of the cell across the cell membrane. Further descriptions of these effects are found later in this textbook.

Movement of fluid across the capillary membrane is quite different. Although not fully understood, the idea of Starling's forces remains the major theory to describe net fluid movement from the interstitial space into or out of the capillary or into and out of the tissue space. Starling's equation is:

$$\text{Net filtration} = K_f\left[\left(P_{cap} - P_{if}\right) - \left(\pi_{cap} - \pi_{if}\right)\right]$$

While seemingly daunting at first, this equation simply describes how fluid moves across the capillary membrane. The net filtration, if positive, means fluid extravasates out of the capillary and if negative means fluid moves into the capillary.

K_f = Filtration coefficient, describes the permeability of the capillary wall

P_{cap} = The hydrostatic pressure inside the capillary (fluid pressure), will tend to drive fluid out of the capillary if elevated

P_{if} = The hydrostatic pressure of the tissues, will tend to drive fluid into the capillary if elevated

π_{cap} = The oncotic pressure in the capillary. This is the pressure generated by plasma proteins (negatively charged) attracting water toward them and thus tending to draw water into the capillary and keeping it there.

π_{if} = Represents the oncotic pressure in the tissues. This tends to exert a pressure maintaining water inside the tissue (interstitial) space.

Disturbances in Starling's law demonstrate why fluid would move out of the capillary space, causing edema, or potentially into the capillary space, causing hypervolemia. If the capillary hydrostatic pressure increases, as caused by congestive heart failure in pulmonary capillaries, water will tend to move out of the capillary and into the interstitial space, thus causing pulmonary edema. If plasma protein concentration drops, such as in hypoproteinemia or hypoalbuminemia, the capillary oncotic pressure drops as well. As this pressure tends to maintain water within the capillary space, when it is not present water will tend to leak out of the capillary and into the tissue bed, also causing edema.

The anion gap

The anion gap is a concept that will be discussed in later chapters in reference to acid-base. As electrolytes have charges and affect fluid balance, disturbances in them can be responsible for causing acid-base conditions. The anion gap can help identify if certain electrolytes are responsible for the acid-base condition, or illuminate other causes. The body exists in a state of electroneutrality, meaning all electrolyte charges sum to zero. All cation charges (positive) when added to all anion charges (negative) are equal and thus maintain a 0 net charge in the body. However, routine analyzers don't measure all known anions and cations. So trying to identify total concentrations of all electrolytes becomes challenging. For example, only sodium and potassium, and chloride and bicarbonate, are routinely measured. Even if phosphorus, magnesium, and lactate are measured, there are still ions that are unaccounted for. Due to limits of technology, analyzers tend to analyze more cations than anions, meaning more anions are not measured in clinical assays. This leads to an overabundance of anion charges/

measures that are not accounted for routinely. If unmeasured anions (UAs) and unmeasured cations (UCs) are represented in a total neutrality equation, one can develop an equation accounting for these unmeasured, yet biologically active, ions.

1 Total cations should equal total anions: $Na^+ + K^+ + UC = Cl^- + HCO_3^- + UA$
2 Rearranging: Measured cations – measured anions = UA – UC = anion gap
3 Final: $(Na^+ + K^+) - (Cl^- + HCO_3^-) = UA - UC$

The result of the third equation will yield a number representing how many more UAs there are than UCs. For example, if lactate (typically a UA) is high, it will make the UA value in the third equation much higher, yielding an elevated anion gap. More on this in later chapters.

Fluid maintenance and loss basics

Although mainly about electrolytes and acid-base, this textbook will cover some measure of discussion on fluids, fluid balance, and gain or loss in the presence of disease. As electrolytes affect fluid balance across compartments, as discussed above, alterations in gain or loss of fluid will also exert osmotic and fluid-moving effects.

Typically, the body exists in a state of equilibrium of fluid movement, called homeostasis. Fluid is lost and gained in equal proportions to maintain hydration and blood volume. All gains and losses end up totaling to zero, meaning no net gain or loss. A gain of fluid is called a positive fluid balance and a loss of fluid is called a negative fluid balance. These can occur in disease states.

Fluid or water loss is described as sensible or insensible. Sensible losses are those that can be measured or quantified easily, and insensible losses are those that must be estimated. Water lost in urine, feces, or saliva is typically called sensible loss and can be measured. Insensible losses include sweating and evaporative losses from the skin and respiratory tract.

Water lost through the kidney (sensible urinary water loss) can take two forms: water with solute (called obligatory water loss), which helps maintain solute balance in the kidney and body, and water without solute (simply H_2O, also called free water loss) which is generated through the action of vasopressin/antidiuretic hormone (ADH) on the kidney. Remember the examples of sodium and water in a beaker with a membrane? The loss of water through the kidney can effectively change sodium or water concentrations in the body. If water and sodium are lost in equal proportions through the kidney (obligatory water loss), all concentrations remain the same. But if free water (simply H_2O) is lost, a concentration gradient is established because the water on one side of the membrane (in this case outside of the cell) is depleted of water but still has sodium. This becomes a hypertonic solution. The same situation could occur if water was lost in great amounts through respiratory or evaporative means. This will cause disease in the body and will be discussed in more detail in later chapters.

Conclusion

Understanding these general concepts of acid-base balance and electrolyte/fluid physiology in the body are essential to move on to later chapters in this text. The veterinary technician cannot understand hypertonic fluid loss in the presence of hypernatremia, or hyperosmolar states or triple acid-base disorders without first mastering the basic physiologic concepts discussed here. Once these concepts are fully understood, alterations in electrolyte or acid-base balance will make sense and allow the veterinary technician to fully comprehend the complex physiologic alterations occurring during the disease conditions. Although confusing and sometimes frustrating, having a strong foundation in electrolyte and acid-base conditions is essential for the veterinary technician working with sick and injured patients. Electrolyte and acid-base abnormalities affect all species, ages, breeds, and disease conditions and can cause life-threatening alterations in heart rate, cardiac conduction, blood pressure, and nervous transmission. The veterinary technician must be ready to quickly identify abnormalities, alert the attending veterinarian, and apply rapid treatment to stabilize the critically ill veterinary patient.

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