Acid base imbalance

The major buffer of extra cellular fluid is HCO_3^-/CO_2 system. The plasma pH is determined by the concentration of bicarbonate (HCO_3^-) and carbonic acid (H_2CO_3). The conventional method of determination of concentration of carbonic acid is the determination of pCO_2 in blood. The carbonic acid concentration can be calculated by multiplying pCO_2 by 0.003. The 0.03 is the solubility constant for carbon dioxide in plasma.

The four primary and their compensatory responses are as below.

Disorder	pH	Concentration of H^+ ion	Primary imbalance	Compensating response
Metabolic acidosis	Decreases	Increases	Low [HCO_3^-]	Low pCO_2
Metabolic alkalosis	Increases	Decreases	High [HCO_3^-]	High pCO_2
Respiratory acidosis	Decreases	Increases	High pCO_2	High [HCO_3^-]
Respiratory alkalosis	Increases	Decreases	Low pCO_2	Low [HCO_3^-]

NB: [HCO_3^-] indicates the concentration of bicarbonate ions.

The metabolic acid base imbalance is mainly caused by changes in bicarbonate concentration. The compensating response is mediated by the respiratory system that within its own limit alters the pCO_2, so as to counterbalance the primary imbalance and to partially restore the pH towards the normal.
The primary imbalance of respiratory disorders is related to alteration in alveolar ventilation resulting in increase in pCO_2 in respiratory acidosis and decrease in pCO_2 with respiratory alkalosis. The compensation is done by kidney by alteration in excretion or retention of H^+ ions or bicarbonate.

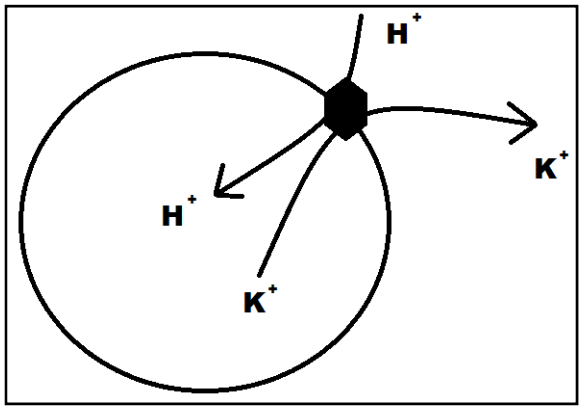
ACIDOSIS

Metabolic acidosis:

It is characterized by decrease in pH and bicarbonate ions.

Initial buffering of acid load is performed by ECF (extra-cellular fluid) buffers, primarily by bicarbonate-carbonic acid buffer pair (HCO^{3-}/H_2CO_3).
Intracellular buffering is done particularly by protein and phosphates. The intracellular movement of H^+ in exchange of K^+ helps to reduce the excessive load of H^+ in extra-cellular fluid.

This exchange is called **CATION SHIFT**. The cation shift causes the hyperkalemia.



Causes of metabolic acidosis:

1. Lactic acidosis.
2. Ketoacidosis.
3. Gastrointestinal problems such as indigestion, colic, diarrhoea, renal failure that may result in decrease ability to excrete the H^+ and thus to retain bicarbonate.
4. Ingestion of toxic compounds such as salicylate, methanol, ethylene glycol or paraldehyde that results in accumulation of exogenous anions.

   Compensation

   1. Increased alveolar ventilation leads to decrease in pCO_2 causing the elevation of pH. This compensation is short lived and lasting for few days only.
   2. Longer term correction of metabolic acidosis required renal bicarbonate retention and enhanced acid excretion primarily as ammonium ions (NH_4^+).

      The complete correction of renal acidosis is difficult in patients with intrinsic renal diseases that would impair the kidney's ability to excrete acid or retain bicarbonate.

Respiratory acidosis

It is characterized by decrease in pH and increase in pCO_2. It develops due to decreased effective alveolar ventilation or breathing in atmosphere with elevated CO_2.

Causes of respiratory acidosis:

Any disorder that interferes with the normal effective ventilation may produce respiratory acidosis:

Common causes:

1. Primary pulmonary diseases ranging from
   a. Acute upper respiratory obstruction.
   b. Pneumonia.

c. Pneumothorax.
d. Chronic obstructive lung disease.

2. Drugs affecting CNS may inhibit medullary respiratory centre.
3. General anaesthesia with volatile agents using a closed system.

Compensation of respiratory acidosis:

- Renal retention of bicarbonate and increased H^+ excretion. It takes several days. Thus seen only in chronic respiratory acidosis.

Metabolic alkalosis

It is characterized by increase in pH and bicarbonate. It is commonly observed in association with digestive disturbances in ruminants. It occurs due to H^+ loss and increased bicarbonate retention.

Causes of metabolic alkalosis

1. Most common cause of H^+ loss are GI loss of chloride rich fluids associated with small animals (vomition).
2. Sequestration of chloride rich fluid in the abomasums and fore-stomach of ruminants.
3. Excessive renal H^+ loss associated with mineralocorticoid excess, diuretic usage and low chloride intake.
4. Deficiency of Na^+ and Cl^-.
5. H^+ movement outside the cells in response to K^+ depletion.

Factors that maintain the metabolic alkalosis:

It includes all factors that are responsible for impairment of renal bicarbonate excretion.

- Decreased glomerular filtration of bicarbonate excretion.
- Increased renal bicarbonate reabsorption that occurs in response to
  - Decreased effective circulating fluid volume.
  - Potassium depletion
  - Chloride depletion.

To maintain fluid volume Na^+ is resorbed in proximal tubule. Now to maintain the electro-neutrality resorbable anions such as chloride must accompany Na^+. In distal tubule Na^+ reabsorption is accompanied by concurrent excretion of H^+ ions and to some extent K^+. In metabolic alkalosis, plasma bicarbonate is increased and Cl^- concentration is generally decreased due to disproportionate loss of chloride (resulting from vomition, sequestration of gastric fluid, heavy sweat loss and diuretic usage). Relative lack of the resorbable anion, chloride in proximal tubule thus allows a larger amount of sodium to reach the distal tubule where the action of aldosterone causes the increased loss of H^+ ions into the tubular lumen in exchange of sodium. Maintenance of effective circulating volume is so critical that the body chooses to maintain it by enhanced Na^+ reabsorption by whatever means.

The hyperkalemia occurs due to extrusion of K^+ from the cells and as a result to maintain the electro-neutrality the cells bring H^+ inside the cell causing the sequestration of H^+ inside the cells causing alkalosis due to lack of H^+ ions in the extra-cellular fluid.

Compensation of metabolic alkalosis

The chemoreceptors of the respiratory centre sense the alkalosis and the respiratory response to a metabolic alkalosis is hypo-ventilation leading to increase in pCO_2.

Respiratory alkalosis

It is characterized by increase in pH and decrease in pCO_2

Causes of respiratory alkalosis:

- Due to hyperventilation that may be stimulated by hypoxemia associated with pulmonary diseases, congestive heart failure or severe anaemia.
- Gram Negative sepsis.
- Psychological stress.

Compensation of respiratory alkalosis

1. Initial response: modest decline in extra-cellular fluid bicarbonate concentration.
2. Subsequent response: reduced renal HCO_3^- reabsorption. That is accompanied by increased renal chloride retention to maintain electro-neutrality. This leads to hyperchloremia.

Students are advised to refer to the below mentioned book for details:

Clinical Biochemistry of Domestic Animals
Author: J. Jerry Kaneko.