بسم الله الرحمن الرحيم

General Systemic States

by

Dr. E.M. Said

Prof. Of Vet. Int. Med.

I. Disturbances in body fluid, electrolytes, and acid-base balance

Disturbance in body fluid

1. Dehydration.

2. Water poisoning.

Dehydration:

A disturbance of body water balance in which more fluid is lost from the body than that is absorbed results in reduction in circulating blood volume and in dehydration of the tissues

i.e. it is a negative water balance.

ETIOLOGY

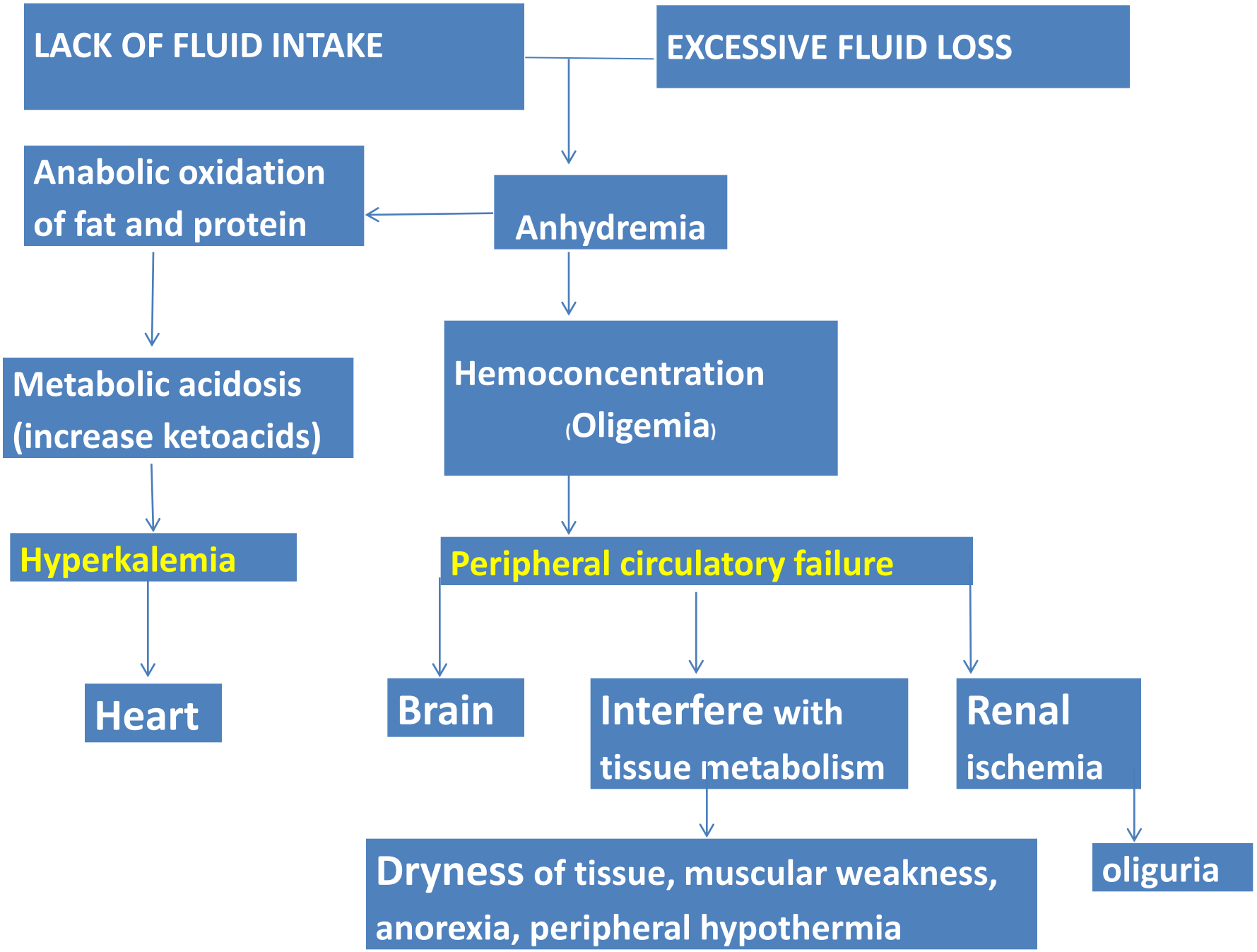
There are two major causes of dehydration:

A- Inadequate water intake

1. **Deprivation,**
2. **Lack of thirst (toxemia).**
3. **Esophageal obstruction**

B. Excessive fluid loss

1. **Diarrhea and/or vomiting.**
2. **Acute carbohydrate engorgement of ruminants.**
3. **Acute intestinal or gastric obstruction, dilatation and volvulus of abomasum**
4. **Polyuria.**
5. **Extensive skin wounds and burning.**
6. **Copious sweating in horses.**
7. **Diffuse peritonitis**


LACK OF FLUID INTAKE
EXCESSIVE FLUID LOSS
Anabolic oxidation of fat and protein
Anhydremia
Metabolic acidosis (increase ketoacids)
Hemoconcentration (Oligemia)
Hyperkalemia
Peripheral circulatory failure
Heart
Brain
Interfere with tissue metabolism
Renal ischemia
Dryness of tissue, muscular weakness, anorexia, peripheral hypothermia
oliguria

CLINICAL FINDINGS

1.The first and most important clinical finding in dehydration is **dryness** and **wrinkling of the skin**, which gives the body and face a shrunken appearance.

2.The eyes recede into the sockets, and the skin subsides slowly after being picked up into a fold. The best indicator of hydration status in dairy calves has been demonstrated to be the **degree of recession of the eye into the orbit**

3. In diarrheic calves, the severity of dehydration, hypothermia, and metabolic acidosis are associated with the degree of **mental depression.**

4.The combined effects of acidemia and dehydration also contribute to **hypothermia.**

5. Loss of BW and milk production occurs rapidly in dehydration, and **muscular weakness and inappetence or anorexia** is common.

6.The degree of thirst present will depend on the presence or absence of other diseases causing an inflammatory response or endotoxemia. In primary water deprivation, dehydrated animals are very thirsty when offered water. In dehydration secondary to enteritis associated with severe inflammation, acidemia, and electrolyte imbalance there may be no desire to drink.

7. Horses that become dehydrated in endurance rides may refuse to drink, and the administration of water by oral intubation and enemas may be necessary.

Assessment of hydration

Eyelid recession test in pet

- Hydration status is assessed by gently rolling the lower eyelid out to its normal position and estimating the distance of eye recession in millimeters.

-This distance is multiplied by 1.7 to provide an estimate of the degree of dehydration as a percentage of euhydrated body weight.

Skin fold test in calves

- The second best indicator of hydration status in calves is the elasticity of the skin of the neck and lateral thorax, which are assessed by pinching the skin between the fingers, rotating the skin fold 90°, and noting the time required after release of the skin fold for the skin fold to disappear (normally <2 seconds).
- The elasticity of the skin fold on the upper or lower eyelid is a poor indicator of hydration status in calves and is not recommended.

- The best method for assessing hydration status in adult cattle and other large animals has not been determined, but it is likely that eye recession and skin tent duration in the neck region provide the most accurate and sensitive methods for estimating hydration status.

Water intoxication

Def. and etiology: Rapid ingestion of large quantities of water

Epidemiology: Access to water by thirsty calves, or calves that have been marginally deprived of water for some time

Clinical findings: Dark red urine, weakness, and depression

Clinical pathology: Hemoglobinuria, hemoglobinemia, hypoosmolality, hyponatremia, and hypochloremia

Necropsy findings: Hemoglobinuria and renal cortical necrosis

Diagnostic confirmation: Epidemiologic, presence of hyponatremia and hypochloremia; rule out other causes of intravascular hemolysis

Treatment: Time, possibly intravenous **hypertonic saline** but usually too late to be effective

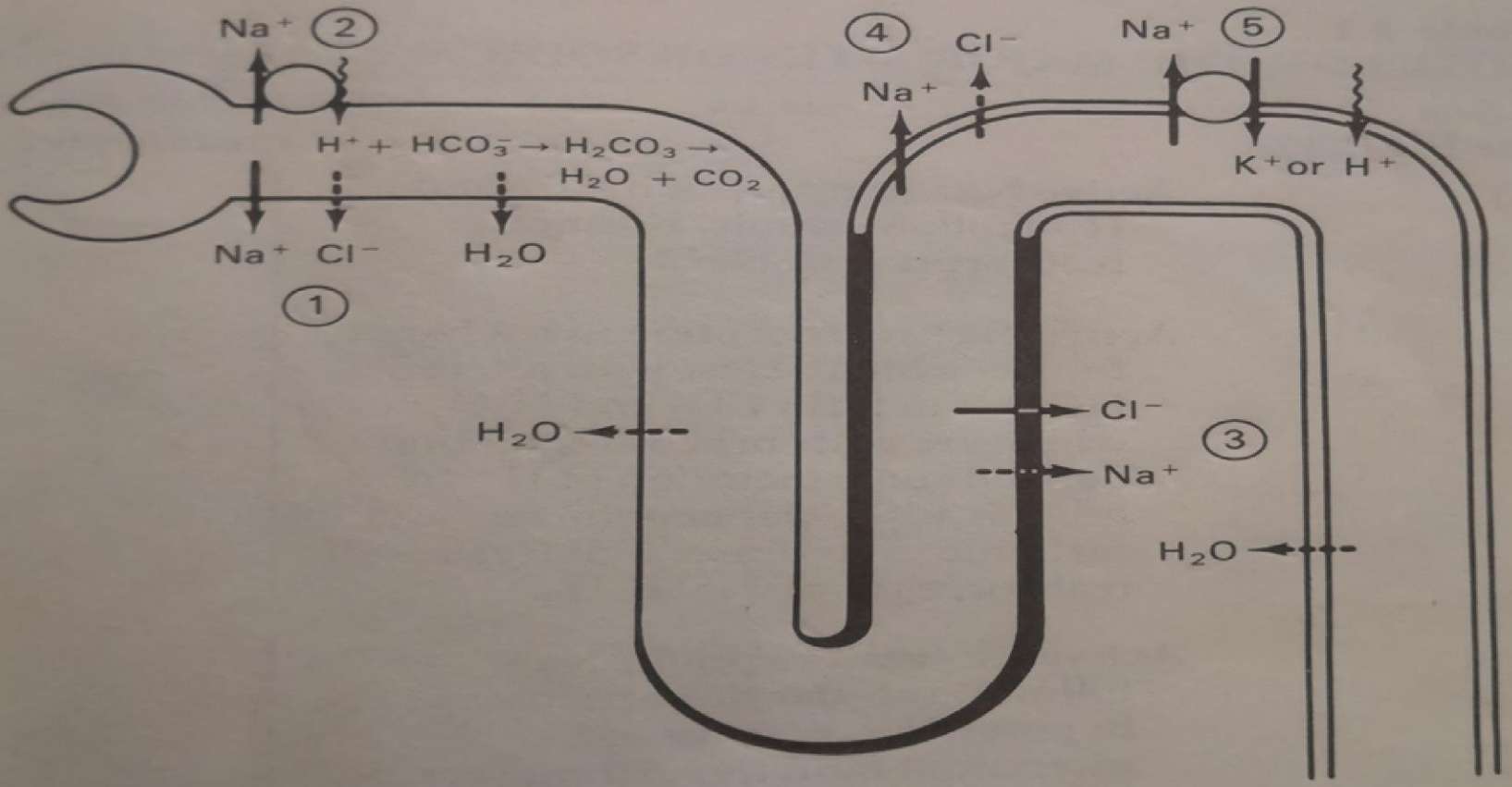
Electrolyte Imbalances

The electrolytes of major concern are:
sodium, chloride, potassium, calcium, phosphorus, magnesium, and bicarbonate.

HYPONATREMIA

Introduction

- Sodium (**Na^+**) is the most abundant ion in the extracellular fluid and is chiefly responsible for **the maintenance of osmotic pressure of the extracellular fluid.**
- Total body sodium average 60 mmol/kg of body weight but of this 60% is readily exchangeable. **The remainder is in bone, cartilage and dense connective tissue.**
- The normal range of plasma sodium concentration is **135-145 mmol/l.**
- Urinary excretion of sodium is tailored to the dietary intake. The sites at which sodium reabsorbed in normal tubules are shown in the following figure.


Na+ 2
H+ + HCO3− → H2CO3 →
H2O + CO2
Na+ Cl− H2O
1
H2O
4
Cl−
Na+
Na+ 5
K+ or H+
Cl−
3
Na+
H2O
Permeable to water
Impermeable to water
Permeable to water
in presence of ADH
Active transport
Passive transport
H+ secretion dependent
on carbonic anhydrase

The major sites of sodium reabsorption in kidney

site	Mechanism	% of total Na reabsorp
1	**Active Na^+** reabsorption, **Cl^-** and **H_2O** follow: result, **iso-osmotic** reabsorption of **NaCl**	70% PCT
2	**Active Na^+** reabsorption in exchange for **H^+** which reacts with filtered **HCO_3^-** to form **CO_2** and **H_2O** which are reabsorbed. Regulation depends on generation of **H^+** by tubular cells, dependent on **carbonic anhydrase activity**; result reabsorption of **$NaHCO_3$**	
3	**Active Cl^-** reabsorption **Na^+** follow: **tubular fluid becomes hypotonic to plasma and interstitial fluid hypertonic**; result reabsorption of **NaCl without H_2O. Ability to concentrate urine (by countercurrent mechanism) depends on this function.**	25% Loop
4	**Active Na^+ reabsorption, Cl^- follow**: result reabsorption of NaCl and water, tubular fluid becoming iso-osmotic with plasma if ADH active; in absence of ADH fluid remains hypotonic **(ability to dilute urine depends on this function).**	

site	Mechanism	% of total Na reabsorp
5	**Active reabsorption of Na^+ in exchange for K^+ and H^+ depending on aldosterone:** balance between K^+ and H^+ as counter ion depends partly on generation of H^+ in tubular cells, which is itself dependent on carbonic anhydrase.	5% DCT

Site of action of common diuretics on sodium reabsorption

Type of diuretic	Site of action	examples
Thiazide	Mainly **site (4)** but also **site (1)** {also **weak carbonic anhydrase inhibitor** so H^+ excretion at site (5) reduced and K^+ secretion increased; **more sodium reaches this site and also favors K^+ loss }**	Bendrofluazide Chlorothiazide Metolazone
Loop	Mainly **site (3)** but **also site (4)** {more sodium reaches site (5) increasing both K^+ and H^+ loss: hypokalemia and alkalosis; inhibition of loop transport reduces corticomedullary osmotic gradient and therefore reduces ability to concentrate urine}	Frusemide Bumetanide Ethacrynic acid
Potassium sparing	**Site (5)** - Spironolactone by acting competitive inhibitor of aldosterone. - Other drugs by different mechanism	Spironolactone Amiloride Triametrene
Carbonic anhydrase inhibitor	**Sites (2)and (5)** by diminishing availability of H^+ for exchange; (weak action; used in treating glaucoma by reducing carbonic anhydrase-dependent secretion of aqueous humor)	Acetazolamide

Type of diuretic	Site of action	examples
Osmotic	**Site (1) and (5)** by maintaining large tubular volume by means of poorly reabsorbed small molecules (electrolytes reabsorption only slightly decreased per liter but volume of urine may be very large).	Mannitol Urea

1.Definition of hypo/natr/emia:

Decrease sodium (Na^+) ions in the blood.

2. Etiology:

The most common cause of hyponatremia is increased loss of sodium through the intestinal tract in

enteropathies:

- This is particularly marked in **the horse with acute diarrhea.**
- In calves with **acute diarrhea caused by *enterotoxigenic Escherichia coli*** the sodium concentration of the intestinal fluid secreted in response to the enterotoxin is similar to that of plasma, and hyponatremia usually occurs (**hypotonic dehydration**).

- Hyponatremia can become severe when sodium-free water or 5% dextrose are used as the only fluid therapy in animals already hyponatremic.

- Hyponatremia can also occur in animals ***with proximal tubular dysfunction***.

Hyponatremia causes an increase in the renal excretion of water in an attempt to maintain normal osmotic pressure, which results in a decrease in the extracellular fluid space, leading to a decreased circulating blood volume, hypotension, peripheral circulatory failure, and ultimately renal failure. Muscular weakness, hypothermia, and marked dehydration are common findings.

Clinical signs:

1. There is usually ***dehydration.***
2. ***Polyuria and polydipsia*** occur in cattle with dietary sodium chloride deficiency.

3. ***Muscular weakness.***
4. ***Mental depression***, which occur with other disturbances of both water and electrolytes and with acid-base imbalance.

Classification of dehydration according to plasma osmolality:

1. Hypotonic dehydration:

- **as in all types of diarrhea especially entertoxigenic diarrhea, Colibacillosis and salmonellosis especially in horses.**
- Hypotonic hyponatremia results in **cerebral edema** by water entry to the brain; chronic hyponatremia has been associated with improvement of neurologic abnormalities; by the development of progressive ataxia, dysphagia, myoclonus, spastic tetraparesis, and death within 2 to 5 days.

2. Isotonic dehydration: occurs when there is a parallel loss of sodium and water e. g. **copious sweating and nephrosis**

3. Hypertonic dehydration:

- **mechanism of thirst:** the osmolality of ECF is regulated by means of the supraoptical nuclei of hypothalamus (osmostat) which normally maintains a constant plasma osmolality because a 1% increase in plasma osmolality triggers both thirst and the release of antidiuretic hormone (ADH) with the result that more water is both taken and retained; a fall in plasma osmolality has the opposite effects.
- In animals that are unable to consume water because of an esophageal obstruction.

HYPERNATREMIA

Definition:

Increase sodium (Na^+) ions in the blood.

Etiology:

- Hypernatremia is most commonly caused by **water restriction or mixing errors in neonatal animals,** particularly in milk-replacer solutions or oral electrolyte formulations administered to neonatal calves with diarrhea as part of the treatment of dehydration.
- Less common causes of hypernatremia include **high-salinity water.**

- Hypernatremia occurs transiently **after hypertonic saline (7.2% NaCl) administration**, but serum sodium concentrations never exceed 170 mEq/L and may occasionally exceed 160 mEq/L for a few minutes. Transient episodes of mild hypernatremia caused by intravenous hypertonic saline administration are not thought to have any clinical consequences

Clinical signs:

A. Clinically relevant hypernatremia occurs when serum sodium concentrations exceed **160 mEq/L**, with significant mortality occurring whenever serum sodium concentrations exceed **180 to 190 mEq/L** before treatment is instituted.

B. The clinical signs of hypernatremia are nonspecific and

1. Weakness, depression, inappetence, abnormal posture, recumbency.
2. Apparent blindness, and muscle twitching, particularly of the facial muscles.
3. Some animals may convulse shortly before death.
4. Cerebral depression is caused by inhibition of neuronal cell glycolysis.
5. Less severely affected animals may exhibit a mania for water.

Treatment:

- Correction of hypernatremia is challenging because too rapid a rate of correction can result in **cerebral edema and brain herniation** through the foramen magnum, particularly in animals with chronic hypernatremia.

- Treatment of hypernatremia focuses on identifying and **removing the underlying cause (such as incorrectly mixed milk replacer).**

- slowly reducing the serum sodium concentration, (10 mEq/L decrease per day representing an ideal goal).

- The preferred method for decreasing serum [Na^+] concentration is by oral administration of sodium containing electrolytes.

HYPOCHLOREMIA

Def.: decrease chloride ions (Cl^-) in the blood.

Etiology:

- Vomiting in monogastric animals.
- abomasal diseases (dilatation, impaction, volvulus and displacement).
- Acute proximal intestinal obstruction.
- Enteritis and gastroenteritis
- All conditions of hypochloremic, hypokalemic, metabolic alkalosis.

Clinical findings:

- Anorexia, weight loss and lethargy.
- Mild polydipsia, and polyuria.
- A marked metabolic alkalosis occurs resulting in hypokalemia, hyponatremia

HYPOKALEMIA

Definition: Decrease potassium ions (K+) in the blood.

Etiology:

- Decreased dietary intake.
- Increased renal excretion, e.g. diuretics.
- Abomasal stasis, proximal intestinal obstruction and enteritis and gastroenteritis.
- Repeated administration of corticosteroids with mineralocorticoid activity.

- The prolonged use of **potassium-free solutions** in fluid therapy.
- **Alkalosis** may result in an exchange of potassium ions for hydrogen ions in the renal tubular fluid, resulting in hypokalemia

Clinical Signs:

- Hypokalemia can cause muscle weakness, recumbency, and inability to hold up the head, anorexia, muscular tremors and paradoxic aciduria, if severe enough, coma. **The treatment of ketosis in lactating dairy cows with multiple dosages of isoflupredone, a glucocorticoid with some mineralocorticoid activity, can cause hypokalemia and recumbency, with a high case fatality rate.**

- Metabolic alkalosis and hypokalemia in cattle are often accompanied by muscular weakness by lowering the resting potential of membranes, resulting in decreased excitability of neuromuscular tissue and. Thus, the differential diagnosis of the animal with muscle weakness should always include hypokalemia.
- The most common occurrence of hypokalemia in ruminants is in diseases of the abomasum that cause stasis and the accumulation of fluid in the abomasum. Potassium becomes sequestered in the abomasum along with hydrogen and chloride, resulting in **hypokalemia, hypochloremia and metabolic alkalosis.**

Relationship between hypokalemia and metabolic alkalosis:

- Hypokalemia and alkalosis also are often ***directly related*** because of the renal response to either. Hypokalemia from true body deficits of potassium will cause decreased intracellular concentration of this ion. The intracellular deficit of potassium and excess of hydrogen will cause hydrogen secretion into the urine when distal sodium reabsorption is required.
- This situation exists in metabolic alkalosis, where sodium bicarbonate reabsorption in the proximal nephron is decreased because of the excess of plasma bicarbonate.

- Distal nephron avidity for sodium is increased to protect extracellular fluid volume, and the increased distal sodium reabsorption is at the expense of hydrogen secretion, although it is contrary to the need of acid retention in the presence of alkalosis. *In other words, the kidney prioritizes maintenance of plasma volume above that of acid-base balance, presumably because respiratory compensation can usually keep blood pH within the normal physiological range*

- Because **electroneutrality** of extracellular fluid must be maintained by reabsorbing an equivalent charge of cations and anions, the reabsorption of chloride and of bicarbonate in the kidneys are inversely proportional to each other. Thus, with excess trapping of chloride in the abomasum, the kidneys will compensate for the resulting hypochloremia by increasing bicarbonate reabsorption, which may proceed until metabolic alkalosis develops.

Treatment of Hypochloremia and Hypokalemia

- Hypokalemic alkalosis requires correction of extracellular fluid volume and sodium and chloride deficits with **0.9% NaCl infusions and oral KCl**. Providing adequate chloride ion allows sodium to be reabsorbed without bicarbonate. Increased proximal reabsorption of sodium will decrease distal acid secretion because less sodium is presented to the distal nephron. As, less bicarbonate is reabsorbed and less acid secreted, the metabolic alkalosis is resolved. Specially formulated solutions containing potassium are necessary in cases of severe hypokalemia and small intestinal obstruction.

- Hypokalemia also occurs following treatment of the horse affected with metabolic acidosis and hyponatremia, and probably reflects whole-body potassium depletion.
- Horses used for **endurance rides** may be affected by ***hypokalemia, hypocalcemia and alkalosis*** due to loss of electrolytes during the competition. ***Synchronous diaphragmatic flutter*** also occurs, which may be the result of the electrolyte imbalance (particularly hypocalcemia) causing hyperirritability of the phrenic nerve.
- Since potassium is the major intracellular cation, the measurement of plasma or serum potassium is not a reliable indication of whole-body potassium status.

- In severe alkalosis, for example, potassium leaves the extracellular space and becomes concentrated in the cells. Conversely, in severe metabolic acidosis, the potassium leaves the cells and moves into the extracellular fluid. This results in hyperkalemia in some cases where the body potassium is normal or even decreased. When changes occur in the concentration of intracellular and extracellular potassium, the ratio of intracellular to extracellular potassium may decrease by as much as 30-50%, which results in a decrease in the resting membrane potential. This is thought to be the explanation for the effects of hypokalemia and hyperkalemia on muscle function

- The potassium concentration of Rbcs may be a more accurate indicator of whole-body potassium deficit.

- Potassium should be administered ***intravenously or orally***. **The intravenous route is used only for the initial treatment of recumbent ruminants with severe hypokalemia and rumen atony, as it is much more dangerous and expensive than oral treatment.** The most aggressive intravenous treatment protocol is an ***isotonic solution of KCl (1.15% KCl),*** which should be administered at less than 3.2 mL/kg/hour, equivalent to a maximal delivery rate of 0.5 mEq of K+ /kg B.W./hour. Higher rates of potassium administration run the risk of inducing arrhythmias, including ventricular premature complexes that can lead to ventricular fibrillation and death.

- A less aggressive intravenous treatment is an isotonic equimolar mixture of NaCl (0.45% NaCl) and KCl (0.58% KCl), and the least aggressive intravenous treatment is the addition of 10 mmol of KCl/L of Ringer's solution, which will increase the solution osmolarity to 329 mosmol/L. Clinical experience with oral administration of KCl has markedly decreased the number of adult ruminants treated with intravenous KCl.

- **Oral administration of potassium is the method of choice for treating hypokalemia.**
- **Inappetent adult cattle should be treated with *30-60 g of feed grade KCl twice with a 12-hour interval, with the KCl* placed in gelatin boluses.**
- **Adult cattle with severe hypokalemia (< 2.5 mEq/L) should initially be treated with 120 g of KCl, followed by two 60 g KCl treatment at 8-hour intervals, for a total 24-hour treatment of 240 g KCl.**

Higher doses have been administered to dairy cows but these are accompanied by diarrhea, and oral administration of 0.58 g KCl/kg B.W. was toxic in 6 -month-old. Holstein calves, manifest by excessive salivation, muscular tremors of the legs and excitability, and a peak plasma [K+] of 9.0 mEq/L.

HYPERKALEMIA

Def. Increase potassium ions (K+) in blood.

Etiology:

- Hyperkalemia is not as common in farm animals as hyperkalemia, occurring most commonly in severe ***metabolic acidosis.***
- A more likely mechanism is that metabolic acidosis is accompanied by acidemia and a decreased intracellular pH; during intracellular acidosis the function of all enzyme systems is decreased. As a direct result of the intracellular acidosis, the **Na-K ATPase activity** is decreased, with potassium leaving the cell down its concentration gradient.

- Hyperkalemia is potentially more life threatening than hypokalemia. Hyperkalemia (when over 7-8 mmol/L) has a profound effect on cardiac function. There is usually marked bradycardia and arrhythmia and sudden cardiac arrest may occur.
- The changes of **ECG** include four successive stages as hyperkalemia increased. There was **a widening and lowering of amplitude followed by inversion and disappearance of the P wave, an increase in the amplitude of the T wave, an increase in the QRS interval, with some irregularity in the ventricular rate, and periods of cardiac arrest** that became terminal or were followed by ventricular fibrillation.

- The minimum plasma potassium concentration required to induce ECG changes was **6-7 mmol/L** and severe cardiotoxic effects occurred at levels between **8-11** mmol/L. The effects of hyperkalemia on the ECG are exacerbated by the presence of hyponatremia.
- **Hyperkalemia has traditionally been treated by intravenous administration of sodium bicarbonate, glucose, insulin and sometimes calcium.**

- **Hyperkalemic periodic paralysis**

It occurs in heavily muscled **Quarterhorse**. Affected horses become weak, may stand base-wide and are reluctant to move. Sweating commonly occurs and generalized muscle fasciculations are apparent.

- Affected horses remain bright and alert but may **yawn and do not eat or drink**. Some horses be come recumbent and may appear to be in a state of flaccidity.

- Attacks may occur in a rest period following exercise or at random. During the episode the **serum potassium concentration is elevated by up to twofold and returns to normal values when the animal recovers.**

- Treatment consists of sodium bicarbonate, or 5% dextrose given intravenously, possibly with insulin.

Disturbance of acid base balance

Introduction

pH

- The acidity of the ECF (blood) is generally expressed as **pH**
- The normal pH range of **7.36-7.44 (7.35-7.45 in animals)**.
- corresponds to a hydrogen ion concentration of **44 to 36 nmol/l**
- A pH outside the range **6.8-7.8** (corresponding to a H^+ concentration of **158-16 nmol/l**) is incompatible with life, and values **below 7.2 or above7.5** are potentially dangerous

Buffering system

- Buffers, by **absorbing or donating** hydrogen ions according to circumstances, mitigate the pH changes which would otherwise result from the amount of H^+ ions added or withdrawn.
- Buffering follows the general equation

- Whenever **H^+** ions are added, they combine with **the buffer base A^-** to form the **weak acid HA**. By this process the H^+ ion is prevented from expressing its activity(which in turn determines the pH of solution). Conversely, when **H^+** ions are wanting, the above reaction is driven to the right, **H^+** ions are donated by the weak acid and the change in pH of the buffered solution is less than would be expected from the addition of deficit of H^+ ions .
- **Only weak acids and their salts** can act as buffering substances within body fluids.

- As a general rule the salts of weak acids with a **pK** close to **the normal or physiologic pH of the body fluid act as the most efficient buffers.**
- The **pK**, the negative logarithm of the ionization constant, is the point at which an acid or an alkali is 50% dissociated; the closer this point is to the plasma pH, the better able a weak acid and its salt is to donate or bind hydrogen ions respectively .

- **Carbonic acid/bicarbonate pK = 6.1**
- **H_2PO_4/ HPO_4 pK = 6.8**
- **Protein buffers pK= 6.8**
- **Hemoglobin pK= 6.8**

- All acts as the most important buffering systems stabilizing the blood pH
- Their in vitro importance is reflected by the number of mmol of hydrogen ions which would be required to lower the pH of the amount of each buffer contained in the liter of the blood from 7.4 to 7.0

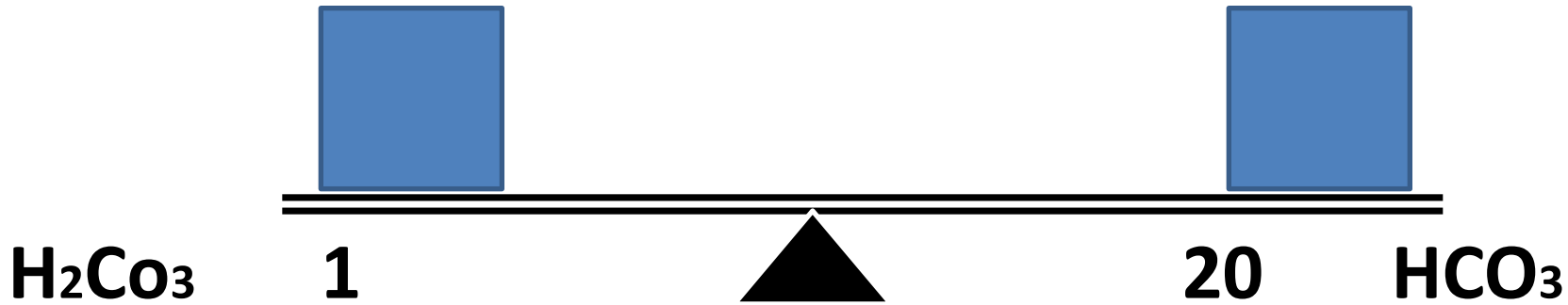
- **Bicarbonate 18**
- **Phosphate 0.3**
- **Plasma protein 1.7**
- **Hemoglobin 8**

28 mmol H^+

- The buffering capacity of bone and the intra cellular compartment approximately equals that of the extracellular compartment.

Buffer system

- The state of acid-base balance or imbalance of the extracellular fluid depends primarily upon **the relative quantities of carbonic acid and base bicarbonate present in the extracellular fluid.**
- Normally these are present in a ratio of **1 part of carbonic acid to 20 parts of bicarbonate.**
- When this ratio is disturbed, the acid-base balance is also upset, and there is a deviation from the **normal pH 7.35-7.45** of the body fluid.



Normal pH of extracellular fluid 7.36-7.44 (7.35-7.45 in animals).

Other buffer systems; play only a minor role in the regulation of acid-base balance

- **Monosodium phosphate: Disodium phosphate**
- **Monopotassium phosphate: Dipotassium phosphate**
- **Plasma protein system.**
- **Oxyhemoglobin: Reduced hemoglobin**

Acidosis and alkalosis

- ***The ratio*** of **1 part** of carbonic acid to **20 parts** of bicarbonate determines the pH of the extracellular fluid, and as long as this ratio is maintained the pH will lie within the normal range of **7.36-7.44 (7.35-7.45 in animals)**.
- If the carbonic acid and the bicarbonate are both **divided by 2 or both multiplied by 2,** the ratio remains 1:20 and the pH of ECF remains between**7.36-7.44 (7.35-7.45 in animals)**.
- , so the animal is in a state of acid-base balance.
- If either the carbonic acid or bicarbonate is increased or decreased so that the ratio no longer holds an acid-base imbalance results.

- Two general types of acid-base imbalance occur:

a. Metabolic disturbance: affect bicarbonate

1. Bicarbonate deficit: acidosis

2. Bicarbonate excess: alkalosis

b. Respiratory disturbance: affect carbonic acid

1. Carbonic acid deficit: alkalosis

2. Carbonic acid excess: acidosis

Metabolic acidosis (acidemia)

Definition: Bicarbonate ions deficit in the ECF (blood).

Causes metabolic acidosis can be divided into three categories

- Excessive loss of base (bicarbonate)
- Accumulation of endogenous or exogenous acid
- Combination of both of these process.

1. Excessive loss of saliva except in horse.
2. Extreme diarrhea and lower intestinal obstruction.
3. Acute carbohydrate engorgement.
4. Renal insufficiency and failure.
5. Ketosis:
    i. Starvation
    ii. ketosis in cattle
    iii. Pregnancy toxemia
    iv. Diabetes mellitus

6. Hypovolemic shock.

7. Urea, methanol and ethylene glycol poisoning

8. Administration of acidic fluid:

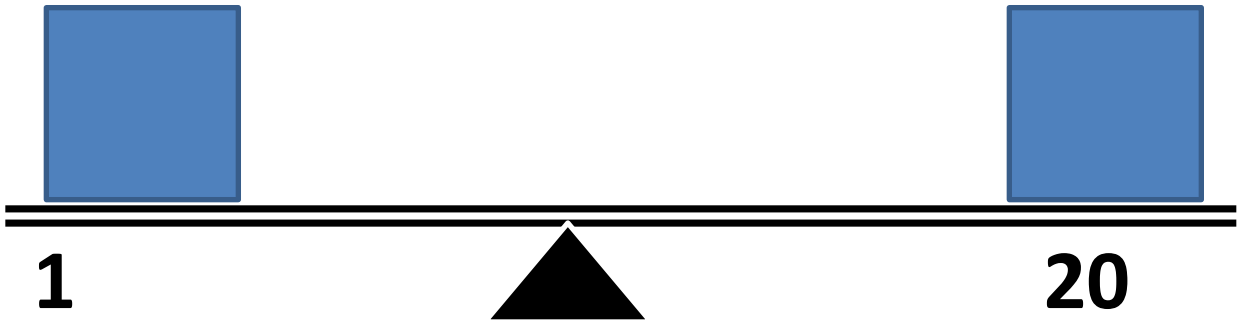
   i. Excessive parenteral administration of **sodium chloride** solution.

   ii. **Ammonium chloride**

9. Severe infectious diseases

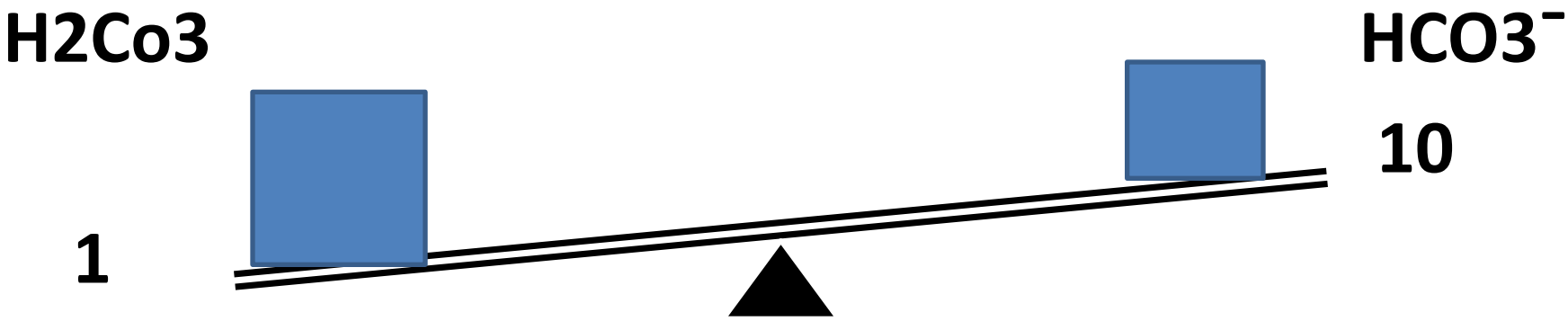
Pathophysiology

A. Normal balance

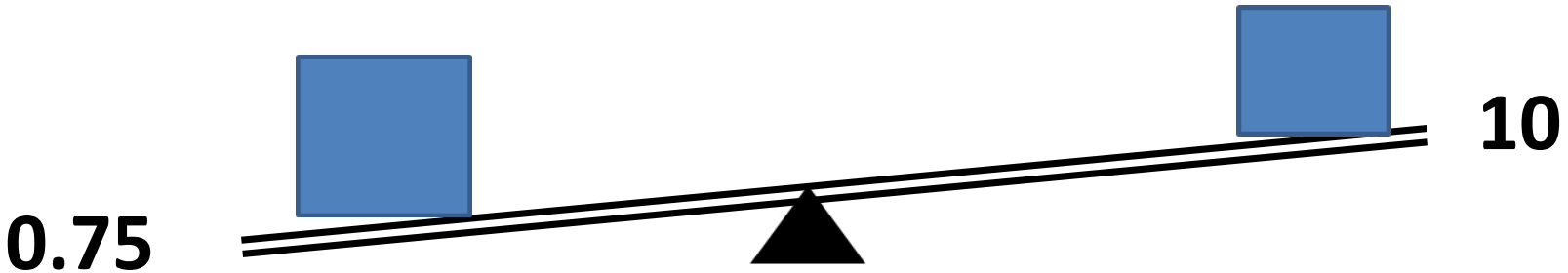


Normal pH of extracellular fluid 7.36-7.44

(7.35-7.45 in animals)



B. Acidosis



C. Body compensatory action:

1. **Breathing** hyperactive to remove carbonic acid.
2. **Kidneys** conserve bicarbonate ions and excrete hydrogen ions and non carbonate (chloride ions)

Clinical signs:

1. Hyperpnea increase the rate and depth of respiration.
2. Depression of CNS:
    i. Disorientation
    ii. Stupor
    iii. Coma

3. Hyperkalemia bradycardia, cardiac arrhythmia and arrest

Laboratory findings:

1. **Urine pH:** **More acid**
2. **Blood pH:** **Below 7.36**
3. **Plasma bicarbonate:** **Low**
4. **Plasma chloride:** **Variable but usually**

Principal therapy: administer bicarbonate ions

1. Sodium bicarbonate solution:

i. The **carbon dioxide** will be blown off through the lungs, leaving behind **sodium hydroxide** which change pH of the plasma toward the alkaline side.

ii. It can be given **orally**, which will be slower or **intravenous** which may be rather toxic especially in small animals due to less dilution by the blood.

2. **Sodium lactate:** converted to bicarbonate ions in the liver

i. Not as alkaline as sodium bicarbonate, so it is important to be as cautious in administration

ii. Orally or intravenously

3. Sodium gluconate

Metabolic Alkalosis (ALKALEMIA)

Def. Bicarbonate (**HCO^-_3**) excess in the blood.

Etiology: Alkalemia is caused by

- Excessive loss of acid.
- An increased absorption of alkali.
- A deficit of carbon dioxide.

I. **Excessive loss of acid (loss of chloride**

Hypochloremia) as in

- Diseases of the stomach and pyloric obstruction.

- Diseases of stomach of horse

- Diseases of abomasum.

- Upper (high) intestinal obstruction.

II. Potassium loss (Hypokalemia).

1. X-ray therapy.

2. Prolonged administration of K^+- solution.

3. Hyperadrenocorticism.

   i - Over activity of anterior pituitary.

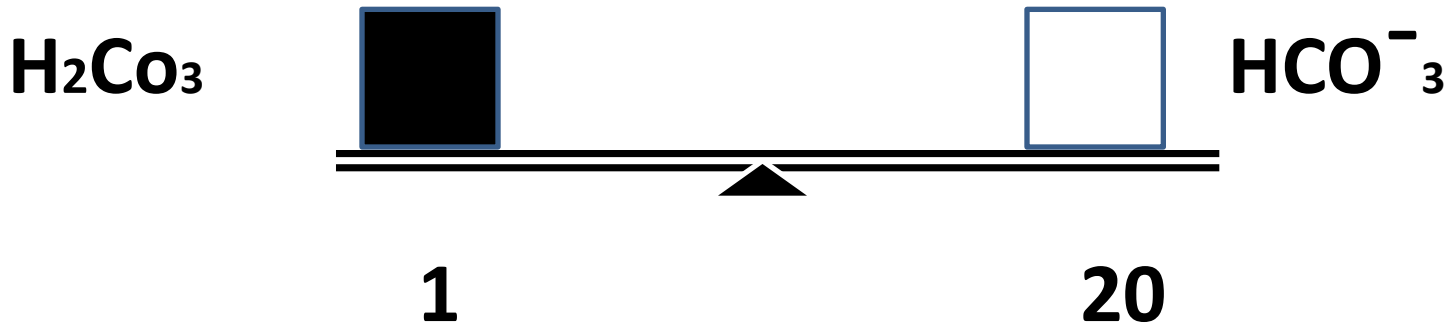
   ii- Adrenal tumor. iii - Overdosage of ACTH.

4. Excessive loss of saliva in horses.

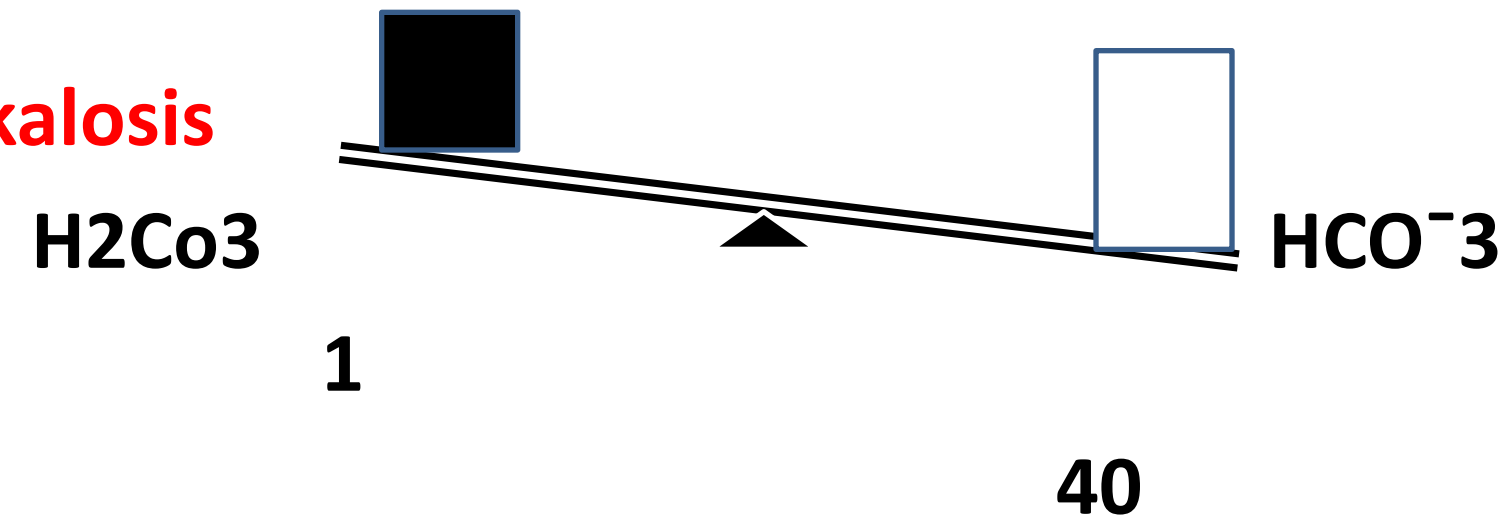
III. Excessive alkaline therapy

Pathophysiology

1. Normal balance



2. Alkalosis

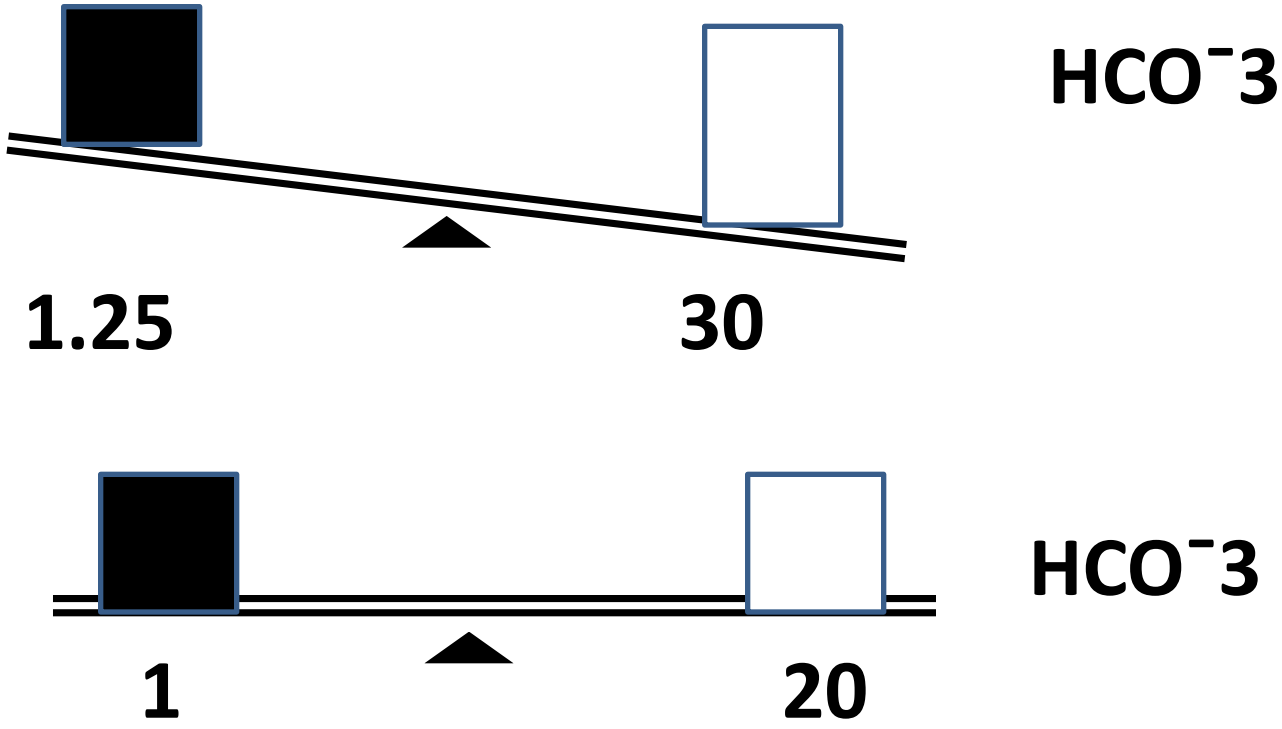


3. Body compensatory action:

i. **Breathing suppress**: lungs hold **Co_2**

ii. **Kidneys:** excrete **Hco^-_3** and retain **H^+** and **Cl^-** **to**

produce more alkaline urine



Therapy:

Using chloride ions to replace bicarbonate ions.

1. Sodium chloride **(NaCl)**.

2. Ammonium chloride **(NH_3Cl)**.

Respiratory acidosis (Hypoventilation)

Def.: Carbonic acid (H_2CO_3)excess

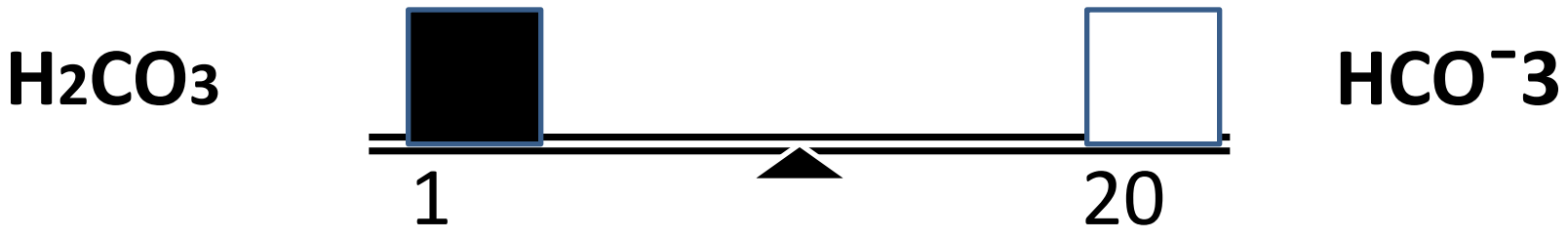
Etiology: impaired respiration causing **retention of carbon dioxide CO_2**

1. Pneumonia.
2. Emphysema.
3. Pulmonary congestion and edema.

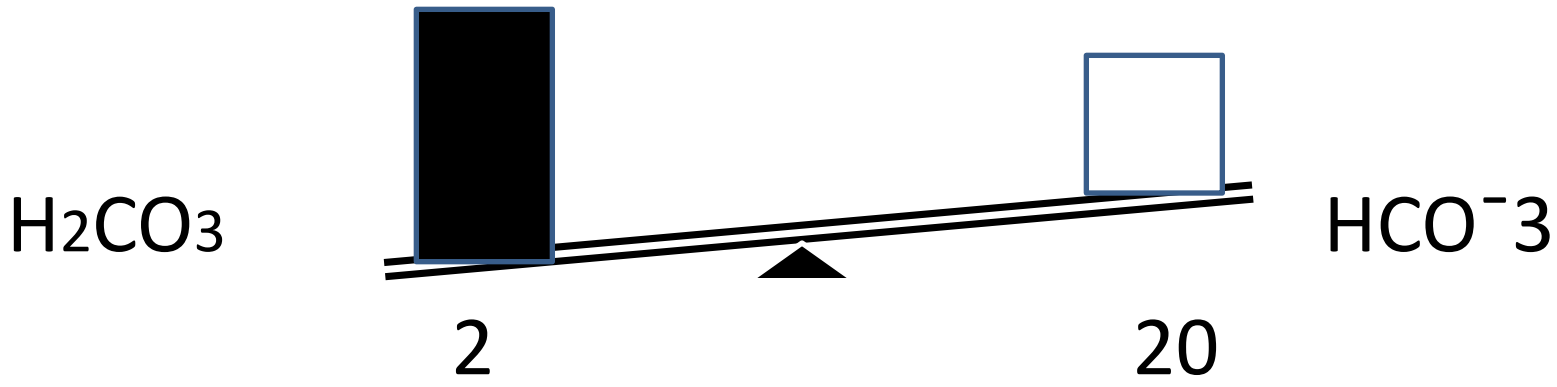
4. Pneumothorax, Hydrothorax, Hemothorax and pyothorax.
5. Pulmonary atelectasis.
6. Paralysis of respiratory muscles.
7. Occlusion of breathing passage.
8. Morphine and barbiturate poisoning

- Pathophysiology:

1. Normal balance

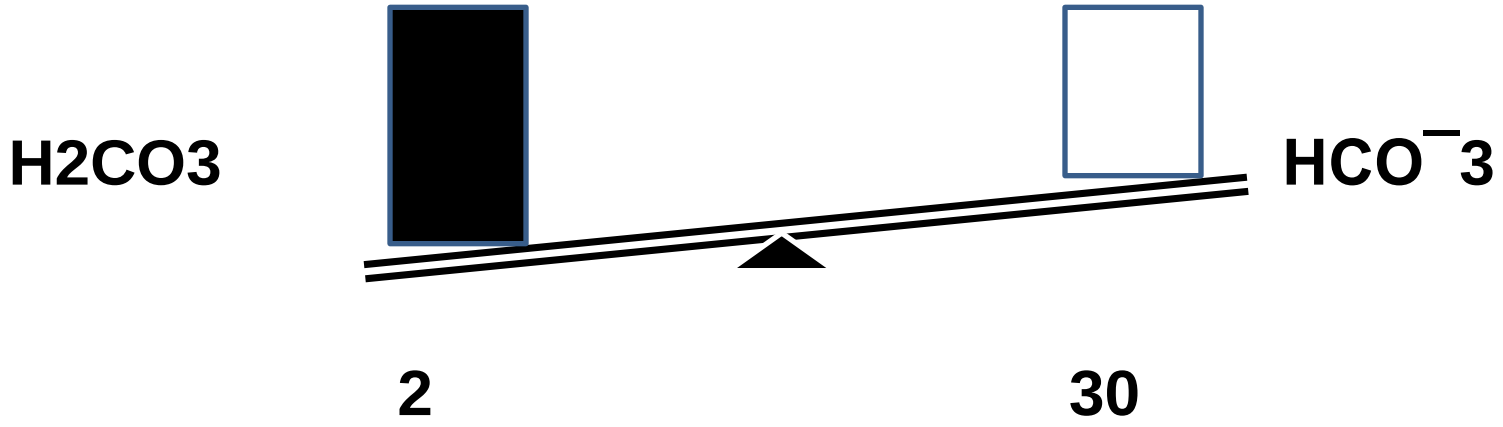


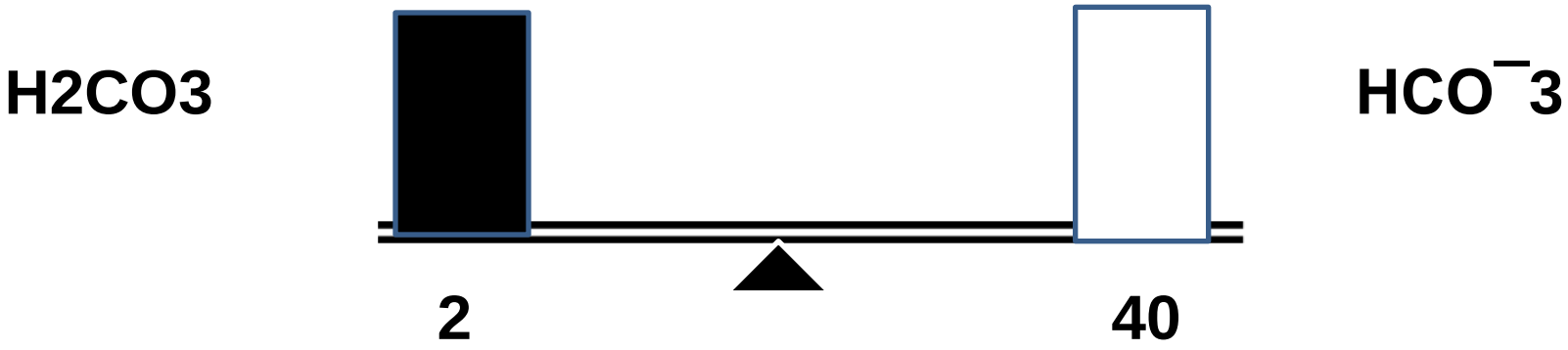
2.Respiratory acidosis



3. Body compensatory action:

Kidney: conserve bicarbonate and excrete hydrogen and Chloride ions and produce more acid urine.





Clinical signs

1. Respiratory embarrassment
2. Depression of the nervous system;
    1. Disorientation
    2. Coma

Laboratory findings:

1. Urine pH: more acid
2. Blood pH: below 7.35
3. Plasma bicarbonate: normal to high
4. Plasma Chloride: low

Therapy:

Do not use alkalinizing solution

1. ***As they decrease cerebral blood flow and***
2. ***decrease ability of hemoglobin to release oxygen to the tissues;***

instead, change the respiratory rate by treating the primary condition

Respiratory alkalosis (Hyperventilation)

Def.: Carbonic acid deficit.

Etiology: increase rate and depth of respiration

1. **Fever**

2. **Anemia**

3. **Acute and congestive heart failure**

4. Oxygen lack (altitude)

5. Respiratory center stimulation:

    i. Encephalitis

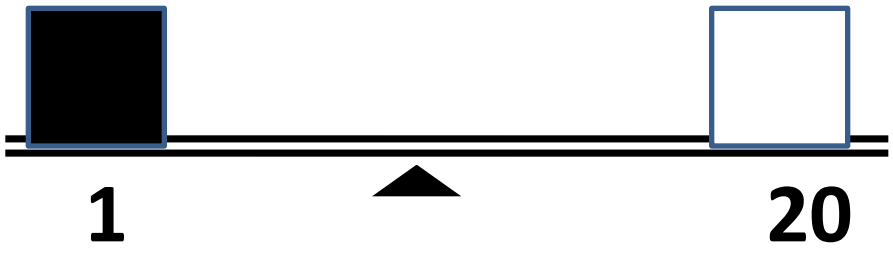
    ii. Drug salicylates

6. Hysteria and anxiety

Pathophysiology

i. Normal

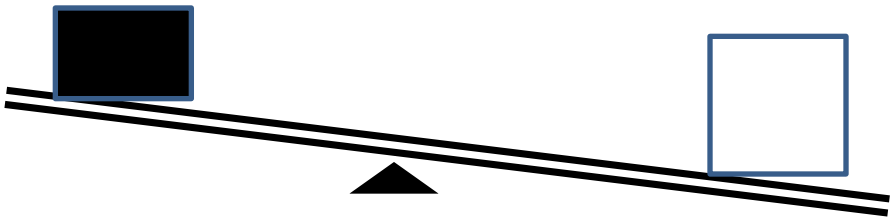
H_2CO_3



HCO^-_3

ii. Alkalosis

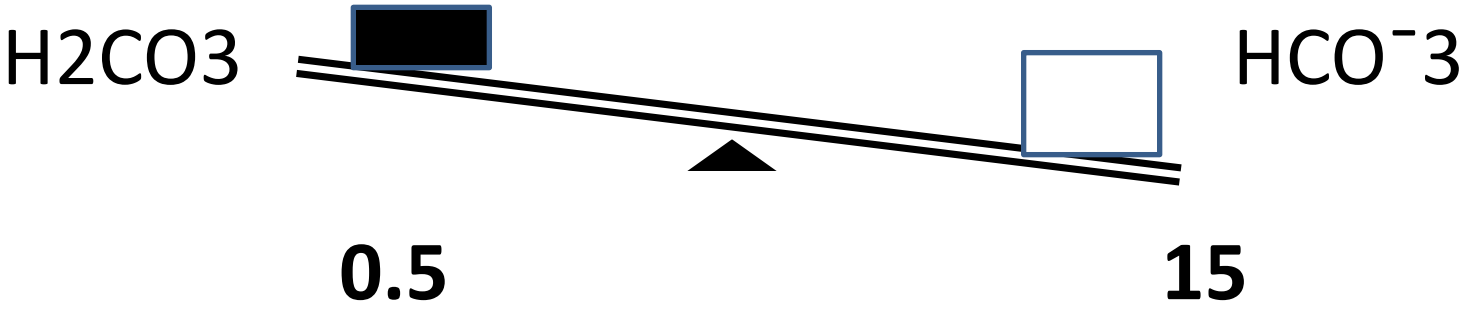
H_2CO_3

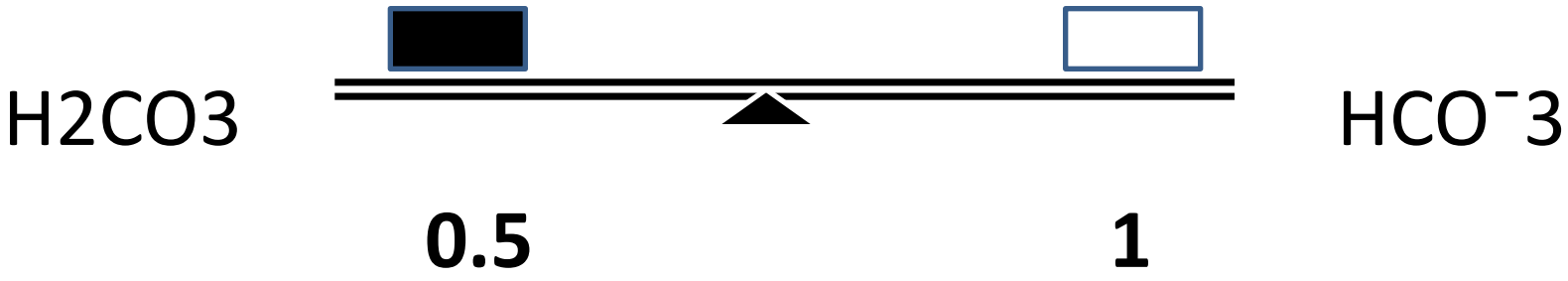


HCO^-_3

iii. **Body compensation action:**

Kidney: excrete Bicarbonate ions and retained Hydrogen and Chloride ions





Clinical signs:

1. Deep rapid breathing.

2. Tetany progressing to convulsions.

Laboratory findings:

Urine pH: more alkaline

Blood pH: over 7.45

Plasma bicarbonate: normal to low

Plasma Chloride: normal to high

Therapy:

Acidifying solutions are not indicated; Increase the

***pCO2* in the atmosphere**

Naturally Occurring Combined Abnormalities

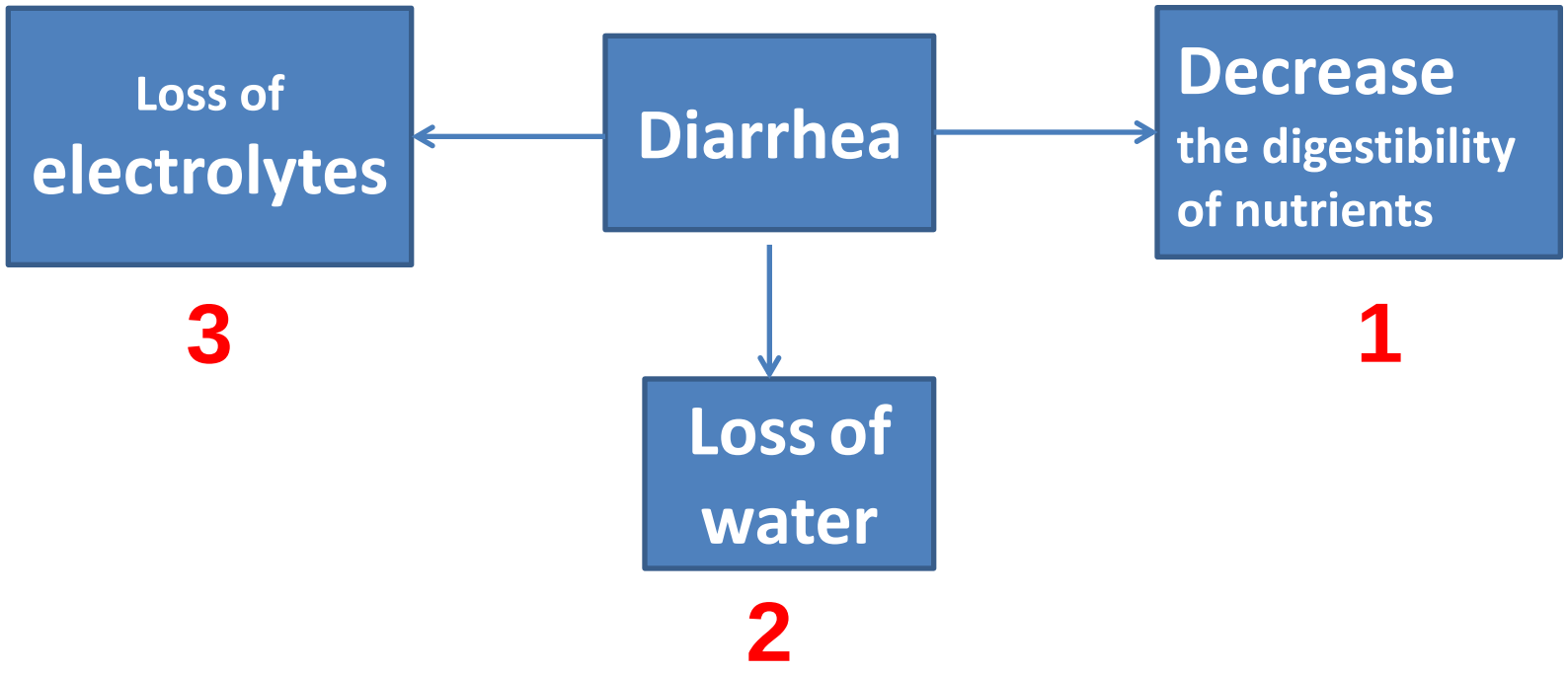
of Free Water, Electrolytes, Acid-Base Balance, and Oncotic Pressure

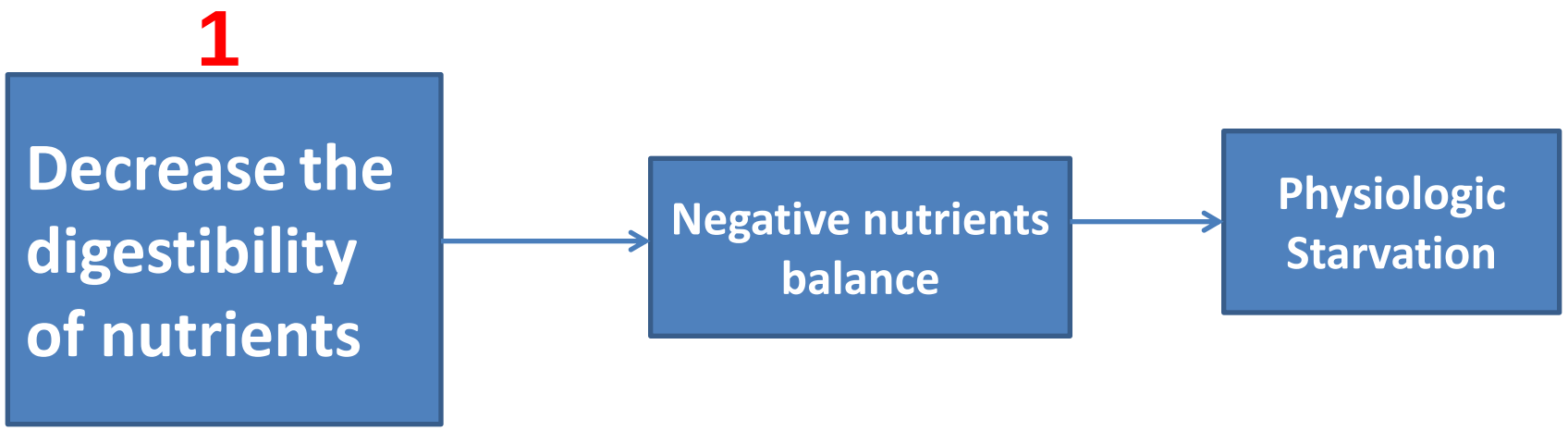
- These abnormalities are seldom **primary** and are usually **secondary** to a serious disease
- **Diseases that are in themselves life-threatening.** state such as abomasal volvulus, rumen overload, or acute intestinal obstruction**.**

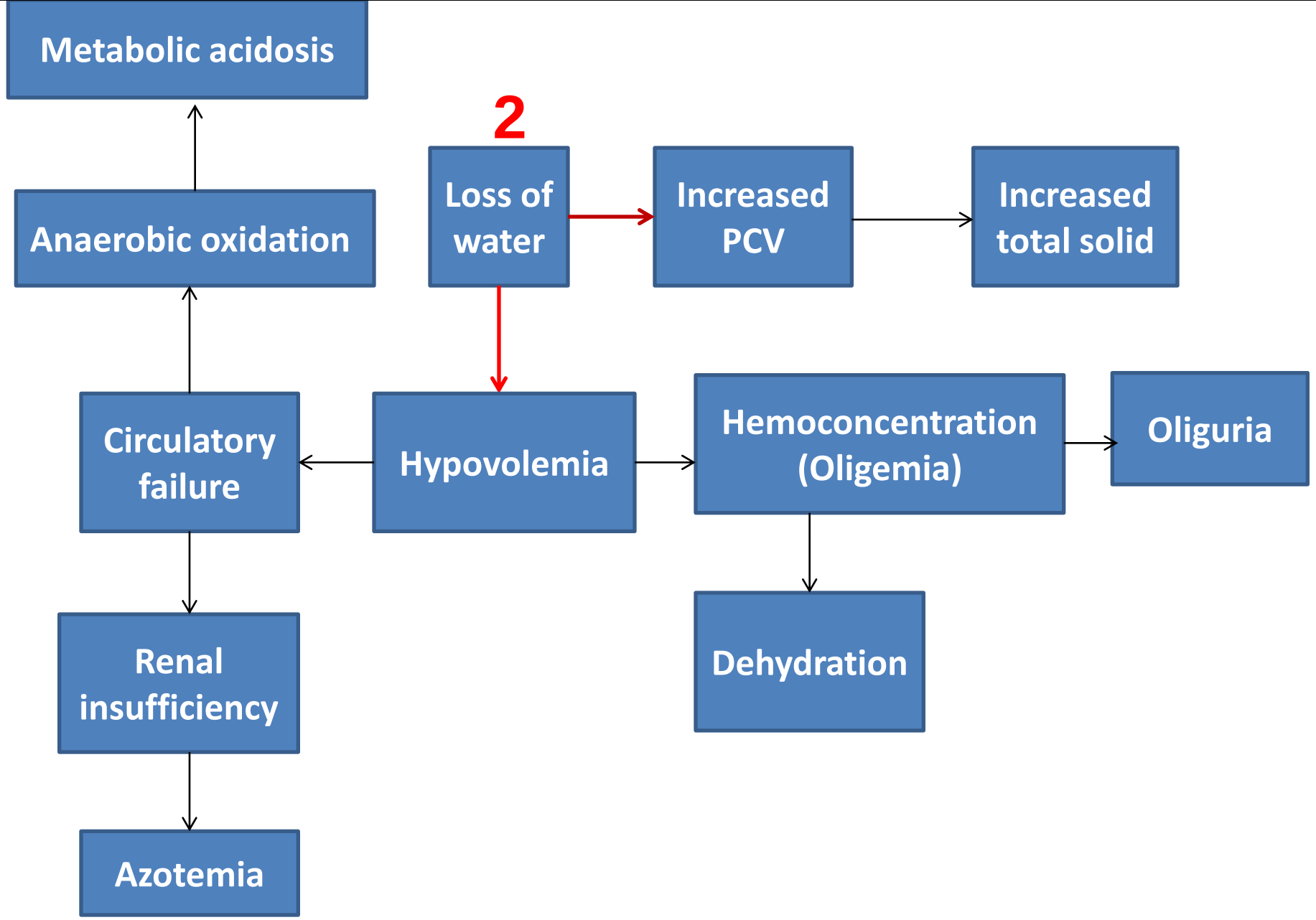
- Fluid and electrolyte abnormalities are also **life-threatening**
- simple correction of the primary abnormality, for example, removal of a large section of a horse's small intestine, is **valueless unless the dehydration, hyponatremia, and acidosis are also corrected.**

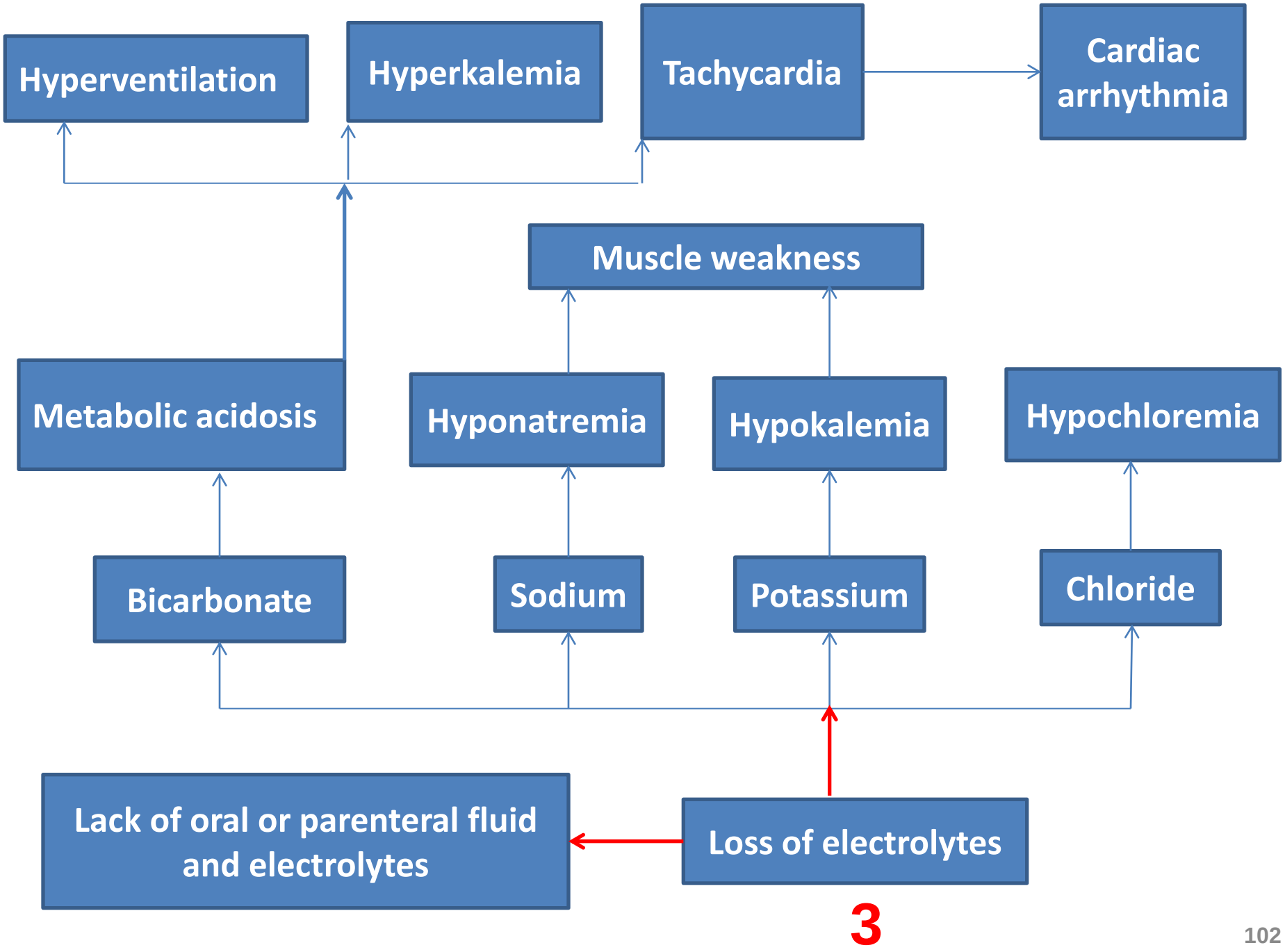
- In most naturally occurring diseases, the abnormalities are complex. For example, the probable events in a case of acute diarrhea are set out diagrammatically in the following Fig.

It is important to remember that the variation in fluid and electrolyte imbalance is **dynamic** as a result of the compensatory changes occurring in various organs, especially **the respiratory and circulatory systems and the kidneys.**


Loss of electrolytes
3
Diarrhea
Decrease the digestibility of nutrients
1
Loss of water
2


1
Decrease the digestibility of nutrients
Negative nutrients balance
Physiologic Starvation


Metabolic acidosis
2
Loss of water
Increased PCV
Increased total solid
Anaerobic oxidation
Circulatory failure
Hypovolemia
Hemoconcentration (Oligemia)
Oliguria
Renal insufficiency
Dehydration
Azotemia


Hyperventilation
Hyperkalemia
Tachycardia
Cardiac arrhythmia
Muscle weakness
Metabolic acidosis
Hyponatremia
Hypokalemia
Hypochloremia
Bicarbonate
Sodium
Potassium
Chloride
Lack of oral or parenteral fluid and electrolytes
Loss of electrolytes
3

Pillars of Diagnosis (Diagnoses):

- History
- Clinical findings
- Special methods for examination
- Clinical laboratory diagnosis
- Necropsy findings

- **HISTORY**

the chronological order; the **length of time** the animal has been affected the severity of the disease could be detected by:

- **The onset of the disease .**

- **The first clinical sign(s).**

- **Sequences of clinical findings may indicate to the severity of the disease**

Sign: Diarrhea

Animal: Ruminants and pets (adult and young),and only foal

Duration: 12-18 hr.

Organ (s) and/or system(s): Small intestine

The disease(s): S.I. Enteritis

Disturbances: Dehydration, electrolytes dis. and metabolic acidosis

- Animals that have had a **profuse watery diarrhea** for 18 to 24 hours may be severely acidemic.
- **Acute intestinal obstruction in cattle** is not as severe as in the horse.
- **Acute gastric** or **intestinal rupture** in the horse or in cattle is usually rapidly fatal.
- Acidosis in **grain overload** in cattle may be fatal in 24 to 48 hours; acidosis in the horse with grain overload may be much more rapidly fatal.

- **Muscular tremors and leg buckling are grave signs in the horse** and are commonly followed by collapse and death.
- The inability of any dehydrated animal to stand (other reasons being eliminated) is ominous.
- **Severe depression and dullness** are commonly observed in acute conditions, and **coma** is usually terminal.

CLINICAL FINDINGS

In disturbance in body fluid, electrolytes and acid-base balance, only is Dehydration usually obvious clinically.

The degree of dehydration could be assessed by

- **PCV**
- **serum or plasma total protein concentration**

Temperature

- A normal rectal temperature is not a good prognostic guide.
- A subnormal temperature suggests a worsening situation.

Heart beat and pulse

- A gradually progressive **tachycardia** indicates that the patient is deteriorating.

Generally, in the horse, a heart rate:

- **up to 39 beats/min** indicate to normal
- of **40 – 59 beat/min** suggests a minor lesion (but not always),
- of **60 to 79 beats/min** is in the danger area,
- of **80 to 99 beats/min** is serious (critical),
- **more than 100 beats/min** is commonly premortal (except in intestinal tympany that may be relieved).

Respiration

- Rapid respiration (three to four times normal) with intermittent hyperpnea and apnea suggest a poor prognosis.

Skin fold test (skin resiliency test)

- **A cold clammy skin** that remains tented for more than 30 seconds suggests severe dehydration.
- 1-3 second may consider normal
- 4 second, mild dehydration without further clinical signs
- 5-6 second moderate dehydration
- >6 second severe dehydration

Mucus membrane

Cyanosis of the oral mucous membranes suggest poor prognosis

Capillary refill time (CRT)

- **up to 2 second is normal**
- **more than 4 seconds suggests a poor prognosis.**

CLINICAL PATHOLOGY

- **The PCV** and the **total serum protein (**historically called **total solids)** will indicate:
- The severity of water loss.
- Anemic animals.
- Hypoproteinemia.
- The normal range depends on the **age** and **species** of animal, **previous excitement**, and the presence of **anemia or hypoproteinemia.**

PCV (%)

- **30% to 40%** is considered normal.
- **40% to 50%,** fluid therapy may or may not be necessary;
- **50% to 60%,** fluids are necessary for recovery.
- **above 60%** intensive fluid therapy is necessary and the prognosis is unfavorable.

A total serum protein concentration (g/dL)

- 6.0 to 7.5 g/dL is usually considered normal.
- 8 to 10 g/dL fluids are needed and the prognosis is favorable.
- Above 10 g/dL the prognosis is unfavorable.

Leukocytes

- **Degenerative left shift suggest bad prognosis**
- **Regenerative left shift indicate good prognosis**
- **Lymphopenia indicate to severe stress**

Blood pH

Normal pH for most domestic animals varies from 7.35 to 7.45 (venous blood). pH of:

- 7.30–7.25 indicate to moderate acidemia,
- pH 7.25–7.20 suggest severe acidemia. and grave
- pH 7.10–7.00 associated with a high fatality rate, except in neonatal animals

Blood or Plasma L-Lactate Concentration

- The blood or plasma l-lactate concentration provides valuable information about:
- The adequacy of oxygen delivery to the tissues.
- Assessing the severity of cardiovascular or pulmonary dysfunction.
- Monitoring the response to treatment.
- Formulating a prognosis for survival.

- The normal plasma L-lactate concentration in large animals is less than **1.5 mmol/L.**
- **2.5–4.9 mmol/L** categorized as mild acidemia
- **5.0–9.9 mmol/L** categorized as moderate acidemia
- **≥10 mmol/L** categorized as severe acidemia.

Bicarbonate (HCO^-3)

- 24-30mEq/L indicate to normal.
- 20-24mEq/L indicate to mild acidosis.
- 14-18mEq/L indicate to moderate acidosis.
- Less than 10 mEq/L indicate to severe acidosis.

Serum Electrolytes

- **Serum electrolyte** concentrations indicate the severity of the electrolyte losses and the necessity for replacement with either balanced electrolyte solution or specific electrolyte solution.
- Serum concentrations of **sodium, chloride, and potassium** are usually determined.

Urea and Creatinine

- Urea and creatinine are metabolic breakdown

constituents that can be used to assess the degree of dehydration and to distinguish among **prerenal, renal, and postrenal uremia**.

- The plasma/serum concentrations of urea and creatinine concentration will be elevated, depending on the severity of the dehydration and decrease in circulating blood volume.

- **Creatinine** concentration varies directly with

the **muscle mass** in healthy animals, and, consequently, is much higher in beef bulls than dairy cows.

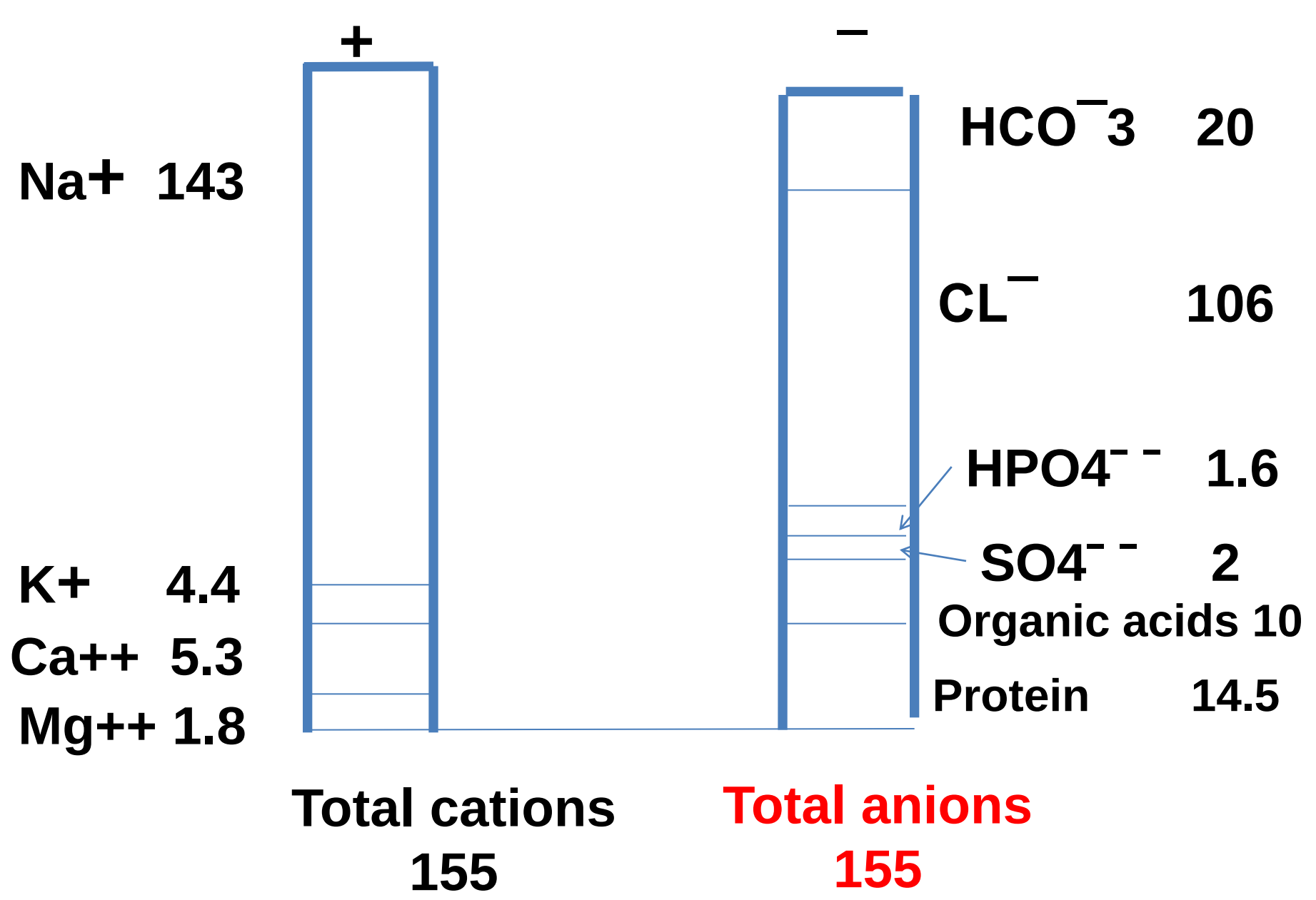
- **Plasma urea** concentration varies directly with the **protein intake** in healthy animals, and, consequently, is increased in ruminants on a high-protein diet.

Blood or Plasma Glucose

- Plasma glucose concentration can be determined using conventional laboratory techniques **(hexokinase assay),**
- which require submission of **heparinized blood** samples to a laboratory as soon as possible to avoid erroneous results caused by erythrocyte glycolysis

- Quantitative, rapid, low-cost methods for determining blood glucose concentrations are now widely available.
- Many units are designed for analysis of human blood and are **not suitable for use in large animals** because they incorrectly assume intraerythrocyte glucose concentration is the same as plasma glucose concentration (which is the case in most primates).

- In all of the domestic animals examined, intraerythrocyte glucose concentration is lower than plasma glucose concentration, and, consequently, the measured blood glucose value depends on the hematocrit, which is usually assumed to be fixed and approximately 44%.


+
−
Na+ 143
K+ 4.4
Ca++ 5.3
Mg++ 1.8
HCO−3 20
CL− 106
HPO4− − 1.6
SO4− − 2
Organic acids 10
Protein 14.5
Total cations
155
Total anions
155

Anion gap (AG)

- The AG represents the difference between the concentration of [UA] and [UC] in serum which can be expressed in the equation:
- $[Na+]+[K+]+[UC]=[Cl-]+[HCO3-]+[UA]$

which can be rearranged to

- $AG = [UA]- [UC]= ([Na+]+[K+]) – ([Cl-]+[HCO3-])$
- A change in [UA] or [UC] will cause a change in AG

- The 95% confidence interval for the range of AG for adult animals varies for different species:
- **8 to 13 mEq/L (horse),**
- **14 to 20 mEq/L (cow),**
- **17 to 29 mEq/L (sheep).**
- The AG values greater than 30 mEq/L have been observed in critically ill cattle; the increase is attributed to an increase in blood lactate and ketoacids concentration as well as to anions

Osmolal Gap

- Evaluation of the osmolal gap is a means of detecting an **increased amount of abnormal osmotically active solute in the blood**.
- The osmolal gap is the difference between the measured plasma osmolality and the osmolality calculated from the plasma concentration of normally measured solutes.

Osmolal gap

1.9[(Na+)+(K+)]+(glucose/18)+urea/2.8+0.5

Examination of the triad of calculated osmolality, measured osmolality, and the osmolal gap is beneficial in the diagnosis and prognosis of a number of diseases

PRINCIPLES OF FLUID AND ELECTROLYTE THERAPY

There are at least four possible abnormalities and must be corrected:

- **Fluid volume deficit**
- **Plasma osmolar deficits**
- **Specific electrolyte imbalances**
- **Acid-base imbalance.**

- The two major problems are
- to determine the ***nature and degree of the abnormalities present***
- ***to decide which fluid and electrolyte replacement solution*** should be used.
- The ideal situation would be to make both a ***clinical and laboratory evaluation*** of the animal

Water

1- No clinical evidence or slight symptoms of dehydration, but history of vomiting and/or diarrhea:

Replace water in amount of ***4%*** of body weight.

2- Moderate clinical evidence of dehydration:

Replace water in amount of ***6%*** of body weight.

3- Severe dehydration:

Replace water in amount of ***8%*** of body weight.

- **B-*Calculation of electrolyte requirements***

The total milliequivalent deficit =

(ΔmEq/L)) X (estimated body weight in kg) X

(0.3 or 0.5).

(ΔmEq/L)= the difference in electrolytes

- **Example**: for diarrheic horse of 500 kg body weight, the measured bicarbonate is 12 mEq/L

(the normal 24mEq/L)

The total milliequivalent of bicarbonate required=

(24 - 12) X 500 X 0.3

- If a large quantity of fluid is to be administered to the patient to replace the deficit of water, this fluid also enters into the calculations. It is reasonably accurate to assume that the extracellular fluid comprises approximately one third of the total water of the body.
- ***Body wt in kg/5 x (ΔmEq/L)) + liters water retained/3 x normal electrolyte conc.***

Example: A dog weighing 44lb (20kg) displayed **moderate** clinical evidence of dehydration and have a concentration of 86mEq/L of plasma chloride. (normal chloride 106 mEq/l)

Water to be replaced at the rate of **6%**

6%x20 (20,000) =1.2 (1200 ml) = water retained

20x20/100x (106-86) +1.2/3x106=122.4mq chloride necessary to replace deficit

- **Conversion from mg/L to mEq/L**

$$\text{mEq/L} = \frac{mg/lXvalence}{formula\ weight}$$

- **Conversion from mEq/L to mg/L**

$$\text{mg/L} = \frac{mEq/lXformulaweight}{valence}$$

Where as formula weight is molecular weight

Some formula weight of some essential elements

Element	Formula weight	Element	Formula weight
Hydrogen (H)	1	Sodium (Na)	23
Carbon (C)	12	Magnesium (Mg)	24
Nitrogen (N)	14	Chloride (Cl)	35.5
Oxygen (O2)	16	Potassium (K)	39
Calcium (Ca)	40		

Types of intravenous fluid

Fluids are categorized on the basis of **Physical nature (crystalloid or colloid):**

- ***Crystalloid solutions***: A crystalloid is a substance that forms a true solution and is capable of being crystallized. Examples of crystalloid solutions are **Ringer's solution**, **lactated Ringer's solution**, **acetated Ringer's solution**, **0.9% NaCl**, **7.2% NaCl (hypertonic saline), 1.3% NaHC03**, **8% NaHCO3; calcium gluconate** and **50% dextrose**. Sodium chloride is the classic crystalloid.

- ***Colloid solutions:***

A colloid is a substance that is too large top as through a semipermeable membrane. Examples of colloid solutions administered to ruminants are whole blood, stroma-free hemoglobin, plasma, dextrans, hydroxyethyl starches and gelatins.

- Colloid solutions are excellent for sustained expansion of plasma volume, which is in marked contrast to the effect of crystalloid solutions.
- Colloid solutions are contraindicated in:

1. **Congestive heart failure** because these animals have increased plasma volume.

2. **Oliguric or anuric renal failure** because the sustained volume overload may lead to pulmonary edema.

- **Crystalloid classified according Osmolarity into:** (isotonic or hypertonic):

1- **Isotonic solution:** Isotonic solutions contain crystalloid concentration similar to that of plasma e.g. **NaCl 0.9% ,KCl 1.1%, $NaHCO_3$ 1.3%, dextrose 5%.**

- solutions are defined as isotonic (300-312 mosmol/L); the normal plasma osmolarity for large animals is 306 mosmol/L.

- **Isotonic solutions (300 to 312 mosmol/L) are subdivided into:**

- **Alkalinizing**

- Tromethamine,1. 3% $NaHC0_3$, Carbicarb, McSherry's solution, and Darrow's solution.

- **Acidifying**

Ringer's solution, 0.9% Na Cl, 1. 1 5 % K Cl.

2- Hypertonic solution(>312 mosmol/L):

- There are two main types of hypertonic solutions:

- **High sodium, alkalinizing solution**

e.g. 8.4% NaHC03, 5.0% NaHC03, 1 0 % NaH2PO.

- **High potassium acidifying solution**

e.g.50% dextrose, 7.2% Na Cl 25% magnesium sulfate, 23% calcium borogluconate

3- Hypotonic solution(<300 mosmol/l):

- **Alkalinizing solution**

e.g. Acetated Ringer's and Lactated Ringer's

- **Acidifying solution**

- **e.g.** 5% dextrose .

- **Precautions of using alkalinizing solution containing acetate or lactate:**

- It should not be administered in case of liver insufficiency as they exaggerated metabolic acidosis.

- For all hypertonic solutions, it should be followed by isotonic solutions.

Quantity of fluids required and routes of administration:

The fluids are usually given in two stages:

- **Hydration therapy:**

It is administered in the first 4-6 hours at a rate of

100-150 mL/kg BW. I/V.

- **Maintenance therapy:**
- It is administered in the next 20-24 hours, depending on the severity and the course of the disease, **at 60-80 mL/kg BW/24 hours I/V.** (approximately 3-4 mL/kg BW/hour).
- In some cases of profuse diarrhea, the continuous losses and maintenance requirements will be about **150 mL/kg BW over a 24-hour period.**

- **Responses of fluid therapy administration:**

During the intravenous administration, the animal must be monitored for clinical and laboratory evidence of improvement or deleterious effects.

- **A favorable response:**

It is indicated by urination within 30-60 minutes, an improvement in mental attitude and some evidence of hydration.

- **Unfavorable responses:**

Include dyspnea because of pre-existing pneumonia or pulmonary edema because of too rapid administration, failure to urinate because of renal failure or paralysis of the bladder, and tetany because of the excessive administration of alkali.

Rate of administration:

- **Isotonic solution:**

Saline (0.9% NaCl) and sodium bicarbonate solutions may be given at the rate of **10-12 L/h. in adult animals and 3-5 L/h in young animals.**

- **Hypertonic solutions:**

Such as 5% sodium bicarbonate can be given to a mature animal at the rate of **3-5 L/h, followed by balanced electrolytes at 10-12 L/h.**

- **Solutions containing potassium:**

It should be given cautiously, at the rate of **3-5 L/h.**

Adverse reactions in all species:

- Include sudden muscle weakness (**suggests hypokalemia)**
- Sudden tachycardia and hyperventilation, which suggest **over hydration.**
- When these occur the fluids should be stopped and the clinical findings assessed.