NYMAHE - DL-CLS Program - Lynn Jones

Blood Gases, pH and Buffering Systems – A Review

An important function of the Biochemistry Lab is to provide timely, accurate, and precise information to the clinical staff. Of utmost importance is blood gas and acid/base status. Often times this information is a matter of life and death.

Important processes involved in maintaining homeostasis:

1. Buffering systems used to maintain blood pH
2. Exchange of gases, specifically carbon dioxide (CO_2) and oxygen (O_2)

I. Acid/Base Balance

Shifts in acid/base balance cause alterations in the rate of chemical reactions in the cell and change metabolic processes in the body. The level of hydrogen ion concentration in the blood is determined by measuring pH in the blood gas panel.

The pH scale, using the following equation, expresses H^+ concentration in the blood:

$$pH = \log \frac{1}{cH^+} = -\log cH^+$$

c = concentration of hydrogen ion
Normal H+: 36-44 nmol/L
Normal pH: 7.40 (Equivalent to 40 nmol/L of H^+)

Hydrogen ion concentration has a reciprocal relationship with pH (as expressed in the above equation), so an ***increase in H^+ decreases pH*** (acidosis), while a ***decrease in H^+ increases the pH*** (alkalosis).

Acidosis, a shift below the normal pH, can lead to altered consciousness, coma and death.

Alkalosis, a shift above the normal pH, can lead to neuromuscular irritability, tetany, loss of consciousness, and death.

Arterial blood pH is controlled by in vivo buffering systems (electrolyte balance), the respiratory system, and the kidney.

II. Buffering Systems

1. Role of Carbonic Acid

The bicarbonate-carbonic acid buffer system is the body's first line of defense against changes in H^+ concentration in all body fluids.

H_2CO_3 (carbonic acid) is a weak acid that can *partially dissociate* into H^+ (free hydrogen ion) and HCO_3^- (bicarbonate). When an acid is added to the bicarbonate-carbonic acid buffer system, the HCO_3^- will combine with the excess H^+ to form H_2CO_3. When a base is added, H_2CO_3 will combine with the excess OH- group to form H_2O and HCO_3^-. This process allows for only a small change in pH, rather than dramatic pH changes seen with strong acids or bases.

$$H_2CO_3 \Longleftrightarrow H^+ + HCO_3^-$$

2. The Role of Hemoglobin

Buffering of whole blood is largely done by hemoglobin. Hemoglobin, once oxygen is released, binds to hydrogen ions.

The RBC membrane contains carbonic anhydrase, which allows CO_2 to combine with water to form H_2CO_3.

Co-Oximetry: measurement of various hemoglobins and their O_2 content:

Carboxyhemoglobin (COHb) – Hemoglobin bound to CO_2.
Deoxyhemoglobin (HHb) – Reduced hemoglobin. In this form hemoglobin is able to accept O_2 when it is available.
Methemoglobin (MetHb) – Oxidized hemoglobin. In this form hemoglobin is unable to bind O_2 because iron is in an oxidized rather than reduced state.
Oxyhemoglobin (O_2 Hb) – O_2 reversibly bound to hemoglobin

3. Role of Phosphate

The phosphate buffer system (HPO_2^{-2} & $H_2PO_4^-$) plays a role in plasma and erythrocytes and is involved in the exchange of sodium ion of hydrogen ion in the urine.

4. Role of Plasma Proteins

Most circulating proteins have a net negative charge so they are capable of binding hydrogen ions.

II. Respiratory System

Respiration affects the blood pH by altering the rate of ventilation (breathing rate) in an effort to restore the blood pH to normal. The respiratory system can rapidly regulate blood pH through hypo- or hyperventilation – this is called the ***respiratory component*** of acid/base regulation.

In the Lungs: H^+ is carried by deoxyemoglobin in venous blood to the lungs. There it combines with HCO_3- to form H_2CO_3 which dissociates into H_2O and CO_2. The CO_2 diffuses into the alveoli and is eliminated through respiration. The inhaled O_2 diffuses from the alveoli into the blood and is taken up by the hemoglobin, forming oxyhemoglobin which is delivered to the tissues in the arterial blood. Because of this even exchange of gases, there is minimal effect on H^+ balance.

If CO_2 is not removed by the lungs at the rate of its production, it will accumulate in the blood, causing an increase in H^+ concentration. If CO_2 is removed faster than its production, the H^+ will decrease.

In the Tissues: Aerobic metabolism produces CO_2 in the tissues. For this reason dissolved CO_2 (dCO_2) is more concentrated in the tissues and easily diffuses out into the plasma and RBC's. In plasma, the CO_2 combines with carbonic acid (H_2CO_3) which quickly dissociates into H^+ and HCO_3^-. The freed H^+ is buffered by plasma proteins and plasma buffers.

In the RBC: CO_2 is handled in three ways, a small portion stays as dCO_2, some combines with hemoglobin to form carbamino hemoglobin, but most of the CO_2 combines with water to form H_2CO_3 (accelerated by carbonic anhydrase) which quickly dissociates.

O_2 picked up from the lungs is unloaded from oxyhemoglobin at the tissues. The hemoglobin then readily accepts any H^+, forming deoxyhemoglobin. As the HCO_3^- concentration rises in the RBC, it diffuses out into the plasma while Cl^- diffuses into the cell (Chloride Shift). In this way electroneutrality is maintained.

III. Renal System

The kidney affects the blood pH by selectively excreting or reabsorbing hydrogen, sodium, chloride, phosphate, potassium, and bicarbonate ions in order to restore equilibrium between the production and removal of hydrogen ions. These processes help determine the pH of both the blood and the urine.

Bicarbonate concentration is controlled mainly by the kidneys; this is the nonrespiratory, or ***metabolic component*** of acid/base regulation.

IV. Assessing Acid/Base Homeostasis

Henderson-Hasselbalch equation:

$$pH = pK_a' + \log \frac{cA-}{cHA}$$

A = pronton acceptor (HCO_3^-)
HA = proton donor (H_2CO_3)
pK_a' = pH at which there is an equal concentration of protonated and unprotonated ions

This equation expresses the acid/base relationship in a mathematical formula.

Under normal conditions the ratio of bicarbonate to carbonic acid is 20:1, resulting in a pH of 7.40.

Evaluation of a patient's oxygen status is possible using the partial pressure of oxygen (pO_2), measured along with pH and pCO_2 in the basic blood gas panel.

Blood Gases consist of the following analytes:

- pH: Hydrogen ion concentration, used to evaluate acid/base status.
- pCO_2: Partial pressure of carbon dioxide, used to evaluate acid/base status.
- pO_2: Partial pressure of oxygen, used to evaluate respiratory ability and oxygen status.
- sO_2: Saturated oxygen – the amount of oxygen bound to hemoglobin (can be determined by direct analysis or by calculation).
- HCO_3^-: Bicarbonate, used to help determine metabolic or respiratory disorder.

Arterial Blood Gas Components and basic Reference Ranges:

	Arterial	Venous
pH	7.35-7.45	7.33-7.43
pCO_2	35-45	38-50 mmHg
pO_2	80-110	30-50 mmol/L
sO_2	>95%	60-85%
HCO_3^-	22-26	23-27 mmol/L

A change in the pCO_2 level is termed a primary **respiratory** acidosis or alkalosis.

A change in the HCO_3^- level is termed a primary **metabolic** acidosis or alkalosis.

Mixed metabolic and respiratory disorders are also common.

The body is constantly trying to maintain a normal pH level (20:1 ratio), so any imbalance will cause an equal response in order to **compensate** for the imbalance. The body does this by altering the function not primarily affected by the pathologic condition. When compensation is not adequate, a **secondary compensation** will come about through the primary source of the disorder.

V. Acid/Base Disorders

Acid/Base disorders are caused by a shift in the acid/base balance from the normal 20:1 bicarbonate to carbonic acid ratio (pH 7.4) maintained in vivo and expressed mathematically by the Henderson-Hasselbalch equation.

1. Primary Metabolic Acidosis: Decrease in bicarbonate (<22 mmol/L) resulting in a decreased pH. Caused by diabetic ketoacidosis, starvation, renal disease, and excessive loss of bicarbonate from diarrhea or fistula.

Expected Results:		
	pH	Low
	pCO_2	Normal to Low
	HCO_3^-	Low

Primary compensation is through hyperventilation helping to remove CO_2 through the lungs. The acid/base ratio will return to normal, if this mechanism is not enough to restore pH levels *secondary compensation* will be through the kidney (the original source) to correct the ratio by retaining bicarbonate.

2. Primary Respiratory Acidosis: Decrease in CO_2 level (<23 mmol/L) resulting in a decreased pH. Caused by lung diseases, emphysema, pneumonia, and congestive heart failure all leading to hypoventilation.

Expected Results:		
	pH	Low
	pCO_2	High
	HCO_3^-	Normal to High

Compensation occurs through the kidney by increasing the excretion of H+ and increased reabsorption of HCO_3^-.

3. Primary Metabolic Alkalosis: An increase in bicarbonate leading to an increase in pH. Caused by ingestion of increased use of antacids, excess vomiting, nasogastric suctioning or prolonged use of diuretics.

Expected Results:		
	pH	High
	pCO_2	Normal to High
	HCO_3^-	High

Compensation is through the respiratory center, hypoventilation increases the retention of CO_2.

4. Primary Respiratory Alkalosis: An increased rate of respiration leads to excessive elimination of CO_2 by the lungs and an increase in pH. Caused by drugs, especially salicylates, fever, hysteria, PE, and cystic fibrosis.

Expected Results:		
	pH	High
	pCO_2	Low
	HCO_3^-	Normal to Low

Compensation is through the kidneys by excreting bicarbonate and retaining H^+.