Fluid and Electrolyte Balance

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Abstract

Many of the body's cellular operations use water as a medium. When water intake equals water loss, the body's water equilibrium is maintained. Water disperses throughout the body in distinct compartments. Several factors influence the distribution of water in different fluid compartments. Water and electrolyte intake and outflow are more strictly regulated to maintain total body water and total body osmolarity. Water intake is controlled by water consumption, whereas water loss is controlled by urine output. Electrolytes serve a critical function in controlling bodily water content, distribution, and osmolarity. Calcium, sodium, chloride, and bicarbonates are the major electrolytes in extracellular fluid; potassium, magnesium, phosphates, proteinates, and sulphates are the major electrolytes in intracellular fluid. Sustaining acid-base balance is another essential part of maintaining homeostasis. The chemical buffer system, respiratory system, and renal system are the three primary systems that manage the acid-base balance in the body. Clinical disorders impacting hydration, acid-base balance, and electrolyte status can have serious, even life-threatening repercussions; therefore, it is critical to recognise and treat them.

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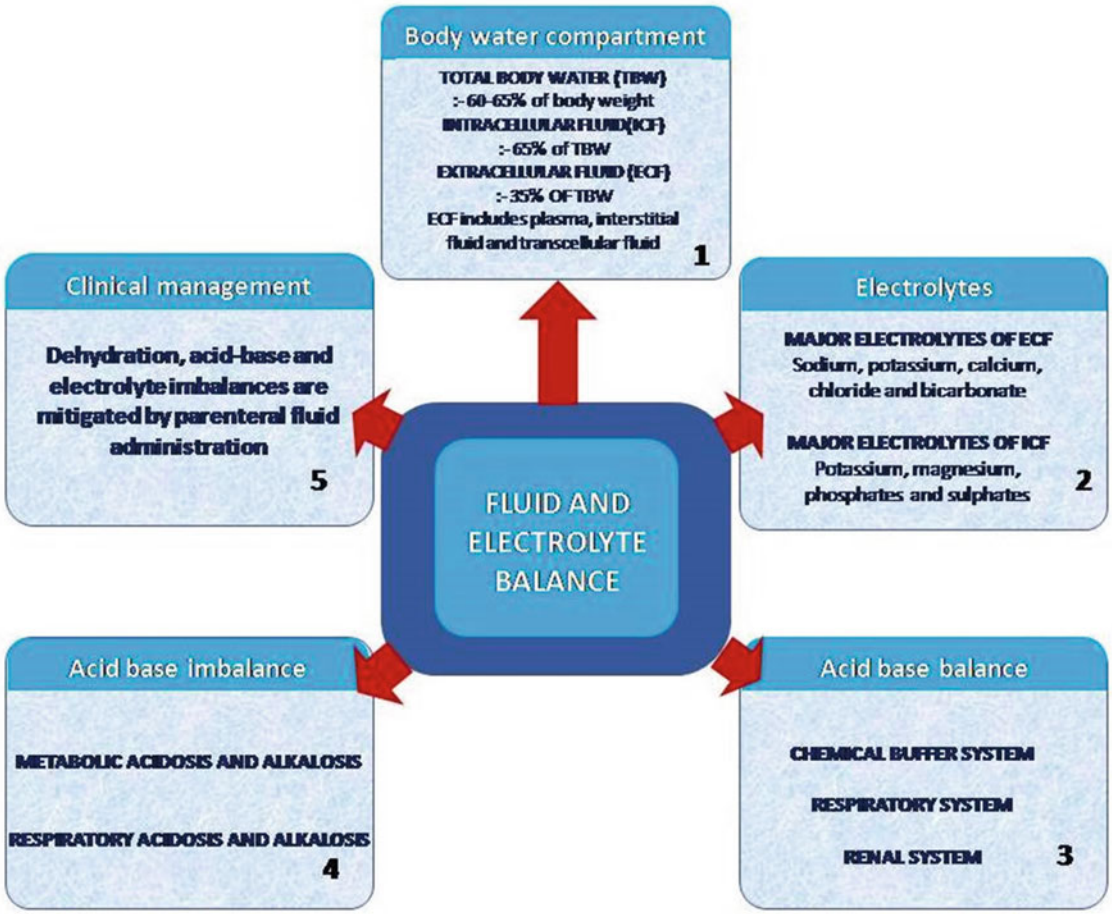
Graphical Abstract



Description of the graphic: Total body water (TBW) constitutes 60–65% of body weight (**1**). About 65% of TBW is ICF and 35% is ECF. Electrolytes are differentially distributed with respect to the concentration in both ECF and ICF, sodium being the major extracellular cation and potassium being the major intracellular cation (**2**). Along with the chemical buffer system, respiratory and renal systems are also involved in the acid-base regulation of the body (**3**). Respiratory or metabolic alterations can cause acidosis or alkalosis (**4**). Clinical management by parenteral fluid administration is decided by the level of dehydration, pH, and electrolyte imbalance (**5**)

Keywords

Acid-base balance · Electrolytes · Dehydration and fluid therapy · Total body water · Transcellular fluid

Learning Objectives

- To know about the different body water compartments and regulation of water balance
- The physiological importance of electrolytes and various causes of electrolyte disturbances
- Different types of transcellular fluids and their physiological importance
- Various systems involved in maintaining acid-base balance
- Causes for acid-base balance disturbances
- Clinical management of dehydration, acid-base imbalance, and electrolyte disturbances

8.1 Water, Electrolytes, and Body Fluids

8.1.1 Introduction

Osmoregulation is **osmotic balance** maintained across membranes within the body's fluids. Osmotic balance is contributed by the electrolytes and non-electrolytes.

Electrolytes* are the** solutes that dissociate into ions during water dissolution, and ***non-electrolytes do not dissociate into ions during water dissolution. Electrolytes in living systems include zinc, sodium, potassium, magnesium, chloride, copper, bicarbonate, manganese, calcium, iron, phosphate, molybdenum, and chromium. Sodium, bicarbonate, phosphate, potassium, calcium, and chloride are the major electrolytes involved in various body functions. These electrolytes perform a variety of functions in the animal body such as transmission of electrical impulses in neurons and muscles, release of hormones, stabilisation of protein structure, acid-base regulation, and also osmoregulation of body fluids. The hydrostatic pressure and osmotic pressure control the movement of water along the cell membrane. Among these two physical factors, osmosis can only be directly controlled by the movement of electrolytes. Maintenance of an electrical and chemical balance within and outside the cell is accountable for an electro-chemical gradient existing between extracellular and intracellular fluids. This gradient is actually made use of in the movement of electrolytes and also in the movement of water across the cellular compartments.

Osmoconformers are organisms that maintain their internal salinity same as their environment (e.g., most marine invertebrates). *Osmoregulators* tightly maintain body osmolarity even after fluctuations in salt levels in the environment and are more common in the animal kingdom.

Osmosis is a physical process, by which diffusion of water occurs across a semipermeable membrane, from an area of high water potential (low solute concentration) to an area of low water potential (high solute concentration) without input of energy. The force per unit area that halts osmosis is called the *osmotic pressure* of the solution. Colloid osmotic pressure, also known as plasma oncotic pressure, is the effective osmotic pressure exerted by plasma proteins on fluid flow between the two compartments. A colloid is a term that refers to the big molecular weight (MW >30,000) particles that are present in a solution. Plasma proteins are the most common colloids found in plasma. The osmotic pressure of a solution is a colligative feature. It is determined by the number of particles dissolved in a unit volume of solvent, not by the particle's valence, weight, or shape. Because most biological membranes are semi-permeable, osmosis is vital in living systems. Large-molecule solutes, such as polysaccharides, are impermeable, but water and tiny, uncharged solutes are permeable. The number of molecules of dissolved particles is represented by the osmole. Each osmole (Osm) has 6.023×10^{23} molecules since one osmole is defined as 1 g molecular weight of any non-dissociable material. (According to Avogadro's law, 1 mol of any substance contains the same number of particles 6.023×10^{23}, independent of its molecular weight.) *Osmolarity* is the measure of solute concentration in 1 L solution (osmol/L). The osmoles of solute per kilogramme of solvent (osmol/kg) are a measure of osmolality. However, unlike osmolarity, osmolality is the preferred physiological term because it is unaffected by the temperature of the solution. Weight is a temperature-independent variable, whereas volume is dependent on temperature. Electrolyte concentrations are commonly represented in terms of milliequivalents per litre (mEq/L), which is equal to the ion concentration (in millimoles) multiplied by the number of electrical charges on the ion. Since electrolytes create ions in aqueous solutions, the milliequivalent unit takes into account the ions present in the solution as well as the charge on the ions. One milliequivalent is equal to 1 millimole for ions with a charge of one, and one milliequivalent is equal to 0.5 millimoles for ions with a charge of two (such as calcium). The milliosmole (mOsm), which is the number of milliequivalents of solute per kilogramme of solvent, is another unit for expressing electrolyte concentration. The osmotic pressure of body fluids is normally kept between 280 and 300 mOsm.

When a solution has a higher concentration of solute than a solution with a lower concentration of solute, it is referred to as hyperosmotic. If two solutions are having the same solute concentration, they are said to be isosmotic.

Tonicity is determined by the number of solutes that cannot penetrate the membrane and the effective osmotic pressure gradient. To put it another way, tonicity refers to the relative concentration of dissolved solutes in a solution that determines the direction and extent of diffusion. It describes what a solution would do to a cell's volume at equilibrium if the cell was placed in the solution. The solutes that are unable to penetrate the cell dictate the tonicity of an infused solution. As a result, the terms isosmotic, hyperosmotic, and hyposmotic are not interchangeable with tonic, hypertonic, and hypotonic. Isosmotic refers to the osmolalities of various physiological fluids having the same value, such as plasma versus cerebrospinal fluid. The terms *isotonic*, *hypotonic,* and *hypertonic* are used to describe the osmolalities of solutions used in clinical practice to restore bodily fluid losses. When compared to plasma, a hypertonic solution has a higher effective osmotic pressure. A hypotonic solution has lower effective osmotic pressure compared to plasma. A solution having effective osmotic pressure identical to that of plasma is called isotonic solution. Plasma has an osmolality of 0.3 Osm or 300 mOsm. 0.15 M solution of NaCl is equal to 0.3 osmol solution because NaCI ionises into two ions, Na^+ and Cl^-; half the molar NaCI (0.15) solution contributes to 0.3 osmole. Isotonic saline solution for clinical applications is prepared with sodium chloride concentration of 9 g/L of water or 0.9% (w/v), i.e. 0.167 M NaCI.

If water or hypotonic saline is added to extracellular fluid (ECF) or plasma, the osmotic concentration of this compartment is lowered and water moves into cells—this may interfere with normal metabolism of cells or may even lead to

death of cells—this over-hydration is known as *water intoxication*. When isotonic saline solution is given to ECF, it spreads evenly throughout the ECF but has no effect on ICF. When a hypertonic saline solution is added to ECF/plasma, the osmotic concentration of ECF rises, and water moves from within the cells (ICF) to ECF; however, the cell membrane is less permeable to sodium ions, so sodium ions accumulate within the cells, raising intracellular osmotic pressure; this is known as *cellular dehydration*.

8.1.2 Body Water Compartments

Water is the most important component of life and the body's main component. The body's water is divided into compartments separated by a selectively permeable membrane. The chemical composition of these compartments varies. The compartments are as follows: Intracellular fluid (ICF) is the water contained within the cells and accounts for approximately (two-thirds of body water) 65% of total water; extracellular fluid (ECF) is the water outside the cells and accounts for approximately (one-third of body water) 35% of total water. Intravascular fluid or plasma (one-fifth of ECF), interstitial fluid (four-fifths of ECF), and transcellular fluid make up extracellular fluid. The fluid that surrounds the cell is known as interstitial fluid. The fluid contained in body cavities such as cerebrospinal, peritoneal, synovial, ophthalmic fluids, and fluids in the gastrointestinal system (which is the major component in ruminants) is known as transcellular fluid ("third space," which is generally neglected in calculations). Urine and bile are also considered as transcellular fluids.

8.1.2.1 Total Body Water (TBW)

The sum of water in intracellular and extracellular body compartments is referred to as total body water. It is influenced by factors, like species, age, size, gender, and nutritional status. Water makes up 60–65% of the body weight of an adult animal with little fat. Water makes almost 70% of a lean cow's body weight, but it makes up just approximately 40% of a fatty cow's. Water content is highest in newborn and lowest in aged adult animals. Males have higher water content than females. About 60% of body weight is considered water in adult males and 55% in adult females. Water makes up around 75% of the weight of lean muscle tissue. Water makes up 95% of blood, 14% of body fat, and 22% of bone. Skin also contains much water.

Out of 60% TBW, intracellular fluid accounts for 40% of total body weight, whereas extracellular fluid accounts for 20%. The amount of water in each of these compartments is controlled by the body. To keep the amount of water in each compartment generally constant, water is transported across most of the cell membranes as needed.

8.1.2.2 Water Balance

Homeostasis (coined by W. B. Cannon) is the existence and preservation of stability within the internal environment. The term internal environment or internal milieu was put forth by Claude Bernard. When daily water intake equals daily water loss, the body's water equilibrium is maintained. In most cases, the body's water content varies very little.

Ingestion and metabolic water (end product of cellular metabolism) provide water to the body. One gram of carbohydrate, fat, and protein on oxidation supplies 0.6 mL, 1.1 mL, and 0.4 mL of water, respectively. Metabolic water provides 5–10% of total body water requirements. The importance of metabolic water in many desert rats cannot be overstated. It may provide 100% of their water consumption, allowing them to subsist on dry food and no water. One of the examples is the kangaroo rat.

Water is lost from the body through various routes like urine, skin, expired air, faeces, and milk (lactating animals). The body's natural regulatory mechanism regulates water losses through several routes in order to maintain equilibrium (Table 8.1).

8.1.2.2.1 Regulation of Water Intake

Water intake is intermittent, whereas water loss is continuous. A gradual dehydration problem is constantly present in an animal's life. The osmolarity in all fluid compartments is almost equal. It ranges from 301.5 to 303 mOsm/kg of water in human. Water will be shifted from the cell into the ECF during gradual dehydration since the ECF is the immediate source of water loss. Water ingestion is used to replenish this water deficiency on a regular basis. Water consumption is influenced by habit or a daily routine of eating and drinking without being thirsty.

Any significant loss of bodily fluid results in a sensation of thirst as well as a behavioural desire to drink. When there is a water shortage, both thirst and the desire to drink grow. There are a number of regulating mechanisms in place to ensure that the amount of water consumed equals and corrects a bodily water deficit.

Table 8.1 Water balance in a cow

	Intake (L)				Output (L)				
Animal status	Drinking	In feed	Metabolic water	Total	Urine	Faeces	Evaporation	Milk	Total
Non-lactating	26	1	2	29	7	12	10	0	29
Lactating	51	2	3	56	11	19	14	12	56

Dehydration causes a decrease in blood volume and blood pressure, as well as an increase in blood osmolarity. The thirst centre of hypothalamus reacts to a variety of dehydration signals, including angiotensin II (subjected to release in reaction to low blood pressure), vasopressin (released in response to increased blood osmolarity), and osmoreceptor cues (neurons in hypothalamus monitoring extracellular fluid osmolarity).

When the thirst centre receives the signals, it inhibits salivation by activating the sympathetic nerve supply to the salivary gland. Salivation is also reduced in dehydration due to decreased capillary filtration produced by low blood pressure and high blood osmolarity. Reduced salivation causes the animal to feel thirsty, which leads to water consumption. Drinking water cools and moistens the mouth while also causing stomach and intestinal distension. These will suppress thirst for a brief period of time.

Water consumption rehydrates the blood, lowering osmolarity. It reduces osmoreceptor response and enhances capillary filtration. As a result, saliva becomes more watery and profuse. Long-term thirst inhibition is caused by water absorption from the small intestine and a decrease in blood osmolarity.

8.1.2.2.2 Regulation of Water Output

The only means by which water output can be significantly controlled is through regulation of urine volume. Antidiuretic hormone (ADH) is involved in controlling water output. In dehydration, elevated blood osmolarity stimulates the osmoreceptors in the hypothalamus. As a result of the stimulation of osmoreceptors, the posterior pituitary is stimulated to release ADH. In the kidney, ADH interacts with V_2 receptors present on the basal side of epithelial cells of late distal convoluted tubule, collecting tubule, and collecting duct. Binding of ADH with V_2 receptor will cause formation of second messenger cAMP. cAMP will in turn increase the number of water channels (aquaporin 2) in the epithelial cytoplasm. Aquaporin 2 is inserted on the luminal surface of the epithelium and thus increases water permeability. Water is reabsorbed till osmotic equilibrium is reached. Thus, kidney will increase water reabsorption resulting in reduced urine output. ADH helps in elevating blood volume and lowering blood osmolarity in dehydration.

On the other hand, if blood osmolarity is very low or blood volume and blood pressure are very high, ADH release is blocked. The renal tubule's ability to reabsorb water decreases, resulting in an increase in urine volume. This will lower the total blood water level and return it to normal.

Adjustments in sodium reabsorption are also linked to urine volume regulation. Sodium reabsorption and excretion are accompanied by a proportionate amount of water. With regard to electrolyte balance, maintaining water balance by regulating sodium excretion is better understood.

8.1.2.3 Measurement of Body Water

The difference in the weight of fresh carcasses and dried carcasses was used to compute the total body water at earlier times. The total body water was afterwards estimated using the dilution approach. The volume of bodily water can be determined by injecting a known-concentration indicator chemical into the bloodstream, allowing it to diffuse equally throughout the plasma, and then evaluating the amount of dilution (Table 8.2). The total body water (TBW) can be calculated from the formula given below:

Table 8.2 Different substances used to determine body fluid volume

Body fluid	Substance used to measure the body fluid	Characteristics of substance used
Total body water	Radioactive water (tritium), heavy water (deuterium), antipyrine, urea, thiourea, sulphanilamide	Must penetrate the cell membrane and uniformly disperse in ECF and ICF
ECF	Radioactive chloride, radioactive iothalamate, thiosulfate, inulin, sucrose, thiocyanate	Must disperse in plasma and interstitial fluid but do not penetrate the cell membrane
Plasma volume	Serum albumin labelled with radioactive iodine, Evans blue dye (T-1824)	Does not penetrate capillary membrane but remains in vascular system
Blood volume	RBC labelled with radioactive material like chromium or phosphorus	
ICF	ICF = Total body fluid − ECF	

ECF extracellular fluid, *ICF* intracellular fluid, *RBC* red blood cells

$$\text{TBW} = \frac{\text{Volume of indicator solution injected} \times \text{Concentration of indicator solution injected}}{\text{Concentration of indicator solution after equilibration}}$$

An indicator solution that equally spreads in plasma and interstitial fluid but does not infiltrate the cell membrane can be used to assess the volume of extracellular fluid. Because the intracellular fluid volume cannot be directly determined, it must be calculated by subtracting the extracellular fluid volume from total body water. A material that does not readily permeate capillary membranes but persists in the circulatory system after injection is used to quantify plasma volume. Similarly to intracellular fluid volume, interstitial fluid volume cannot be measured directly. It is computed by subtracting the volume of plasma from the volume of extracellular fluid.

The haematocrit (the fraction of total blood volume made up of cells) can also be used to compute the blood volume using the equation below:

$$\text{Total blood volume} = \frac{\text{Plasma volume}}{1 - \text{Haematocrit}}$$

Another approach to estimate blood volume is to insert radioactively labelled red blood cells into the circulation. The radioactivity of a mixed blood sample can be measured after extensive mixing of these cells in circulation, and the total blood volume can be determined using the dilution principle. Radioactive chromium (^{51}Cr), which binds firmly to red blood cells, is a common material used to identify red blood cells.

Newer non-invasive techniques using body composition have been developed to measure total body water. These techniques include bioelectrical impedance analysis, air displacement plethysmography, dual-energy X-ray absorptiometry, and nuclear magnetic resonance. Bioelectric impedance analysis is economical and simple to use. These newly developed techniques measure total body water using empirical equations. These empirical equations are developed by comparing the measurements obtained by new methods with measurements made using reference methods.

8.1.3 Electrolytes

Electrolytes play a crucial role in animal health. Chemically reactive, they have a role in metabolism. They are responsible for determining the electrical potential across the cell membrane. They have a significant impact on the osmolarity of body fluids and the content and distribution of body water. Because ICF and ECF have the same osmolarity, cells do not bulge or shrink, but in terms of electrolyte concentration (Table 8.3), electrolytes are more numerous than non-electrolytes; they regulate water osmosis between bodily compartments. Sodium and calcium are the predominant cations in extracellular fluid, whereas chloride and bicarbonates are the major anions. Blood plasma will contain other proteins. Potassium and magnesium are the most abundant cations in intracellular fluid, while phosphates, proteinates, and sulphates are the most available anions. The erythrocytes of cats, dogs, cattle, and sheep have higher sodium ions than potassium. There is a little osmotic activity difference between plasma and interstitial fluid. The concentration of positively charged ions in plasma is slightly higher (approximately 2% higher) than the interstitial fluid (Table 8.4).

8.1.3.1 Electrolyte Transportation

The electrolytes transfer across a cell membrane in two ways: passive and active transportation. Transportation follows a concentration gradient called passive transportation that requires no energy input. Simple diffusion, facilitated diffusion, filtration, and osmosis are examples of passive transportation. In simple diffusion, electrolytes flow across the cell membrane according to their concentration gradient, from areas of high concentration to areas of low. In facilitated diffusion, electrolytes migrate into or out of the cells down to their concentration gradient through protein channels present in the cell membrane. Molecules move across the cell membrane due to a pressure gradient in the filtration process. Hydrostatic pressure is generally applicable here. The movement of a solvent through a selectively permeable or semi-

Table 8.3 Osmotically active substances in human body fluid (mOsmol/kg H_2O)

Substances	Plasma	Interstitial fluid	Intracellular fluid
Sodium	146	142	14
Potassium	4.2	4.0	140
Calcium	2.5	2.4	0
Magnesium	1.5	1.4	31
Chloride	105	108	4
Bicarbonate	27	28.3	10
Phosphate	2	2	11
Sulphate	0.5	0.5	1
Glucose	5.6	5.6	–
Proteins	1.2	0.2	4
Urea	4	4	4
Other organic substances	3.4	3.4	83.2
Total osmolality	302.9	301.8	302.2
Osmotic pressure at 37 °C (mmHg)	5453	5430	5430

Table 8.4 Plasma concentrations of electrolytes in dogs and cats

Substance	Dog	Cat
Sodium (mEq/L)	140.3–153.9	145.8–158.7
Potassium (mEq/L)	3.8–5.6	3.8–5.3
Ionised calcium (mEq/L)	5.4	5.1
Total calcium (mg/dL)	8.7–11.8	7.9–10.9
Total magnesium (mg/dL)	1.7–2.7	1.9–2.8
Chloride (mEq/L)	102.1–117.4	107.5–129.6
Bicarbonate (mEq/L)	21	20
Phosphate (mg/dL)	2.9–6.2	4.0–7.3
Proteins (g/dL)	7	7
Lactate (mg/dL)	15	15

permeable (cell) membrane, from higher to lower, is called osmosis.

Active transportation necessitates the use of energy to transport molecules into a cell. Primary active transportation and secondary active transportation are two types of active transportation. The transport protein comprises an ATPase, which hydrolyses ATP to create the energy required for transport in primary active transportation. It may also be called as an ion pump. There is no direct coupling of ATP in secondary active transportation; instead, the potential difference established by pumping ions out of the cell via primary active transport is used. Multiple electrolytes are moved across the membrane via secondary active transportation, which combines the uphill movement of one electrolyte (s) with the downhill movement of the other(s). It is called symport or co-transport when electrolytes flow in the same direction and antiport or counter-transport when they move in the opposite direction. ABC transporters, P-type ATPases, and solute carrier family are the three main membrane transporters that transport electrolytes. ABC transporters are key active transporters that transfer a wide spectrum of ions. P-type ATPase enzymes are used in primary active transportation to move cations. Ca^{2+}-ATPases and Na^{+},K^{+}-ATPases are examples of this family. Transporters in the solute carrier family use secondary active transport and facilitative diffusion to move solutes. The Na^{+}/H^{+} exchanger is an example of the solute carrier family.

8.1.3.2 Sodium

Sodium is the primary cation in extracellular fluids. Nearly 45% of sodium in the body is present in the extracellular fluid, 45% in the bones, and the rest in the intracellular fluid. Sodium is a key solute in determining total body water volume and water distribution among fluid compartments. Sodium is responsible for 90–95% of ECF osmolarity, and it accounts for half of the osmotic pressure differential that exists between the inside of cells and their surroundings. The kidneys are primarily responsible for salt excretion. Sodium is freely filtered through the kidneys' glomerular capillaries, and the majority of it is reabsorbed in the proximal convoluted tubule leaving only a small amount in urine.

In ECF, sodium content is relatively constant. In animals, dietary deficiency of sodium is rare, but adequate sodium excretion by the kidney is of primary concern. Four hormones are mainly involved in the regulation of sodium; they are ADH, atrial natriuretic factor, aldosterone, and angiotensin II.

The antidiuretic hormone regulates water absorption and excretion independently of sodium excretion. Osmolarity of ECF increases when sodium concentration rises above the normal level in ECF. The osmoreceptors in the hypothalamus detect it, causing the release of ADH from the posterior pituitary. ADH increases water reabsorption from renal tubules and stimulates the thirst centre. In contrast, the release of ADH is inhibited by a drop in sodium content below normal in ECF, causing diuresis with the excretion of more water followed by the rising of sodium content in the ECF.

The hormone aldosterone (also known as the salt retention hormone) regulates the rate of sodium excretion. The adrenal cortex is directly stimulated to release aldosterone when sodium levels are reduced or potassium levels are elevated. The renin-angiotensin system promotes aldosterone secretion when blood pressure is reduced. The major cells that line the renal tubules, particularly at the later part of the convoluted tubule and collecting duct, are affected by aldosterone. The basement membrane allows aldosterone from the blood to enter the main cell. It induces gene transcription by binding to its receptors in the cytoplasm. The proteins formed cause three effects: (1) attach new sodium-potassium ATPase pumps on the basal surface of principal cells, (2) attach ENaC (epithelial sodium channels) on the luminal surface of principal cells, and (3) activate the existing sodium-potassium ATPase pump on the basal surface and sodium and potassium channels on the luminal surface. Sodium from the tubular fluid is reabsorbed into the main cell and transported to the blood via sodium-potassium ATPase pumps due to these three processes. At the same time, potassium from the blood enters into the principal cell via sodium-potassium ATPase pumps on the basal surface and is excreted into the tubular fluid of the renal tubule via potassium channels on the luminal surface. Sodium, from the blood, enters the principal cell via sodium-potassium ATPase

pumps on the basal surface. As a result, aldosterone causes an increase in salt absorption and a decrease in potassium excretion. Along with sodium and water, chloride is also reabsorbed. The blood volume, blood pressure, and sodium and potassium concentration are restored to normal.

An increase of sodium with the rise in blood volume results in the release of the atrial natriuretic factor (ANF) due to distension of the heart's atria. ANF increases salt and water excretion through the kidneys while inhibiting ADH and renin secretion. As a result, the kidneys excrete more salt and water. It aids in restoring normal blood volume and sodium levels.

Hyponatraemia is a condition in which sodium concentration in the blood is lower than normal. It is mainly caused by an excess of water in the body, which dilutes the sodium. Reduced sodium intake combined with constant excretion through urine, severe sweating, vomiting, diarrhoea, and diseases that cause diuresis, such as diabetes and acidosis, causes extreme hyponatraemia. Relative hyponatraemia can occur as a result of excessive water retention in oedema or congestive heart failure.

Hypernatraemia is a condition in which blood sodium levels are abnormally high. It can be caused by the loss of water from the blood, which causes the haemo-concentration of all blood elements. It can also be caused by hormonal abnormalities involving ADH and aldosterone.

8.1.3.3 Potassium

Potassium is the most abundant as the intracellular cation, and it aids in generating action potentials and establishing the resting membrane potential after depolarisation in neurons and muscle fibres. Potassium, unlike sodium, has minimal effect on osmotic pressure. The sodium-potassium pumps in cell membranes, which maintain appropriate potassium concentration gradients between the ICF and ECF, are responsible for the low potassium levels in the blood and cerebrospinal fluid. The renal tubules, particularly at the distal convoluted tubule and collecting ducts, discharge potassium both actively and passively. Under the effect of aldosterone, potassium participates in the exchange of sodium (discussed earlier).

Aldosterone aids in the control of potassium levels in the ECF. The adrenal cortex will release aldosterone in response to a slight increase in potassium content. The tenfold increase in potassium concentration results in a threefold increase in aldosterone. Aldosterone raises potassium excretion in the urine and returns the ECF potassium concentration to normal.

Hypokalaemia is a condition in which the potassium level in the blood is abnormally low. Hypokalaemia can develop due to loss of potassium in the body or a relative reduction in potassium in the blood due to potassium redistribution. Reduced intake, which is commonly associated with famine, vomiting, diarrhoea, and alkalosis, can cause potassium loss. The redistribution of potassium causes a relative decrease in the blood in some insulin-dependent diabetic individuals. When insulin is given and glucose is taken up by cells, potassium travels through the cell membrane with the glucose, lowering the amount of potassium in the blood and interstitial fluid, leading to hyperpolarisation of neuron cell membranes and reduced sensitivity to stimuli.

Hyperkalaemia, or an abnormally high potassium level in the blood, can harm skeletal muscles, neurological system, and heart. Increased potassium intake in the diet can cause hyperkalaemia. Increased potassium concentration in the ECF can cause partial depolarisation (excitation) of the plasma membrane of skeletal muscle fibres, neurons, and cardiac cells and an inability to repolarise the cells. In such circumstances, the heart will not relax after a contraction, thus seizing and ceasing to pump blood, resulting in death within minutes. An individual with hyperkalaemia may have mental disorientation, numbness, and weaker respiratory muscles due to the effects on the neurological system.

8.1.3.4 Chloride

The most common extracellular anion is chloride. Chloride contributes significantly to the osmotic pressure difference between the ICF and the ECF, and it is essential for optimal hydration. Chloride maintains the electrical neutrality of the ECF by balancing cations in the fluid. Chloride ion secretion and reabsorption in the kidneys follow the same pathways as sodium ions.

Hypochloraemia, lower-than-normal blood chloride levels, occurs mainly due to faulty renal tubular absorption. Hypochloraemic dogs and cats have chloride concentrations of less than 100 mEq/L and 110 mEq/L, respectively. Hypochloraemia can also be caused by vomiting, diarrhoea, or metabolic acidosis. Dehydration, excessive ingestion of food salt (NaCl) or swallowing seawater, renal failure, renal tubular acidosis, diabetes mellitus, congestive heart failure, chronic lung disease, and other factors can cause *hyperchloraemia*, or higher-than-normal blood chloride levels. Pseudo-hyperchloraemia often occurs during serum examinations in the laboratory. It causes excessive loss of water and leads to chloride loss, lipemic serum, and pigments like bilirubin and haemoglobin in the serum. Injection of potassium bromide can also cause pseudo-hyperchloraemia.

8.1.3.5 Bicarbonate

The second most abundant anion in the blood is bicarbonate. Its primary role is to regulate the body's acid-base balance by acting as a component of buffer systems. In body fluids, a small amount of CO_2 may dissolve. It leads to the production of approximately 90% of CO_2 into bicarbonate ions ($HCO3^-$) following the reaction as:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$$

The bidirectional arrows indicate that depending on the concentrations of the reactants and products, the reactions can proceed either way. In tissues with a high metabolic rate, considerable volumes of carbon dioxide are generated. Carbon dioxide converts into bicarbonate in the cytoplasm of red blood cells by the action of an enzyme known as carbonic anhydrase, and then it enters into the bloodstream. The CO_2 is regenerated from bicarbonate in the lungs, causing a reverse reaction and expelling as metabolic waste.

8.1.3.6 Calcium

Calcium, the most abundant mineral in bones and teeth (calcium reservoirs), is responsible for its hardness. Muscle contraction, enzyme function, and blood coagulation require calcium ions (Ca^{2+}). Calcium also aids in the stabilisation of cell membranes and is necessary for the release of neurotransmitters and hormones from endocrine glands.

Nearly 30% of the total calcium in the bone is made up of amorphous salts that can easily be exchanged with ECF. The amount equates to around 5–10 g in total. The amorphous calcium crystals have a wide surface area that can easily absorb extra calcium when hypercalcaemia occurs. The amorphous salts are easily carried into the bloodstream if hypocalcaemia occurs. In about 70 min, any alterations in calcium concentration in the blood are restored to normal levels by this buffering mechanism. Parathyroid hormone, calcitonin, and vitamin D play a role in calcium homeostasis. These hormones regulate eucalcaemia by their effects on bone deposition and bone resorption, urinary excretion, and intestinal calcium absorption. Bone is a long-term regulator of eucalcaemia. When bone is saturated with or depleted with calcium salts, the intestine and kidney regulate eucalcaemia.

Hypocalcaemia, abnormally low blood calcium levels, is seen in hypoparathyroidism that can occur during the dysfunction of the thyroid gland as four nodules of the parathyroid gland are lodged within it. Renal illnesses, insufficient dietary calcium, vitamin D deficiency, low magnesium levels, pancreatitis, hypoparathyroidism, and certain drugs, including anticonvulsants and corticosteroids, cause hypocalcaemia. Primary hyperparathyroidism is characterised by *hypercalcaemia*, or unusually high calcium blood levels. Hypercalcaemia is a side effect of several cancers. Magnesium levels are closely linked to calcium levels; hence, it is common to fix and treat magnesium levels before treating calcium levels.

8.1.3.7 Phosphate

Dihydrogen phosphate ($H_2PO_4^-$), monohydrogen phosphate (HPO_4^{2-}), and phosphate (PO_4^{3-}) are the three ionic forms of phosphate found in the body. HPO_4^{2-} is the most prevalent kind. Calcium-phosphate salts, bone, and teeth bind up 85% of the body's phosphate. Phospholipids, such as those that make up the cell membrane, ATP, nucleotides, and buffers, all include phosphate. They play a crucial role in maintaining acid-base equilibrium by functioning as buffers.

Hypophosphataemia, or abnormally low phosphate blood levels, can occur due to excessive antacid usage or malnutrition. The kidneys generally conserve phosphate when faced with phosphate depletion, although this conservation is substantially hampered by hunger. *Hyperphosphataemia*, or unusually high phosphate levels in the blood, occurs when renal function is impaired or acute lymphocytic leukaemia is present. Phosphate is a major component of the ICF; hence, any considerable cell death might result in phosphate being dumped into the ECF.

8.1.4 Transcellular Fluid

The transcellular fluid is found in epithelial cell-lined bodily cavities. It includes the cerebral fluid, synovial fluid, peritoneal fluid, pleural fluid, pericardial fluid, aqueous humour, and vitreous humour of the eye, bile, and fluid from the digestive, urinary, and respiratory tracts.

8.1.4.1 Cerebrospinal Fluid

Cerebrospinal fluid (CSF) is a unique fluid found in and around the brain and spinal cord. It presents in the brain's ventricles, the spinal cord's central canal, and the subarachnoid region. The choroid plexus of the brain's lateral and third ventricles produces the majority of the cerebrospinal fluid (two-thirds). Ependymal cells that line the ventricles and spinal canal create cerebrospinal fluid. The pia mater, which covers the central nervous system, produces a minor amount. A layer of pia mater and choroid epithelial cells covers the choroid plexus, which resembles a cauliflower-like proliferation of blood vessels (modified ependymal cells). Microvilli cover the apical surface of choroid epithelial cells. Many fenestrae in the capillary endothelium's wall allow many tiny molecules to flow through. Tight connections connect adjacent choroid epithelial cells preventing water-soluble compounds from passing into the cerebrospinal fluid. The blood-cerebrospinal barrier (BCB) or blood-brain barrier (BBB) is made up of several tight junctions. Blood pressure and cerebrospinal fluid pressure both have little effect on cerebrospinal fluid secretion, which is an active process. The sodium is actively transported into the ventricles by epithelial cells. Chloride and bicarbonate are diffused into the ventricles to preserve electrical neutrality. As a result, the concentration of sodium chloride in the ventricles rises, causing osmosis to sip water into the ventricles. By facilitating diffusion, carrier proteins will aid in moving essential chemicals from the blood into the cerebrospinal fluid.

Table 8.5 Biochemical constituent of cerebrospinal fluid of cow

Constituent	Cow
Total proteins (mg/dL)	23.4–66.3
Albumin (mg/dL)	8.21–28.71
Creatine kinase (U/L)	2–48
Lactate dehydrogenase (U/L)	2–25
Magnesium (mg/dL)	1.8–2.11
Potassium (mEq/L)	2.7–3.2
Sodium (mEq/L)	13.2–14.2
Glucose (mg/dL)	37–51

Cerebrospinal fluid is a colourless, transparent liquid. The cerebrospinal fluid has plasma's specific gravity, pH, and osmolarity. It contains a tiny amount of protein, the same amount of plasma sodium, 15% more chloride than plasma, 40% less potassium, and 30% less glucose than plasma (Table 8.5). In comparison to plasma, cerebrospinal fluid contains less urea. Except for a few lymphocytes, the cerebrospinal fluid lacks biological components.

The cerebrospinal fluid is generated in the lateral ventricles and enters into the third ventricle through the foramen of Monro. A small volume of CSF can infuse into the third ventricle. The cerebrospinal fluid will subsequently pass through the aqueduct of Sylvius and into the fourth ventricle. A minute volume of CSF can also enter into the fourth ventricle. The fourth ventricle's cerebrospinal fluid will enter the spinal cord's central canal. A portion of the cerebrospinal fluid from the fourth ventricle will reach the subarachnoid space through the foramen of Luschka and the foramen of Magendie.

The cerebrospinal fluid is replaced by new cerebrospinal fluid four to five times a day. The rate of formation of the CSF varies in different species (Table 8.6). Arachnoid villi absorb the cerebrospinal fluid. Microscopic extensions of the arachnoid membrane into the dorsal sagittal sinus are known as arachnoid villi. Arachnoid granulation is a macroscopic structure formed by the aggregation of these villi. The arachnoid villi operate as a valve, allowing cerebrospinal fluid to flow quickly into the sagittal sinus while preventing backflow. The cerebrospinal fluid pressure is 1.5 mmHg higher than that of the plasma.

Cerebrospinal fluid helps cushion the central nervous system against shock, thus protecting the brain against a blow to the head. Cerebrospinal fluid significantly lowers the brain weight by providing a buoyancy effect. It helps to maintain the consistent extracellular environment of cells of the nervous system. It is an effective waste control system that can remove potentially harmful cellular metabolites. It transports and distributes some peptide hormones and various substances of the brain into general circulation. It serves partially as nutritive media for the brain and spinal cord.

Table 8.6 Rate of cerebrospinal fluid formation in various species

Species	Cat	Dog	Sheep	Goat	Cow	Human
Rate (μL/min)	20–22	47–66	118	164	290	350–370

8.1.4.2 Synovial Fluid

Synovial fluid is a thick, viscous liquid found in the cavities of joints, tendon sheath, and bursae. A thin layer of synovial fluid surrounds the articular cartilage and penetrates its interior regions. The synovial fluid within the auricular cartilage acts as a reserve. The reserve synovial fluid is forced out of the cartilage during joint movements to keep a fluid layer on the cartilage surface.

Synovial fluid is generated by ultrafiltration from blood plasma. The pH of synovial fluid is usually between 7.2 and 7.4. It contains proteins acquired from plasma through filtration and synthesised by synovial cavity cells. It contains small amounts of albumin, globulin, mucin, proteinase, collagenases, prostaglandins, and hyaluronic acid, but no fibrinogen. Thus, synovial fluid does not clot. Small molecules like electrolytes and glucose have similar concentrations in the synovial fluid to plasma. Large molecules are found in lower concentrations in synovial fluid than in plasma. The synovial fluid contains hyaluronic acid produced by fibroblast-like cells (type B cells) in the synovial membrane. Hyaluronan is a lubricant that enhances the viscosity and flexibility of articular cartilage. Lubricin, a glycoprotein, is secreted by chondrocytes on the surface of the articular cartilage in the synovial joint. Lubricin is involved in lubrication and helps regulate synovial cell growth.

The synovial fluid contains only a few phagocytic cells (mainly mononuclear cells). These cells remove germs and debris from the joints caused by wear and tear. Less than 10% of these cells are neutrophils, and the remaining cells present are lymphocytes, monocytes, and macrophages. The usual synovial fluid volume in dogs and cats is 0.24 mL.

Synovial fluid acts as a lubricant in the joints, reducing friction. Because of its rheopectic characteristics, it functions as a thick absorbent. It provides oxygen and nutrition to the synovial tissues, nourishing them. It gets rid of metabolic waste. In the joint, it also serves as a molecular sieve.

8.1.4.3 Peritoneal Fluid

Peritoneal fluid is present between the peritoneal layers that line the abdominal cavity. It separates the peritoneum into two layers having an odourless, non-turbid, and clear or pale yellow colour. The pH ranges between 7.5 and 8.0. Peritoneal fluid has a specific gravity of less than 1.016. It is a blood ultrafiltrate, and water is the most important component. Simple diffusion allows electrolytes and tiny compounds to enter the peritoneal cavity. Electrolyte concentrations in the peritoneal fluid are similar to those in plasma. The total protein content is less than 2.5 g/dL, and the cell count is less than 3000–5000/μL. The cells present are leukocytes and desquamated mesothelial cells. The packed cell volume of

the fluid in horses is less than 1%. The volume of peritoneal fluid increases during pregnancy. Lymphatics drain peritoneal fluid from the peritoneal cavity. The drainage is proportionate to the rate of its production. The purpose of peritoneal fluid is to lubricate abdominal organs and reduce friction between them during digestion and movement.

8.2 Fluid Balance

8.2.1 Acid-Base Balance

Sustaining acid-base balance is one of the most crucial parts of maintaining homeostasis. The negative logarithm of hydrogen ions (H^+) determines the pH of a solution. In mammals, the pH varies from 7.0 to 7.8. A mild alteration in pH threatens various physiological functions, impairs cellular functions, and affects the structure and functions of macromolecules. Acids are constantly generated in the body. The formation of bases balances the acids produced. Hence, the acid-base balance is maintained. An acid is any substance that donates a proton (releases H^+ in a solution). Among acids, some are strong acids, and some are weak. Strong acids freely ionise by giving up most of their hydrogen ions; thus, they reduce pH substantially. Weak acids have a minor effect on pH because they ionise only slightly, maintaining most of the H^+ in chemically bound form. Any substance that can take proton is referred to as a base (accept an H^+ ion). Bases can be strong or weak bases. A strong base affects the pH markedly by raising the pH as it has a stronger tendency to bind with hydrogen ions. Because it binds with fewer hydrogen ions, a weak base has little effect on pH.

Arterial blood has a pH of 7.36–7.44 (7.4), while interstitial fluid and venous blood have 7.35. The pH of the intracellular fluid lies between 6.0 and 7.4. (7.0). The body can maintain pH balance when the pH ranges from 7.0 to 7.8. The body tries to bring back the pH to a normal physiological level through various compensatory mechanisms whenever there is an alteration in pH beyond the normal range. Three basic systems regulate the concentration of hydrogen ions in body fluid:

1. Chemical buffer system: Mixes with acid or base right away to prevent excessive hydrogen ion concentration shifts.
2. Respiratory system: Controls carbon dioxide removal from extracellular fluid.
3. Kidney: Excretes acid or alkali, bringing the hydrogen ion concentration in the extracellular fluid back to normal.

Within a fraction of a second, the chemical buffer system (first line of defence) reacts to reduce the change in hydrogen ion concentration. The respiratory system (second line of defence) will intervene within minutes to keep hydrogen ion concentrations from fluctuating too much. Both the first and second lines of defence do neither remove nor add hydrogen ions to the body; instead, they bind them until a balance can be restored. Kidneys, the body's third line of defence, react slowly and remove excess acid or base. Kidneys are the most potent acid-base balance mechanism, and they are responsible for the final correction of acid-base balance.

8.2.1.1 Chemical Buffer System

A buffer prevents pH fluctuations by converting a strong acid or base to a weak one. A chemical buffer system is made up of a weak acid and the conjugate base of that acid. Bicarbonate phosphate, protein, and haemoglobin are all essential chemical buffer systems in the body.

8.2.1.1.1 Bicarbonate Buffer System

It is a mixture of carbonic acid (a weak acid) and bicarbonate ions in a protonated state (an unprotonated substance—a weak base). In extracellular fluid, it is the most significant buffer system. Carbonic acid is formed when carbon dioxide is hydrated in the presence of carbonic anhydrase, which dissociates into HCO_3^- and H^+:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$$

Carbonic acid behaves as a weak acid as the reaction progresses to the right, releasing H^+ and reducing pH. When the reaction moves to the left, $HCO3^-$ functions as a weak base, binds H^+, and raises the pH. When the pH drops, the reaction shifts to the left to raise the pH and restores it to normal. When the pH rises, the reaction will move to the right to lower the pH and return it to normal.

The pK of the bicarbonate system (6.1) and the pH of the extracellular fluid are very different (7.4). As a result, the bicarbonate system is less effective than other chemical buffers. Compared to other chemical buffer systems, it plays a critical role in maintaining the pH of bodily fluids. The kidney and respiratory systems regulate this buffer system's bicarbonate and carbon dioxide components separately. These two regulating systems operate continuously and simultaneously, resulting in a more productive and efficient bicarbonate buffer system.

8.2.1.1.2 Phosphate Buffer System

It is the combination of hydrogen phosphate, HPO_4^{2-} (weak base—unprotonated substance), and dihydrogen phosphate, $H_2PO_4^-$ (weak acid—protonated substance). It works the same as the bicarbonate system:

$$H_2PO_4^- \leftrightarrow HPO_4^{2-} + H^+$$

When the reaction goes to the right, H^+ is liberated and pH is lowered, and when the reaction goes to the left, H^+ is bound and pH is raised. The optimal p*K* for this system is 6.8, which is close to the pH of body fluids. Hence, phosphate buffer has a more substantial buffering effect than an equal $HCO3^-$ buffer. But phosphates are less in extracellular fluid than bicarbonates, and they are important in renal tubules and intracellular fluid.

8.2.1.1.3 Protein Buffer System

Proteins are more concentrated in intracellular fluid than bicarbonates and phosphates. Intracellular proteins are responsible for 60–70% of chemical buffering within cells. The capacity to buffer is attributed to the side groups of their amino acid residues. Some have a carboxyl (-COOH) side group that releases H^+ as pH rises, lowering pH:

$$-COOH \leftrightarrow -COO^- + H^+$$

Others have amino ($-NH_2$) side groups, which bind H^+ when pH drops too low, thus raising pH towards normal. The most important buffering amino acid is histidine:

$$-NH_2 + H^+ \leftrightarrow NH_3^+$$

The protein buffer system is more powerful in the plasma since their p*K* value is very near to 7.2 due to their high concentration in plasma.

8.2.1.1.4 Haemoglobin Buffer System

It is the most effective protein buffer and the second most essential blood buffer. Because haemoglobin has a higher concentration than plasma proteins, it has a sixfold better buffering capacity. Haemoglobin in the form of reduced haemoglobin (Hb^-) and their weak acid (HHb) form buffer. It works the same as the bicarbonate system:

$$H^+ + Hb^- \leftrightarrow HHb$$

The chemical buffer system as a whole works together. Whenever the concentration of H^+ in extracellular fluid changes, the equilibrium of the buffer system changes as well, and the isohydric principle describes this phenomenon.

8.2.1.2 Respiratory Regulation

The bicarbonate buffer system equation demonstrates that adding carbon dioxide to bodily fluid boosts H^+ concentration and reduces pH, while removing carbon dioxide has the opposite effect. It is the foundation for the respiratory system's high buffering capacity. This technology neutralises 2–3 times the amount of acid that a chemical buffer system can balance:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$$

Pneumatic ventilation is stimulated by an increase in partial pressure of carbon dioxide (PCO_2) and a decrease in pH. As a result, excess carbon dioxide is ejected. The reaction shifts to the left. As a result, the concentration of H^+ is reduced, and free H^+ becomes a member of the water molecule. When H^+ levels decline, pH rises and inhibits pulmonary ventilation. Carbon dioxide builds up as a result of this process. As the reaction progresses to the right, the pH decreases. Chemoreceptors are responsible for this impact. Based on their location, chemoreceptors are divided into central chemoreceptors and peripheral chemoreceptors.

Central chemoreceptors are chemosensitive areas on the ventral surface of the medulla. They stimulate the respiratory centres, generating a rise in tidal volume and breathing rate. These receptors are sensitive to variations in the concentration of H^+ ions in the brain's interstitial fluid and cerebrospinal fluid (CSF). Because H^+ ions have a difficult time crossing the blood-brain barrier (BBB), changes in H^+ ion concentration in the blood have a much smaller effect on stimulating the chemosensitive area. Carbon dioxide passes through BBB easily.

Carbon dioxide may easily cross the BBB; hence, increased blood PCO_2 raises the PCO_2 of interstitial fluid and cerebrospinal fluid. CO_2 is quickly hydrated in the interstitial fluid and CSF, forming carbonic acid. Carbonic acid breaks down into H^+ and HCO_3^-. Chemoreceptors detect a rise in hydrogen ion concentration, which causes the respiratory centres to be stimulated. Increased alveolar ventilation is caused by an increase in breathing rate and depth.

Aortic and carotid bodies are peripheral receptors. The aortic arch contains a cluster of chemoreceptors known as aortic bodies. The vagus nerve provides a signal to the dorsal respiratory group in the medulla oblongata. Carotid bodies are oval nodules found in the left and right common carotid arteries' walls. The glossopharyngeal nerve provides an impulse to the dorsal respiratory group. The aortic and carotid bodies will be stimulated by an increase in PCO_2 and hydrogen ions in the blood. They then activate the brain's respiratory regions, resulting in enhanced breathing.

8.2.1.3 Renal Regulation

The kidneys neutralise more acid and base than the respiratory system or chemical buffers. The kidneys remove hydrogen ions from the body, and the other buffer systems can lower their concentration by attaching it to other molecules. Three primary mechanisms regulate the extracellular fluid hydrogen ion concentration: (1) hydrogen ion secretion,

(2) reabsorption of filtered bicarbonate ions, and (3) bicarbonate ion generation. The rate of H^+ secretion by renal tubules is primarily determined by the intracellular pH of renal tubular cells. An increase in pH lowers H^+ secretion by the kidney, and lowering of pH increases hydrogen ion secretion. Intracellular pH of cells of renal tubule changes as blood pH or PCO_2 changes. Therefore, acidaemia and hypercapnia increase hydrogen ion secretion. In contrast, alkalaemia and hypocapnia reduce hydrogen ion secretion.

The proximal convoluted tubule secretes 85% of hydrogen ions. In contrast, the intercalated cells of the second half of the distal convoluted tubule, collecting tubule, and collecting duct secrete the remaining 15%.

Secondary active transport secretes hydrogen ions in the proximal convoluted tubule (sodium-hydrogen counter-transport). Carbon dioxide is either diffused into tubular cells or produced by cell metabolism. In the presence of carbonic anhydrase, it will mix with water to generate carbonic acid, which will then dissociate into HCO_3^- and H^+. Sodium-hydrogen counter-transport transports hydrogen ions into the tubular lumen. Carbon dioxide and water will result from the reaction of H^+ with filtered bicarbonate. Carbon dioxide penetrates tubular cells and becomes carbonic acid when it reacts with water.

Primary active transport secretes hydrogen ions in intercalated cells (second half of distal convoluted tubule, collecting tubule, and collecting duct). Carbonic acid is formed when dissolved carbon dioxide in the cell reacts with water to create bicarbonate ions (which are reabsorbed in the blood) and hydrogen ions, released into tubules by the hydrogen ATPase process.

As a result, whenever hydrogen ions are secreted into the renal tubules, the same amount of filtered HCO_3^- is reabsorbed. Only a small percentage of surplus H^+ in ionic form can be eliminated in the urine when more hydrogen ions are produced than HCO_3^- filtered into the tubular fluid. Urine can only be acidified to roughly a pH of 4.5, and it means that most of the hydrogen ions expelled must be bound by bases rather than being free in solution.

When hydrogen ions are titrated with bicarbonate ions in the tubular fluid, a bicarbonate ion is reabsorbed for each hydrogen ion released. In the tubular fluid, excess hydrogen ions will mix with buffers other than bicarbonates, such as ammonia buffer and phosphate buffer, resulting in new bicarbonate, which enters the blood. When extracellular fluid includes surplus hydrogen ions, kidneys reabsorb filtered bicarbonate from the tubular fluid and generate new bicarbonate ions. Although urea and citrate buffer systems exist, they are of minor consequence.

8.2.1.3.1 Phosphate Buffer

As the tubular fluid is acidified with hydrogen ion secretion, hydrogen phosphate (HPO_4^{2-}) takes up and binds hydrogen ions to form dihydrogen phosphate, $H_2PO_4^{2-}$, predominantly. Part of the cation (Na) that electrically balances $H_2PO_4^{2-}$ in the glomerular filtrate is exchanged with a secreted hydrogen ion and thus is returned to the blood.

8.2.1.3.2 Ammonia Buffer

Tubular epithelial cells produce ammonia, which diffuses into the tubules. In the renal tubular fluid, ammonia interacts with hydrogen ions to generate ammonium ions and then combines with chloride ions to form ammonium chloride. Each time an ammonia molecule combines to generate ammonium, the concentration of ammonia in tubular fluid decreases, which causes more ammonia to diffuse from epithelial cells. Chloride ions make up the majority of anions in the tubular fluid. The tubular fluid will fall below 4.5 if all hydrogen ions are carried with chloride ions. Still, ammonia mixes with hydrogen ions and chloride ions to generate ammonium chloride, a weak acid.

Glutamine produced in the liver is transferred to the proximal convoluted tubule, thick ascending limb of the loop of Henle, and distal convoluted tubule epithelial cells. A single glutamine molecule is digested inside the cell to produce two ammonium ions and two bicarbonate ions. The sodium-ammonium counter-transport mechanism secretes ammonium ions into the tubular lumen. This method reabsorbs two bicarbonate ions into the bloodstream for every glutamine molecule digested. As the level of acidity rises, the amount of glutamine digested by collecting duct tubular cells increases.

Urine pH is used to determine the amount of hydrogen ions present in the urine. It reflects the acid-base state of an animal. The ability of the kidneys to regulate hydrogen ion and bicarbonate concentrations in the blood determines the pH of urine. The pH of a dog's or cat's urine is between 6.0 and 7.5. Dairy cows have an average urine pH of 8.10, with a range of 7.27–8.71, and the mean urine pH of beef cows is 7.73, with a range of 7.42–8.12. The pH of an animal's urine fluctuates based on its diet. Urine produced by high-protein diets, such as those consumed by carnivores, is neutral to acidic. The urine of herbivores is more alkaline than that of carnivores. Forages having high K-salt concentrations cause a high dietary cation–anion difference resulting in alkaline urine. Further, with the buffering that happens in reaction to gastric acids, any animal can produce alkaline urine shortly after eating.

8.2.2 Acid-Base Balance Disturbances

The rate of the conjugate base to their weak acids determines the pH of the ECF. Buffer base refers to the overall amount of buffer base in whole blood, including bicarbonate, haemoglobin, and other minor bases (BB). These bases are

called metabolic components, and they play a role in setting blood pH. Acid-base disruption occurs when the ECF gains or loses strong acid or base (Cl^- or HCO_3^-). At a pH of 7.4, the ratio of bicarbonate to carbonic acid in the extracellular fluid is 20:1. When carbonic acid levels rise, the ratio changes, resulting in a lower pH. Acidosis occurs when the pH goes below 7.5 due to a lack of bicarbonate or an increase in carbon dioxide partial pressure in the blood. In contrast, alkalosis happens when the pH rises above 7.4 due to an excess of bicarbonate or a decrease in carbon dioxide partial pressure in the blood.

Hydrogen ions diffuse into the cells to maintain electrical neutrality in acidosis, while potassium flows out of the cell. Intracellular proteins buffer hydrogen ions that enter the cell. As a result of the exchange between hydrogen and potassium, the cell loses a net amount of cation. Hyperpolarisation occurs when a cation is lost from a cell. The formation of the action potential in muscle cells and neurons is hindered. Acidosis reduces the activity of both the central nervous system and the muscles. Severe acidosis can result in unconsciousness and death. In alkalosis, hydrogen ions diffuse out of the cell, and potassium enters the cell. The membrane potential becomes more positive with the net gain of cations in the cell. As a result, neural tissue hyperexcitability and muscular overstimulation occur, resulting in tetany, convulsions, or respiratory paralysis.

Respiratory disturbances are acid-base imbalances caused by changes in the partial pressure of carbon dioxide in the blood. Acid-base imbalances due to alterations in bicarbonate levels are called metabolic disturbances. Metabolic acidosis, metabolic alkalosis, pulmonary acidosis, and respiratory alkalosis are acid-base abnormalities.

8.2.2.1 Metabolic Acidosis

Metabolic acidosis is defined as a gain of strong acid or a loss of base from the ECF. In metabolic acidosis, acidaemia will be present. It happens in ketosis, diabetes mellitus, and renal acidosis, where bicarbonate is lost in the urine due to tubular reabsorption failure. It also occurs in diarrhoea, where bicarbonate is lost. Due to a decrease in bicarbonate ions, the pH drops.

As a result, all blood buffer bases drop. In most cases, the partial pressure of carbon dioxide in the plasma does not vary. A drop in pH causes increased alveolar ventilation and reduced carbon dioxide partial pressure. Reduced carbon dioxide partial pressure will restore the natural ratio of conjugate base to weak acid. However, the total bases will be lower than usual, necessitating renal correction, i.e. H^+ ion excretion and plasma HCO_3^- restoration.

8.2.2.2 Metabolic Alkalosis

ECF results in the acquisition of base (OH^- or HCO_3^-) or the loss of strong acid. The symptoms of metabolic alkalosis are chronic vomiting (loss of stomach acid), potassium deficit (due to excessive renal excretion of hydrogen ions), and oxidation of organic acids. The parenteral introduction of bicarbonate solutions also causes metabolic alkalosis.

There is an increase in HCO_3^- in ECF, increasing the base content in all of these situations. The body's reaction is the polar opposite of that seen in metabolic acidosis. Alkalaemia causes a rise in pH, reducing lung ventilation and raising carbon dioxide partial pressure. Respiratory compensation brings the pH back to normal. Kidneys correct the condition by decreasing the secretion of H^+ ions and increasing the excretion of HCO_3^-.

8.2.2.3 Respiratory Acidosis

When the rate of CO_2 clearance by the lungs falls below the rate of CO_2 creation in the body, respiratory acidosis develops. It raises the partial pressure of carbon dioxide in the blood (hypercapnia). The inability of the lungs to exhale CO_2 at a regular pace is the primary cause of respiratory acidosis. It can occur by a lack of ability to enlarge the thorax due to a defect in the chest wall or respiratory muscles or any obstruction in the respiratory system that limits normal gas movement in the lungs.

A rise in PCO_2 causes an increase in H_2CO_3, and buffer reaction prevents the fall of pH caused by the increase in H_2CO_3. Renal compensation then follows. With a surge in plasma HCO_3^-, low pH enhances H^+ secretion into the urine.

8.2.2.4 Respiratory Alkalosis

In alveolar hyperventilation, the rate of removal of CO_2 exceeds the rate of creation in the body developing respiratory alkalosis. Low plasma PCO_2 (hypocapnia) and alkalaemia will be present. Increased alveolar ventilation is induced by aberrant activation of respiratory centres in the brain, either directly (as in ammonia poisoning) or indirectly (through peripheral chemoreceptors) through lower partial pressure of oxygen. Even when the partial pressure of carbon dioxide falls, there will be no change in the plasma concentration of bicarbonates at first. Non-bicarbonate buffers cause an immediate reaction. Thus, HCO_3 falls, and haemoglobin proteinate ions increase. Alkalaemia depresses H^+ ion secretion by renal tubules and increases the outflow of filtered HCO_3^- within a few hours, causing renal compensation. These result in further lowering of plasma HCO_3^-, and the ratio of HCO_3^- to H_2CO_3 moves back to normal.

8.2.3 Dehydration and Clinical Management

Clinical conditions affecting the hydration, acid-base, and electrolyte status are common in veterinary practice. As these conditions may result in harmful, often life-threatening consequences, recognition and management are vital.

8.2.3.1 Dehydration and Its Management

In small animal practice, dehydration is frequently linked to gastro-enteric diseases such as vomiting and diarrhoea that change electrolyte and acid-base status. Neonatal calf diarrhoea is a severe illness that causes severe dehydration in newborns. Dehydration status is assessed by physical examination and laboratory tests. Skin elasticity (skin turgor) is a valuable guide for evaluating dehydration. It can be carried out in the forehead in dogs and the neck region in cattle. With dehydration of about 5–6%, the loss of skin elasticity is mild, whereas in 10% dehydration, the skin often remains 'tented'. With higher percentages of dehydration, the animal becomes moribund. If the dehydration level is less than 5%, it cannot be reliably assessed by clinical findings. The relatively higher percent of body water in neonates and the variation in skin elasticity in older animals make the skin turgor test a less reliable tool in these age groups. Obesity can also affect skin tenting. Tacky mucous membrane on examination is suggestive of early stages of dehydration. With dry mucous membranes, the dehydration will be more than 6%. Eyeballs sunken in orbit are also noticed as dehydration increases. Rapid and weak pulses, coldness of extremities, animal appearing depressed, and prolonged capillary time indicate severe dehydration; shock may manifest. These clinical findings are noticed with more than 12% dehydration and have a grave prognosis. Eyeball recession (mm) and skin tent duration (seconds) are good indicators of calves' percentage dehydration and fluid replacement requirement. Dehydration is measured in the lab using packed cell volume (PCV) and total solids. Dehydration causes a rise in PCV and total solids. An increase in urine specific gravity can also detect dehydration. The aetiology of the existing disease should also be considered when interpreting laboratory findings, as disorders such as anaemia and hyperproteinaemia can cause variances. Fluid therapy for the management of dehydration has a quantitative aspect that is based on the correction of existing deficiencies, ongoing losses, and maintenance requirements.

The existing deficit is calculated as:

$$\text{Deficit (hydration) in litres} = \%\text{of dehydration (in decimals)} \times \text{body weight in kg}$$

Based on the formula used, a 300 kg cow with 8% dehydration would require about 24 L to correct the existing deficit. For ongoing losses, general thumb rules dictate the volume of fluid that needs to be replaced and may vary based on age and species. To meet daily needs, a volume of 50 mL/kg is required in dogs. Owing to the higher percent of extracellular fluid in young animals, their maintenance requirements are greater. A rate of 5 mL/kg/h or 120 mL/kg/day is required in calves, almost double the adult maintenance needs. The guidelines of the American Animal Hospital Association–American Association of Feline Practitioners suggest 2–6 mL/kg/h as maintenance rate in dogs; the formula suggested for 24 h is 132 × body weight in $kg^{0.75}$. Correction of ongoing losses depends on the type of loss (e.g. vomiting) and the number of episodes. The primary aim is to correct ongoing losses in 2–3 h. In 24 h, the patient's hydration status should be restored based on the total volume needed. Careful monitoring of the patient is essential during fluid therapy for signs of fluid overload. In such a case, reassess the status and adjust the rate of fluid administration. Tachypnoea crackles on auscultation, and watery nasal discharge suggests fluid overload. The volume requirement and rate of administration would be considerably different in animals with diseases affecting the organs like kidney and heart and in shock states.

Common routes of administration include intravenous, subcutaneous, and oral routes. Severe dehydration warrants intravenous fluid therapy. In patients with minimal dehydration, subcutaneous fluid administration can be considered. Isotonic fluids (normal saline and Ringer's lactate) are utilised for subcutaneous delivery. If vomiting is not present, the oral route may be used. Oral rehydration treatments are useful in preventing dehydration and electrolyte loss in calves. It is best to keep the amount of fluid given to calves to roughly 1–1.5 L at a time. Because of the practical challenges in intravenous fluid delivery in terms of the volume that needs to be provided, oral rehydration salts are now frequently suggested in adult cattle to overcome dehydration. However, if the animal is recumbent, the volume that can be administered orally will be reduced. An oral rehydration mix for cattle is sodium chloride 7 g, potassium chloride 1.25 g, and calcium chloride 0.5 g added to 1 L of water. This preparation is not an alkalinising solution, like other oral rehydration therapy preparations in calves. Calves with diarrhoea develop metabolic diseases in many instances due to hypovolaemia or specific diseases. Oral rehydration formulas for calves primarily have sodium and potassium, glucose, and chloride. Sodium bicarbonate, magnesium, acetate, and propionate are also included in some preparations for calves. Acetate and propionate act as metabolisable bases, which are converted to bicarbonate in the liver. These bases are considered superior to direct administration of sodium bicarbonate.

Moreover, they can act as an energy source and support sodium and water transport out of the small intestine. Fluid is administered intraosseously in paediatric patients and small dogs and cats when access to the intravenous route is difficult. The intraperitoneal route is also considered in such patients, provided that conditions like ascites and peritonitis are absent.

8.2.3.2 Types of Parenteral Fluids

The fluids utilised in clinical practice are divided into crystalloids and colloids. In veterinary medicine, crystalloid fluids are often used to treat dehydration. Fluids are classed as

isotonic, hypertonic, or hypotonic based on their osmolality. Fluids having an osmolality similar to that of extracellular fluids (about 270–310 mOsmol/L) can be regarded as isotonic for all practical purposes. Normal saline (0.9% NaCl) and lactated Ringer's solution are two common examples. These fluids 'seep' into other body compartments and are redistributed within extracellular compartments. Only less than one-third of the total volume of fluids administered intravenously will be present in circulation after 1 h of administration. When administered, hypertonic fluids are useful to draw large quantities of fluid into circulation and are preferred in conditions like gastric dilatation and volvulus in dogs. Hypertonic fluids should not be used in cases of dehydration. Dextrose 50% is a hypertonic crystalloid used to manage ketosis in bovines. Sodium bicarbonate as a 5% solution is employed to treat carbohydrate engorgement of ruminants. Hypertonic saline (3% or 7% NaCl) is used in veterinary practice to manage intracranial pressure in head trauma conditions. Hypertonic saline is also used in hypovolaemic shock management, as the volume required for resuscitation is relatively less than isotonic fluids. Hypertonic saline should not be used in dehydrated patients. Preparations like 0.45% NaCl and dextrose 5% are hypotonic fluids. Crystalloid fluids can further be classified, based on usage, as replacement fluids and maintenance fluids. Replacement fluids (e.g. normal saline) have higher sodium concentration and lower potassium levels than maintenance fluids and are indicated in cases of ongoing fluid and electrolyte losses, as in vomiting. A combination of half-strength dextrose (2.5%) and NaCl (0.45%) is also isotonic and is used as a maintenance fluid along with potassium chloride supplementation. It can be used after the ongoing electrolyte imbalances, and dehydration is corrected. The pH of the fluids may also vary. Normal saline has a pH of 5.5 and that of lactated Ringer's is 6.5.

Know More. . . . . .

Dehydration Management in Birds

Panting during periods of increased ambient temperature can lead to respiratory alkalosis in birds as excessive carbon dioxide losses occur. Dietary electrolyte ($Na^+ + K^+$-Cl^-) balance and electrolyte [$(K^+ + Cl^-)/Na^+$] ratio in the feed need to be monitored to alleviate the physiological and metabolic changes of heat stress. These electrolytes are considered important in managing acid-base balance and osmotic pressure of body fluids. In heatstroke, cooling the bird is an emergency measure that owners can try before veterinary aid is available. It involves the use of tap water or tepid water, and cold water should not be used for the purpose. The birds can also be misleading with water making sure that the water has good contact with skin. Moistening the feet and beak is also required.

Colloids can be broadly classified into natural colloids and synthetic colloids. Blood and blood products (albumin) are examples of natural colloids. Hydroxyethyl starch and dextran are synthetic colloids. Due to their higher molecular weight, these intravenous preparations remain in circulation for more extended periods ('crystalloids seep fast'). A veterinary product of hydroxyethyl starch available in India has a molecular weight of 130 kDa. Indications for the use of synthetic colloids are in the management of acute hypovolaemia and maintenance of plasma oncotic pressure. The volume required for fluid resuscitation when plasma expanders are used would be considerably less than that of crystalloids. A clinician needs to be aware of the potential signs of hypersensitivity and organ injury when natural and synthetic colloids are used (Table 8.7).

8.2.3.3 Acid-Base Imbalances and Electrolyte Abnormalities

Acid-base imbalances and electrolyte abnormalities often have life-threatening effects on animals. The disorders vary from carbohydrate engorgement in ruminants to hypokalaemia associated with diabetic ketoacidosis in dogs. The use of blood gas and electrolyte analysers would be beneficial in detecting these variations and monitoring treatment.

Carbohydrate engorgement of cattle (lactic acidosis) results in metabolic acidosis and dehydration, requiring intravenous sodium bicarbonate therapy to manage the acidosis and intravenous fluids to correct the dehydration. Base deficit measurement is the ideal method for deciding on the bicarbonate quantity to be administered. In a severe case of metabolic acidosis, sodium bicarbonate required (in mmol) is base deficit (from blood analysis) × 0.5 (or 0.3) × body weight in kg. Half the calculated dosage needs to be administered for 3–4 h, and the patient values need to be reassessed before administering sodium bicarbonate further. In dogs with chronic renal disease, bicarbonate medication may be required to keep the bicarbonate level between 18 and 24 mmol/L. Thumb guidelines are also employed in ruminant practice to determine the amount of sodium bicarbonate to deliver in cases of lactic acidosis, depending on the clinical severity, because direct access to the laboratory may not be possible in many farms. In urea toxicosis of ruminants, dilute

Table 8.7 Types of dehydration and fluids administered

Type of dehydration	Fluids preferred[a]
Isotonic dehydration (normal serum sodium levels)	Isotonic fluids like normal saline and Ringer's lactate
Hypertonic dehydration (elevated serum sodium)	Fluids with 'free water' (dextrose 5%)
Hypotonic dehydration (Low serum sodium—Not commonly encountered in clinical practice)	Normal saline

[a] Fluid administration also depends on the severity of the condition, primary aetiology, metabolic status, and electrolyte imbalances. Oral rehydration can be tried in less severe cases, especially when vomiting is absent

acetic acid (vinegar) is administered orally to manage ruminal alkalosis. Hypercapnia can result from airway obstruction and pulmonary disease; respiratory acidosis manifests. In dogs, tracheal collapse, brachycephalic syndrome, and chronic bronchial diseases can result in respiratory acidosis. Two or more separate acid-base abnormalities characterise mixed acid-base disorders. Interpretation of the results is essential in deciding the treatment options in such cases.

Diseases, conditions like vomiting, and drugs can contribute to electrolyte imbalances. Renal failure and hypoadrenocorticism can result in hyperkalaemia in dogs. Hypochloraemia and hyponatraemia were reported in hypoadrenocorticism. Hypokalaemia and hyponatraemia can be associated with diabetic ketoacidosis. In ruminants, hypochloraemic, hypokalaemic alkalosis occurs in left abomasal displacement. Administration of furosemide, a loop diuretic, can cause hyponatraemia. Hypokalaemia, hypocalcaemia, and hypomagnesaemia can also result in this drug's administration. Hyperphosphataemia that arises in many cases of chronic kidney disease may warrant dietary phosphate restriction and the use of phosphate binders. Loss or excess of electrolyte management is challenging in many clinical settings. Intravenous potassium chloride administration is carried out after dilution in normal saline and needs to be monitored carefully due to the cardio-toxic effects of potassium. Fluid and electrolyte therapy will have to be tailored based on the primary disease and the body system involved.

Learning Outcomes

- The water in the body is divided into intracellular and extracellular fluid compartments (plasma, lymph, and interstitial and transcellular fluids). The plasma and interstitial fluid in vertebrates are similar in composition, but the ECF and ICF in all animals are significantly different, with NaCl prevailing in the ECF and potassium and organic molecules dominating in the ICF.
- ECF volume and osmolarity are both regulated in mammals to maintain fluid balance. Controlling ECF osmolarity prevents hyper- or hypotonicity from causing variations in ICF volume. The baroreceptor reflex and plasma–interstitial fluid shifts regulate ECF volume in the short term, which is critical in the long-term regulation of blood pressure. Water and salt balances are used to regulate osmolarity and volume.
- In acid-base balance, the management of free hydrogen ions in physiological fluids is critical to survival. Free hydrogen ions are liberated by acids, whereas bases accept free hydrogen ions. The hydrogen ion concentration is expressed using the pH scale. Hydrogen ion fluctuations affect neuron, enzyme, and potassium ion activity. From metabolic activities, hydrogen ions are constantly added to bodily fluids.
- The major ECF buffer is the bicarbonate buffer system. Intracellularly, the peptide and protein buffer system, which includes haemoglobin in erythrocytes, is crucial. Buffers are only a temporary solution because they do not remove excess hydrogen ions; thus, the second and third lines of defence are required. The second line of defence is the respiratory system, which regulates hydrogen ions by adjusting ventilation. Carbon dioxide is removed when breathing occurs more deeply, but it is retained when breathing happens less deeply. Excretory systems control both bicarbonate and hydrogen ions in the ECF and constitute the third line of defence that aid in acid-base homeostasis. Cells in kidneys can release hydrogen ions and reabsorb bicarbonate, while other cells can do the opposite. Some cells release ammonia trap hydrogen ions as ammonium in acidosis.
- Hypoventilation causes respiratory acidosis, caused by an increase in carbon dioxide. Hyperventilation causes respiratory alkalosis, caused by a reduction in carbon dioxide. A decrease in plasma bicarbonate is linked to metabolic acidosis induced by acute diarrhoea, diabetes, intense exertion, or uraemia. Hyperventilation causes respiratory alkalosis caused

(continued)

by a reduction in carbon dioxide. Vomiting can cause metabolic alkalosis, marked by an increase in bicarbonate.

- Body fluid, electrolyte, and acid-base homeostasis must be maintained and regulated to the sustained body's functions. The body has several compensating processes to keep fluid, electrolytes, and acid-base balance; if its compensating systems fail to maintain homeostasis, it can have profound, even life-threatening implications. Fluid treatment can help with these problems.

Exercises

Objective Questions

Q1. Which is the most effective buffer system in the intracellular fluid?
Q2. Which is the major cation of the extracellular fluid?
Q3. Which is the first line of defence in acid-base regulation?
Q4. What does the isohydric principle state?
Q5. How many bicarbonate ions are returned to the blood for each glutamine metabolised within tubular epithelial cells?
Q6. What are the only means by which water output can be significantly controlled?
Q7. Which hormone is released from the heart when there is an increase in sodium level and blood volume?
Q8. What amount of fluid is required to correct 8% dehydration in a 300 kg cow?
Q9. Which fluid compartment has the major part of the body's water?
Q10. Which electrolyte is the chief determinant of cellular volume and intracellular osmolarity?
Q11. Where does the reabsorption of cerebrospinal fluid occur explicitly?
Q12. Which are the major electrolytes involved in the total osmolarity of the interstitial fluid and plasma?
Q13. Which condition is indicated when there is increased excretion of ammonium chloride in urine?
Q14. What amount of water forms when one gram of fat is oxidised?
Q15. Which type of acid-base imbalance is observed in the carbohydrate engorgement of cattle?

Subjective Questions

Q1. Explain in detail body water compartments.
Q2. Which are the methods for measuring body water?
Q3. What is cerebrospinal fluid? Explain the formation, absorption, and functions of cerebrospinal fluid.
Q4. How is acid-base regulated in the body?
Q5. Which are the acid-base imbalances?
Q6. What is dehydration, and how is it managed?
Q7. Which are the common electrolyte abnormalities?
Q8. Which are the important electrolytes in the body fluids?
Q9. How is water intake and water output regulated?
Q10. Which are the different types of parenteral fluids?

Answer to Objective Questions

A1. Protein
A2. Sodium
A3. Chemical buffering
A4. The buffers of the blood and body fluids do not act independent of each other, but rather react in unison
A5. Two
A6. Through regulation of urine volume
A7. Atrial natriuretic factor
A8. 24 L
A9. Intracellular fluid
A10. Potassium
A11. Arachnoid villi
A12. Sodium and chloride ions
A13. Acidosis
A14. 1.1 mL of water
A15. Metabolic acidosis

Keywords for Answer to Subjective Questions

A1. Intracellular fluid, extracellular fluid, transcellular fluid
A2. Indicator dilution technique, haematocrit
A3. Choroid plexus, arachnoid villi, buoyancy
A4. Chemical buffers, respiratory system, kidney
A5. Metabolic acidosis, metabolic alkalosis, respiratory alkalosis, respiratory acidosis
A6. Diarrhoea, skin turgor test, Ringer's lactate
A7. Hyperchloraemia, hyperkalaemia, hypernatraemia, hypocalcaemia, hypochloraemia, hypokalaemia
A8. Sodium, potassium, phosphate, chloride, hydrogen, bicarbonate, calcium
A9. Antidiuretic hormone, thirst, urine, atrial natriuretic factor
A10. Crystalloids, colloids, isotonic, hypertonic, isotonic

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