Blood Gases: An Introduction

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History: The history of blood gases has perhaps the oldest, best documented and the most interesting in the developments of laboratory tests.

Joseph Priestley: Became fascinated with gases by observing the large volume of gases produced in beer making, isolated ten gases, including oxygen.

Henry Cavendish: A "nerd" even 200 years ago…discovered hydrogen.

Benjamin Franklin: A collegue of many scientists, including Priestley. In 1749 submitted a summary of his experiments in which he called "vitreous" charges "positive" which later necessitated the labeling of excess electrons with the adjective "negative."

Lawrence Henderson/Karl Hasselbalch: Although they never knew one another, their work in acid-base testing forms the foundation of modern blood gas measurements. The H-H equation expresses acid-base relationships in a mathematical formula.

Leland Clark/Richard Stowe: Developed prototypes of today's partial pressure of oxygen/CO2 electrodes.

Physiology: The involuntary responses which include the exchange of gases, carbon dioxide and oxygen, and the body's mechanism to maintain acid-base balance.

The main function of the lungs is to provide continuous gas exchange between inspired air and the blood in the pulmonary circulation, supplying oxygen and removing carbon dioxide, which is then cleared from the lungs by subsequent expiration. Survival is dependent upon this process being reliable, sustained and efficient, even when challenged by disease or an unfavorable environment.

Arterial vs. Venous Blood:

Arterial blood is oxygenated blood flowing directly from the heart. Venous blood is blood returning to the heart. Arterial blood is nearly always preferred over venous blood for gas analysis.

Buffer Systems:

The body's first line of defense against extreme changes in H+ concentration is the buffer systems present in all body fluids.

Bicarbonate-Carbon Dioxide (Carbonic Acid H_2CO_3)

This is the buffer in highest concentration in the blood plasma that is also of importance in acid-base regulation. CO_2 is a volatile gas produced as a major product of energy metabolism. Refer to Interrelationship diagram. Figure 1-1 pg 4

RATIO of 20:1

HCO_3 is regulated by the kidneys and CO_2 is regulated by the lungs. It is the ratio of HCO_3 to H_2CO_3 that determines the pH.

The Respiratory and Metabolic Systems in Acid-Base Regulation: Lungs and Kidneys

Respiratory System

pCO_2 is considered the respiratory component of the bicarbonate-CO_2 buffer system. Buffering and removal of CO_2 are continually required for pH regulation. CO_2 will readily diffuse into the blood. CO_2 quickly combines with H_2O to form the unstable H_2CO_3, which quickly dissociates into HCO_3 and H+. Hb plays a key role by accepting the H+. As it enters a region of high pO_2 in the lungs, Hb picks up O_2 to become O_2Hb, which immediately promotes loss of H+. H+ quickly combines with bicarbonate to produce dissolved CO_2, which diffuses into the alveolar air for ventilatory removal. See Figure 1-1 pg 4.

The arterial pCO_2 represents a balance between tissue production of CO_2 and pulmonary removal of CO_2. Elevated pCO_2 = inadequate ventilation. Decreased pCO_2 = excessive ventilation (hyperventilation).

To maintain electroneutrality (the same # of + and – charged ions on each side of the rbc membrane), chloride diffuses into the cell. This is known as the Chloride shift.

Metabolic (Renal) system

When the H+ conc. deviates from normal, the kidneys respond by reabsorbing or secreting hydrogen, bicarbonate and other ions to regulate the pH. HCO3 is considered the metabolic component of the HCO3-CO2 buffer system.

The kidneys require hours to days to significantly affect pH by altering the excretion of HCO3.

Blood Gas Measurement: WHY??

In assessing acid-base homeostasis, components of the bicarbonate buffering system are measured and calculated.

Metabolic Acidosis: Examples: Advance Article

Decreased pH with low blood bicarbonate. Compensatory response is hyperventilation, to decrease pCO2. Hyperventilation enhances the removal of CO2, decreasing the pCO2 and increasing the pH.

Ketoacidosis: Normal metabolism requires glucose. If glucose cannot enter cells, as in diabetes, fatty acids must be metabolized producing ketoacids in large amounts.

Lactic Acidosis: If adequate oxygen is not available, cellular conditions begin to favor conversion of pyruvate to lactate.

Renal Failure: Accumulation of H+ and/or loss of HCO3 may occur due to kidney failure. Hyperventilation begins to compensate quickly.

Metabolic Alkalosis: Examples: Advance Article

Increased pH with elevated blood bicarbonate. Compensatory response is hypoventilation, to increase pCO2.

Hypokalemia: K ions secreted in urine. K ions move out of cells and lead to intracellular acidosis and extracellular alkalosis.

Excess Admin of Bicarbonate: Infusion of excessive sodium bicarbonate may lead to alkalosis if renal function is compromised.

Vomiting: Loss of gastric acid may be followed by renal loss of K in an attempt to conserve H+.

Corticosteroid Excess: Steroids lead to the excretion of K. Seen in Cushing’s syndrome.

Respiratory Acidosis: Advance Article Case Studies

Respiratory Acidosis is an elevation of pCO_2 above the expected limit (hypercapnia) >42 mmHg. pO_2 values below 60.
Causes: a defect in excretion of CO_2. Most common cause is emphysema or alveolar destruction, airway obstruction, and CNS disorders. = **Hypoventilation.**
Metabolic compensation in about 5 days with the renal retention of HCO_3.

Respiratory Alkalosis: Advance Article Case Studies

Reduction of pCO_2 below the expected limit: <38mmHg with an increase in pH.
Metabolic Compensation: Decrease excretion of acid by the kidneys.
Causes: Hypoxia due to lung disease, high altitude living, pharmacologic stimulation (salicylate), anxiety/hysteria. = **Hyperventilation.**

Because the body's cellular and metabolic activities are pH dependent, the body tries to restore acid-base homeostasis whenever an inbalance occurs. This action by the body is termed Compensation—the body accomplishes this by altering the factor not primarily affected by the pathologic process.

As primary acid-base disorders alter pH, either the lungs or the kidneys try to compensate for the primary disturbance to pH. If the primary disorder alters bicarbonate, resp. compensation adjusts pCO_2 to normalize pH. If the primary disorder alters pCO_2, metabolic compensation adjusts HCO_3. See table 1-2 pg 6. The pH is normal. (fully compensated) The 20:1 ratio restored.

Blood gas components measured in the Clinical Laboratory:

Physical principles applied in Blood Gas Measurements include: Boyle's Law, Charles' Law, Avogadro's Law, Dalton's Law and Henry's Law. Table 27-4 pg 1000 Tietz.

pH: pH is an index of the acidity or alkalinity of the blood.

Normal Ranges: 7.35-7.45 <7.35 = acid >7.45 = alkaline

PO2 and PCO2: Partial pressure of Oxygen and Partial pressure of Carbon Dioxide.
Normal Ranges:

pO2 and pCO2 change markedly from arterial to venous blood. Examples.
pO2 indicates the ability of the lungs to oxygenate the blood.

pCO2 is a measure of the tension or pressure of carbon dioxide dissolved in the blood. The pCO2 of blood represents the balance between cellular production of CO2 and ventilatory removal of CO2. Normally, steady pCO2 indicates the lungs are removing CO2 at about the same rate as tissues are producing CO2. Change in pCO2 = change in ventilatory status. A disorder caused by ventilatory disfunction (change in pCO2) is termed Respiratory Acidosis or Alkalosis.

pO2 is a measure of the tension or pressure of oxygen dissolved in the blood. The pO2 of arterial blood is related to the ability of the lungs to oxygenate blood from alveolar air. Decreased pO2 = decreased pulmonary ventilation (obstruction of airway, brain trauma) Impaired gas exchange caused by emphysema, edema. Altered blood flow within the heart or lungs caused by heart defects.

SO2 is the percentage of hemoglobin that is saturated with oxygen.

HCO3 (Bicarbonate) is calculated from the pH and pCO2 with the H-H equation. HCO3 is an indicator of the buffering capacity of blood. HCO3 is the metabolic component of acid-base balance. A disorder resulting from a change in the HCO3 level is termed Nonrespiratory (metabolic) disorder.
Normal Ranges:

BE (base excess) is a calculated term that describes the amount of bicarbonate relative to pCO2.
Normal Ranges:

Hemoglobin: Binding, Transport, and Release of Oxygen

Hemoglobin is a protein that consists of four heme molecules attached to four globin molecules. Hb has the ability both to transport and release oxygen to the tissues and to transport H+ and CO2 from the tissues to the lungs. Exposing Hb to increasing concentrations of O2 or increasing PO2 will cause it to become saturated. The sigmoidal relationship between pO2 and SO2 is known as the hemoglobin-oxygen dissociation curve. See Fig 1-2 pg 7.
Hemoglobin "holds on" to O2 until the O2 tension in the tissue is reduced to about 60mm Hg. P50 is defined as the pO2 for a given blood sample at which the hemoglobin of the blood is half saturated with O2. The total O2 content of a blood sample is the sum of the concentrations of hemoglobin bound O2 and of dissolved O2.

COHb: Carboxyhemoglobin, hemoglobin bound with carbon monoxide. Normal:
MetHb: Methemoglobin, inactive hemoglobin containing Fe^{+3} Normal:
Fetal Hb: Fetal hemoglobin

Several factors affect the hemoglobin binding of oxygen: PO_2, H^+, temperature, PCO_2 and 2,3 diphospohglycerate. An **increase** in any of these will **decrease** the affinity of hemoglobin for oxygen.

Principles of Measurement: ABL 725

The actual percent oxyhemoglobin (O_2Hb) can be determined spectrophotometrically using a co-oximeter designed to directly measure the various hemoglobin species.

Blood gas analyzers use electrodes as sensing devices to measure pO_2, pCO_2 and pH.

Measurement of pO_2:

PO_2 electrodes, called Clark electrodes, measure the amount of current flow in a circuit that is related to the amount of O_2 being reduced at the cathode.

Measurement of pH and pCO_2:

To measure pH, a glass membrane sensitive to H^+ is placed around an internal Ag-AgCl electrode to form a measuring electrode. The potential that develops at the glass membrane as a result of H^+ from the unknown solution is proportional to the difference in cH^+ between the unknown sample and the buffer solution inside the electrode.

pCO_2 is determined with a modified pH electrode, called a *Severinghaus* electrode. CO_2 in the sample diffuses across a membrane, reacts with a buffer to form H_2CO_3 and dissociates into bicarbonate and H^+. The H^+ is measured by the pH electrode and is related to pCO_2 content.

Calculated Parameters

Several acid-base parameters can be calculated from measured pH and pCO_2 values. The calculation of HCO_3 is based on the Henderson-Hasselbalch equation.

Henderson-Hasselbalch: Expression of Acid Base relationships in a mathematical formula. Used to calculate the bicarbonate and carbonic acid ratio.

Note: The concentration of H_2CO_3 is proportional to the partial pressure exerted by the dissolved CO_2. The solubility constant for pCO_2 and the factor to convert mmHg to mmol/L is 0.03

One basic assumption is that the pK of the bicarbonate buffer system in plasma at 37 degrees is 6.1:

$$pH = 6.1 + \log \frac{HCO_3}{0.03 \times pCO_2}$$

If the HCO3 is 24 and the pCO2 is 40, what is the pH?

Example:

$$x = 6.1 + \log \frac{24}{0.03 X 40} = \frac{24}{1.2} = \log 20 = 1.3$$

$$x = 6.1 + 1.3$$

$$x = 7.40$$

Calculation of Total CO2: Total $CO_2 = HCO_3 + (0.03 \times pCO_2)$

Calculation of SO2: $SO_2 = \frac{O_2Hb}{\text{Total Hemoglobin}}$

Temperature Correction Formulas:

$$pH = pHm + [-0.0147 + 0.006597.4\text{-}pHm)]$$

Example: The pH correction for a blood gas at 40 degrees would be - 0.045 (0.015 for each degree above 37 degrees.)

Reviewing the Results:

Evaluating the Acid-Base and Blood Gas Results: Case Studies

The acid-base and blood gas results may be evaluated in a four step process:

1. Evaluate the pH
2. Evaluate the pCO2 and HCO3 status
3. Determine if a mixed disorder may be present
4. Evaluate pO2

Evaluating pH:

Does the pH indicate Acidosis or Alkalosis?

Evaluating the pCO2 and HCO3 status:

Refer to Table 1-5 pg. 10.
Refer to Table 1-6 pg. 10.

Ventilatory status may be evaluated by the arterial pCO2.
The HCO3 concentration reflects whether a non volatile acid H+ is produced (low HCO3) or lost (elevated HCO3) or whether the kidneys are retaining or losing excess HCO3 by compensation.

Determining if a mixed disorder is present: Table 1-7 pg. 13.
Compensation for the primary disorder is failing.

Check the K level: Hypokalemia (low K) suggests metabolic alkalosis.
Check the pH: A normal pH with abnormal HCO3 and pO2 may show a mixed acid-base disorder.
Check the Chloride/Anion Gap.
Check the Lactate: Increased lactate = metabolic acidosis
Check the Creatinine: An elevated creatinine = renal insufficiency and possible acidosis

Evaluating Arterial Oxygenation:

Hypoxia is defined as an arterial pO2 less than the acceptable limit for a given age group. See Table 1-8 pg. 14.

Blood oxygen transport is assessed by measurements of blood oxygen content. Affected by anemia, hypercapnia (high pCO2) and hyperthermia, which will cause Hb to be less saturated for a given pO2.

Handling of Samples for Blood Gas Analysis:

Blood collected for blood gas analysis is highly susceptible to changes, especially in pO2. Anaerobic conditions during collection are essential. Other factors that must be controlled are the type of anticoagulant, type of syringe, temp of storage before analysis and length of delay between collection and analysis.

Dry heparin should be used as the anticoagulant. Heparinized plastic syringes are used for nearly all gas measurements, but they have a disadvantage due to their ability to absorb oxygen. When transported/stored on ice, blood can absorb oxygen dissolved within the wall of the syringe and transmitted through the plastic. Storage of blood in plastic syringes at room temperature is acceptable if analysis is within 15 min. Evacuated tubes are not appropriate for blood gases.

From: Understanding the Clinical Uses of Blood Gases and Electrolytes by John Toffaletti, Ph.D.