Blood Gasses

Blood pH and Blood Buffer

Normal cell metabolism depends on the maintenance of blood pH within very narrow limits (7.35- 7.45).

Even relatively mild excursions outside this normal pH range can have **deleterious effects**, including reduced oxygen delivery to tissues, electrolyte disturbances and changes in heart muscle contractility; survival is rare if blood pH falls below 6.8 or rises above 7.8.

The problem for the body is that normal metabolism is associated with continuous production of hydrogen ions (H^+) and carbon dioxide (CO_2), both of which tend to reduce pH. The mechanism which overcomes this problem and serves to maintain normal blood pH (i.e., preserve acid-base homeostasis) is a complex synergy of action involving chemical buffers in blood, the red cells (erythrocytes), which circulate in blood, and the function of three organs: lungs; kidneys and brain.

Before explaining how these five elements contribute to the overall maintenance of blood pH, it would be helpful to quickly review some basic concepts.

***pH is a measure of hydrogen ion concentration* [H^+].**

pH is a scale of 0-14 of acidity and alkalinity. Pure water has a pH of 7 and is neutral (neither acidic nor alkaline). pH above 7 is alkaline and below 7 acidic. Thus, the pH of blood (7.35-7.45) is slightly alkaline although in clinical medicine the term alkalosis is, perhaps confusingly, reserved for blood pH greater than 7.45 and the term acidosis is reserved for blood pH less than 7.35.

What is a buffer?

A buffer is a solution of a weak acid and its conjugate base.

The bicarbonate (HCO_3^-) buffer system

Buffers

are chemicals in solution which minimize the change in pH which occurs when acids are added by hydrogen ions. In blood, the principal buffer system is the weak acid, carbonic acid (H_2CO_3) and its conjugate base, bicarbonate (HCO_3^-).

Acid -base balance

Physiology of Acid-Base Balance:

In fact, the lungs ensure removal of carbonic acid (as carbon dioxide) and the kidneys ensure continuous regeneration of bicarbonate.

This role of the lungs is dependent on characteristic of the bicarbonate buffering system and that is the ability of carbonic acid to be converted to carbon dioxide and water, the following equation outlines the relationship of all elements of the bicarbonate buffering system as it operates in the body

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

It is important to note that the reactions are reversible. Direction is dependent on the relative concentration of each element. So that, for example, a rise in carbon dioxide concentration forces reaction to the left with increased formation of carbonic acid and ultimately hydrogen ions.

Lung function, transport of CO_2 and acid-base balance

A constant amount of CO_2 in blood, essential for normal acid-base balance, reflects a balance between that produced as a result of tissue cell metabolism and that excreted by the lungs in expired air.

By varying the rate at which carbon dioxide is excreted, the lungs regulate the carbon dioxide content of blood. Carbon dioxide diffuses out of tissue cells to surrounding capillary blood (Fig. 1a), a small proportion dissolves in blood plasma and is transported to the lungs unchanged, but most diffuses into red cells where it combines with water to form carbonic acid.

The acid dissociates with production of hydrogen ions and bicarbonate. Hydrogen ions combine with deoxygenated hemoglobin (hemoglobin is acting as a buffer here), preventing a dangerous fall in cellular pH, and bicarbonate diffuses along a concentration gradient from red cell to plasma. Thus, most of the carbon dioxide produced in the tissues is transported to the lungs as bicarbonate in blood plasma.

$$CO_2 + H_2O + \xleftrightarrow{slow} H_2CO_3 \xleftrightarrow{fast} H^+ + HCO_3^- \qquad (8\text{-}1)$$

At the alveoli in the lungs the process is reversed (Fig. 1b). Hydrogen ions are displaced from hemoglobin as it takes up oxygen from **inspired air**. The hydrogen

ions are now buffered by bicarbonate which diffuses from plasma back into red cell, and carbonic acid is formed. As the concentration of this rises, it is converted to water and carbon dioxide. Finally, carbon dioxide diffuses down a concentration gradient from red cell to alveoli for excretion in **expired air**.

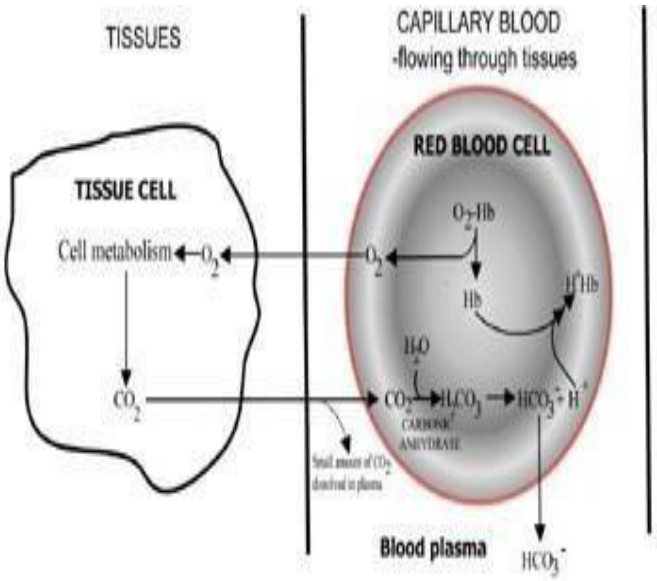


Fig. 1a. CO_2 produced in tissues converted to bicarbonate for transport to lungs.

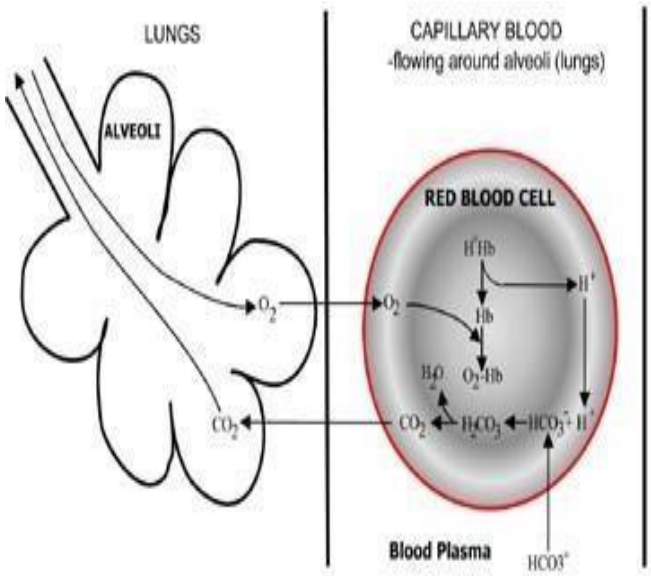
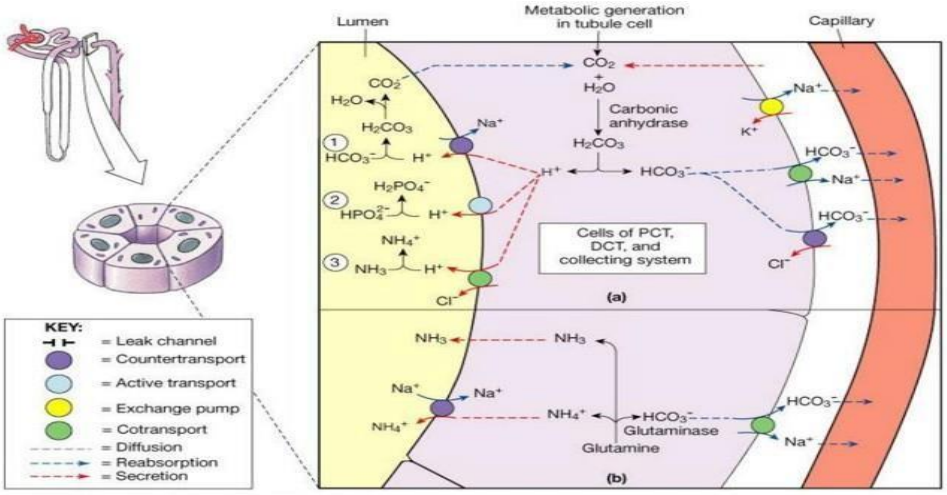


Fig. 1b. At the lungs bicarbonate converted back to CO_2 and eliminated by the lungs.



Respiratory ***chemoreceptors in the brain*** stem respond to changes in the concentration of carbon dioxide in blood, causing increased ventilation (breathing) if carbon dioxide concentration rises and decreased ventilation if carbon dioxide falls.

Kidneys and acid-base balance

These two tasks, elimination of hydrogen ions and regeneration of bicarbonate, are accomplished by the kidneys.

Renal **tubule cells** are rich in the ***enzyme carbonic anhydrase***, which facilitates formation of carbonic acid from carbon dioxide and water. Carbonic acid dissociates to bicarbonate and hydrogen ions. The bicarbonate is reabsorbed into blood and the hydrogen ions pass into the lumen of the tubule and are eliminated from the body in urine.

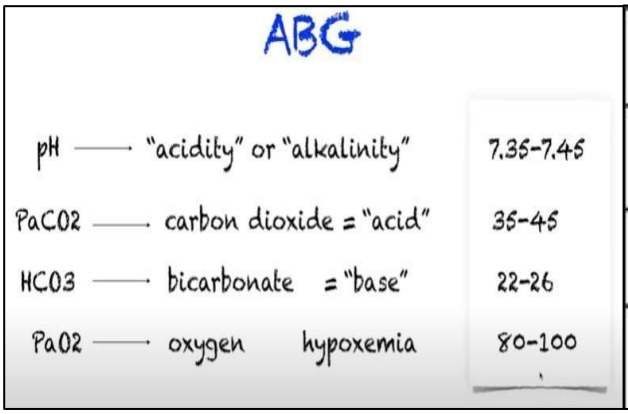
Disturbances of acid-base balance

Most acid-base disturbances result from disease or damage to organs (kidney, lungs, brain) whose normal function is necessary for acid-base homeostasis, disease which causes abnormally increased production of metabolic acids such that homeostatic mechanisms are overwhelmed medical intervention (e.g. mechanical ventilation, some drugs)

Arterial blood gases (ABG) are the blood test used to identify and monitor acid-base disturbances.

Three parameters measured during blood gas analysis:

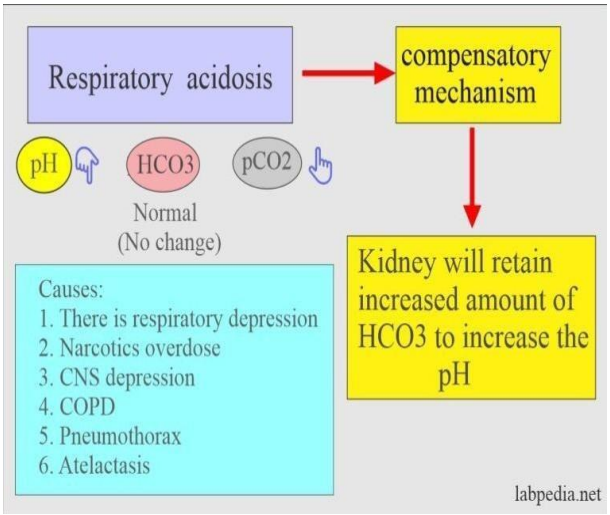
- Arterial blood pH
- Partial pressure of carbon dioxide in arterial blood (pCO2)
- Concentration of bicarbonate (HCO_3^-) are of crucial importance.



pH	$PaCO_2$	HCO_3
7.35 to 7.45	35 to 45	22 to 26
↑Acidosis	↓CO_2 = pH↑	↓HCO_3 = pH↓
↓Alkalosis	↑CO_2 = pH↓	↑HCO_3 = pH↑

Results of these three allow classification of acid-base disturbance to one of four etiological categories:

Respiratory acidosis – (raised pCO_2, reduced pH)



Respiratory acidosis is characterized by

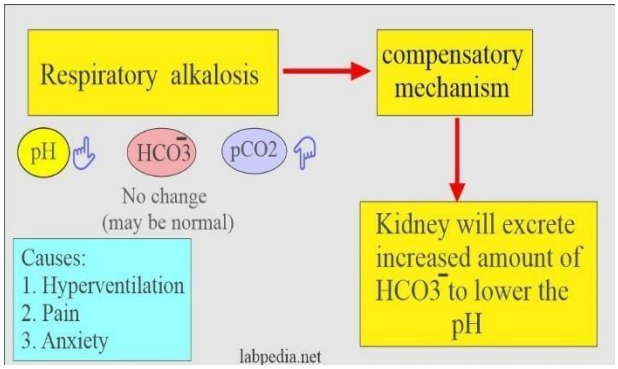
1. increased pCO_2 due to inadequate alveolar ventilation (hypoventilation)
2. consequent reduced elimination of CO_2 from the blood.

Respiratory disease, such as

- **Bronchopneumonia**
- **Emphysema**
- **Asthma**
- **Chronic obstructive**
- **Pulmonary Disease (COPD)** may all be associated with hypoventilation sufficient to cause respiratory acidosis.

- **Some drugs** (e.g., morphine and barbiturates) can cause respiratory acidosis by depressing the respiratory center in the brain.
- **Damage or trauma to the chest** wall and the musculature involved in the mechanics of respiration may reduce ventilation rate.
- This explains the respiratory acidosis that can complicate the course of diseases such as **poliomyelitis**, and recovery from **severe chest trauma**.

Respiratory alkalosis – (reduced pCO_2, increased pH)



respiratory alkalosis is characterized by

1. decreased pCO_2 due to excessive alveolar ventilation
2. resulting excessive elimination of CO_2 from blood.

Disease in which, due to reduced oxygen in blood (hypoxemia), the respiratory center is stimulated can result in respiratory alkalosis.

Examples here include

- **severe anemia**
- **pulmonary embolism**
- **adult respiratory syndrome**.

Hyperventilation sufficient to cause respiratory alkalosis can be a feature of anxiety attacks and response to severe pain.

One of the less welcome properties of **salicylate (aspirin)** is its stimulatory effect on the respiratory center. This effect accounts for the respiratory alkalosis that occurs following salicylate overdose.

Primary disturbances of pCO_2 (respiratory acidosis and alkalosis) are compensated for by renal adjustments of hydrogen ion excretion which result in changes in [HCO_3^-] that compensate appropriately for primary change in pCO_2.

Thus, the renal compensation for respiratory acidosis (raised pCO_2) involves increased reabsorption of bicarbonate, and renal compensation for respiratory alkalosis (reduced pCO_2) involves reduced bicarbonate reabsorption.

Respiratory compensation for a primary metabolic disturbance occurs much more quickly than metabolic (renal) compensation for a primary respiratory disturbance. In the second case, compensation occurs over days rather than hours.

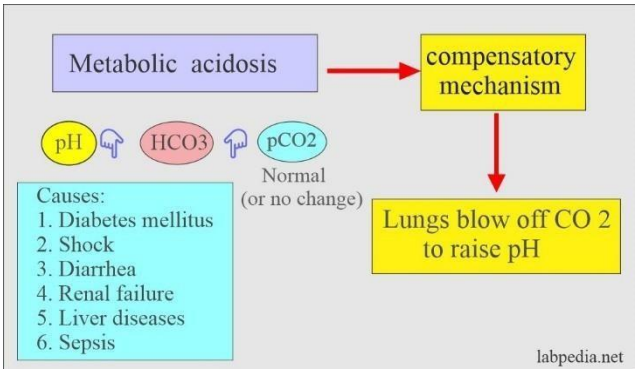
If compensation results in return of pH to normal then the patient is said to be fully compensated. But in many cases the compensation returns pH towards normal without actually achieving normality; in such cases the patient is said to be partially compensated.

For reasons described above, metabolic alkalosis is very rarely fully compensated.

Metabolic acidosis – (decreased HCO_3^-, decreased pH)

Reduced bicarbonate is always a feature of metabolic acidosis. Consider the patient with metabolic acidosis whose

1. pH is low because bicarbonate [HCO_3^-] is low.
2. To compensate for the low [HCO_3^-] and restore the all-important ratio towards normal the patient must lower his pCO_2.



Chemoreceptors in the respiratory center of the brain respond to a rising hydrogen ion concentration (low pH), causing increased ventilation (hyperventilation) and thereby increased elimination of carbon dioxide; the pCO_2 falls and the ratio [HCO_3]: $pCO2$ returns towards normal.

This occurs for one of two reasons:

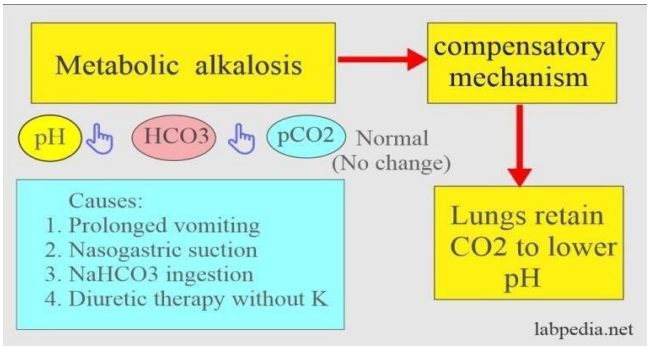
increased use of bicarbonate in buffering an abnormal acid load or increased losses of bicarbonate from the body. **Diabetic ketoacidosis and lactic acidosis** are two conditions characterized by overproduction of metabolic acids and consequent exhaustion of bicarbonate.

In the first case, abnormally high blood concentrations of keto-acids (**b-hydroxybutyric acid and acetoacetic acid**) reflect the severe metabolic derangements which result from **insulin deficiency**.
All cells produce **lactic acid** if they are **deficient of oxygen**, so increased lactic acid production and resulting metabolic acidosis occur in any condition in which oxygen delivery to the tissues is severely compromised.

Examples include **cardiac arrest** and any condition associated with **hypovolemic shock** (e.g., massive fluid loss). Failure to regenerate bicarbonate and excrete hydrogen ions explains the metabolic acidosis that occurs in **renal failure**.

Metabolic alkalosis – (increased HCO_3^-, increased pH)

1. Bicarbonate is always raised in metabolic alkalosis.



Compensation for metabolic alkalosis in which $[HCO_3^-]$ is high, by contrast, involves depression of respiration and thereby retention of carbon dioxide so that the pCO_2 rises to match the increase in $[HCO_3^-]$.

However, depression of respiration has the unwelcome side effect of threatening adequate oxygenation of tissues. For this reason, respiratory compensation of metabolic alkalosis is limited. Rarely, **excessive administration of bicarbonate** or ingestion of bicarbonate in **antacid** preparation can cause metabolic alkalosis, but this is usually transient. Abnormal **loss of hydrogen** ions from the body can be the primary problem. Bicarbonate which would otherwise be consumed in buffering these lost hydrogen ions consequently accumulates in blood. Gastric juice is acidic and gastric aspiration or any disease process in which gastric contents are lost from the body represents a loss of hydrogen ions.

The **projectile vomiting** of gastric juice, for example, explains the metabolic alkalosis that can occur in patients with **pyloric stenosis**. Severe **potassium depletion** can cause metabolic alkalosis due to the reciprocal relationship between hydrogen and potassium ions.

Acid-base disturbance	pH (N 7.35-7.45)	$PaCO_2$ (N 33-45 mm Hg)	$[HCO_3^-]$ (N 22-28 mmol/L)	Primary	Compensatory
Respiratory acidosis	↓	↑	↑	↑ $PaCO_2$	↑ $[HCO_3^-]$
Respiratory alkalosis	↑	↓	↓	↓ $PaCO_2$	↓ $[HCO_3^-]$
Metabolic alkalosis	↑	↑	↑	↑ $[HCO_3^-]$	↑ $PaCO_2$
Metabolic acidosis	↓	↓	↓	↓ $[HCO_3^-]$	↓ $PaCO_2$

Posttest: **What are the characteristics of respiratory acidosis?**