ANALYSIS OF ARTERIAL BLOOD GASES

– An approach

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INTRODUCTION

The state of equilibrium of the internal environment or the state of relative constancy of the physiologic environment is called homeostasis.

Life is an acidogenic process and from birth to death, H⁺ ions are constantly added to the blood. The concentration of the H⁺ ions has to be balanced tightly, so that the input equals the output. This homeostasis is maintained by the Buffers, Lungs, and Kidneys.

Buffers are the body’s first line of defense. When H⁺ ions are added to the blood, the buffers combine with free floating H⁺ ions, thereby decreasing their concentration. The acute buffering capacity of the body is 500–700 mmol, which is ten times the average intake.

After initial buffering, the concentration of the H⁺ ions in the body is decreased by,

i) The lungs, which increase the excretion of CO₂ by hyperventilation.
ii) The kidneys accelerate the excretion of H⁺ ions and regenerate HCO₃⁻ ions.

SOURCES OF HYDROGEN IONS

1. CO₂ added to the blood: (Volatile Acids)

The metabolism of carbohydrate and fat yield CO₂ and H₂O

\[ \text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^- \]

Roughly 22,000 meq of CO₂ are produced each day, which is equivalent to 1500 mmol of H⁺ ions.

2. H⁺ ions added to the blood: (Non-Volatile Acids)

a. Dietary sulfur containing amino acids and proteins contains H⁺ ions.

b. Incomplete oxidation of carbohydrates and fats produce H⁺ ions.

Approximately 50–80 mmol of H⁺ ions are added to the blood each day and the functioning kidneys can excrete all these H⁺ ions.

Urine is the sole channel of H⁺ ions excretion but it is a very slow process. Hence the kidneys make no significant contribution to the control of sudden fluxes in H⁺ ion concentration.
CARBON DIOXIDE TRANSPORT IN BLOOD:

Carbon dioxide produced in the cells by metabolism is transported in the plasma and the red blood cells.

a) In the plasma CO₂ is transported as:
   i) **Dissolved form**, which exerts a partial pressure (PCO₂). The amount of CO₂ carried in the dissolved form is calculated by PCO₂ mm of Hg x 0.03 mmols/mm of Hg, where the solubility coefficient for CO₂ in plasma is 0.03 mmoles/mm of Hg.
   
   **ii) As bicarbonate**: \( \text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^- \). 
   Only a small amount of CO₂ is carried in this way due to a lack of the enzyme carbonic anhydrase in the plasma.

   **iii) As carbamino compound**: CO₂ reacts with plasma proteins to form carbamino compound.

b) In the red blood cells CO₂ is transported as
   i) **Dissolved form**, which exerts a partial pressure that is in equilibrium with plasma PCO₂

   **ii) As HCO₃⁻**: A major portion of CO₂ is carried in the form of HCO₃⁻, due to the presence of the enzyme carbonic anhydrase in the RBCs.

   \[ \text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^- \]

   The hydrogen ions are buffered by the oxyhaemoglobin (HbO₂) releasing oxygen to the issues. A large amount of HCO₃⁻ is present in the RBC. A concentration gradient forces HCO₃⁻ to diffuse out into plasma. In order to maintain electroneutrality, chloride ions from the plasma move into the RBCS. This is called "**CHLORIDE SHIFT**" or "**HAMBURGER PHENOMENON**".

   **iii) As carbamino compound**: CO₂ reacts with the terminal amino acid group of the haemoglobin molecule forming carbamino compound.

   Therefore CO₂ is transported as:
   a. Dissolved form
   b. Carbamino compound
   c. As HCO₃⁻

   The total CO₂ transported is \( = \text{Dissolved form} + \text{The combined form} \)

   \[ = (\text{PCO}_2 \times 0.03) + \text{HCO}_3^- \]

   \[ = 40 \times 0.03 + 24 \]

   \[ = 1.2 + 24 = 25.2 \text{ mmoles/Litre} \]

*A significant increase or decrease in total CO₂ reflects changes in HCO₃⁻ concentration.

*Total CO₂ levels facilitate recognition of metabolic acid-base changes."
CHLORIDE SHIFT

OXYGEN TRANSPORT IN BLOOD:

Oxygen is also transported in two forms: dissolved form (3%) in the plasma and in the RBCs in combination with haemoglobin (97%). The solubility of oxygen in blood at 37°C in the plasma is 0.003ml/100ml of blood per mm of Hg. This dissolved form exerts a partial pressure which is the PO₂. One gram of fully oxygenated blood carries 1.31 ml of oxygen and 15 g of haemoglobin present in 100 ml of blood can carry approximately 19 ml of oxygen.

The PO₂ of dry atmospheric air is 159 mm of Hg. The first drop occurs as result of humidification and PO₂ becomes 150 mm of Hg. The next drop is at the alveolar level where the PAO₂ is 104 mm of Hg and at the arterial level the PaO₂ is 97-100 mm of Hg.

TERMINOLOGIES:

1. ACID, BASE AND ALKALI
   
   Acid – Any substance which provide H⁺ ions; H⁺ ion donor or proton donor.
   
   Base – Any substance that accepts H⁺ ions or Proton acceptor.
   
   Alkali - Is a substance that can donate OH⁺ ions. Alkalies can also accept H⁺ ions.
   
   Acids produced by the body include HCl, Lactic acid, Ketoacid, Pyruvic acid, Uric acid and Proteins. Bases produced by the body include HCO₃⁻, PO₄³⁻, Proteins and Ammonia.

2. BUFFERS:
   
   A buffer may be defined as a substance which can absorb or donate H⁺ ions and thereby mitigate, but not entirely prevent changes in pH. They are primarily weak acids or bases.

   The important buffers in the body are
   
   i)   H₂CO₃/HCO₃⁻ (Carbonic acid / Bicarbonate)
   ii)  H₂PO₄ (Phosphate buffer)
   iii) HPₐ/Hₐ (Protein buffer)
   iv)  Hb (Haemoglobin buffer)
3. BUFFERING SYSTEMS:

i) The Carbonic acid / Bicarbonate buffer:
   If a strong acid is added to the blood, both chemical and physiological buffering occur.
   \[
   \text{HCl} + \text{Na} \text{HCO}_3 \rightleftharpoons \text{NaCl} + \text{H}_2\text{CO}_3
   \]
   – Chemical buffering
   \[
   \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}_2\text{O} + \text{CO}_2 \text{ (Eliminated by lungs)}
   \]
   – Physiological buffering

ii) Phosphate buffering system:
   This system is similar to bicarbonate system.
   The weak acid is Na$_2$HPO$_4$ and the weak base is Na$_2$HPO$_4$.

iii) Protein buffer:
   Proteins are quantitatively the most important buffers in the body.

iv) Haemoglobin buffer:
   Hb is responsible for half of the buffering power of blood. Oxyhaemoglobin gives up oxygen to the tissues and accepts H$^+$ ions.

   The buffers in the blood in order of importance are Haemoglobin, Bicarbonate, Plasma proteins and phosphate. As already stated, after the initial buffering, the remaining excess H$^+$ ions are excreted by the lungs in the form of CO$_2$ and by the kidneys. The lungs control the amount of CO$_2$ excreted, by means of ventilation. In metabolic acidosis, lungs increase the ventilation to blow off CO$_2$ (which is an acid–former).

   One of the major functions of the kidneys is to reabsorb all the filtered sodium. 80% of Na$^+$ is reabsorbed at the proximal tubules. The remaining 20% of Na$^+$ returns to blood in exchange for H$^+$ or K$^+$ ions in the distal tubules.

   In severe metabolic acidosis, kidneys preferentially excrete H$^+$ ions in exchange for Na$^+$. This selectivity promotes accumulation of K$^+$ (hyperkalemia).

   On the other hand, metabolic alkalosis promotes excretion of K$^+$ in exchange for Na$^+$ leading to hypokalemia.

4. STANDARD BICARBONATE:

   It is the HCO$_3^-$ concentration of plasma which has been fully equilibrated with a gas mixture having a PCO$_2$ of 40 mm of Hg at standard temperature and pressure (37°C and 760 of Hg). This equilibration process, removes the respiratory component to the acid-base imbalance and thus reflects only the metabolic contribution.

   But only the H$_2$CO$_3$/HCO$_3^-$ buffering system is taken into account during this equilibration process. It does not measure the activity of the other buffers in trying to maintain the pH in the normal range.

   Therefore the standard bicarbonate underestimates the metabolic changes.

   Normal range of standard HCO$_3^-$ is 21-27 mmol/Litre.
5. ACTUAL BICARBONATE:

Actual bicarbonate is the concentration of $\text{HCO}_3^-$ measured in a sample of blood without any correction. Therefore it reflects the contribution of both, the respiratory and metabolic components of body’s acid base balance.

Normal range is 21-28 mmol/Litre.

6. BASE EXCESS

Base excess is the amount of strong base (or acid) that has to be added to a sample of blood to produce a pH of 7.4, after the blood sample has been equilibrated with a gas mixture containing $\text{PCO}_2$ at 40 mm of Hg at standard temperature and pressure.

*(e.g)* 1. Initial measurement on an ABG sample

\[ \text{pH} = 7.50; \text{PaCO}_2 = 52 \text{ mm of Hg.} \]

This sample is equilibrated with a CO$_2$ gas mixture to make the PaCO$_2$ 40mm of Hg, thus removing the respiratory contribution to the pH abnormality. The pH now becomes 7.59. Now, a strong acid (eg HCl) is added to titrate the pH to 7.4. The amount of acid required per litre of blood is found to be 15 mmol/Litre. Therefore the *base excess* of the original sample is 15 mmol/litre.

*(e.g)* 2. Initial measurement on an ABG sample.

\[ \text{pH} = 7.22; \text{PaCO}_2 = 22 \text{ mm of Hg} \]

After equilibration with CO$_2$ at 40mm of Hg at STP, the pH becomes 7.1. Now, a strong alkali is added to make the pH 7.4. The amount of alkali required is found to be 18 mmol/Litre. Therefore the *base deficit or the Negative base excess* of the original sample is 18 mmol/Litre.

‘Base Excess’ quantifies the metabolic contribution to the acid-base disorder. Normal value is ‘0’.

CONCEPT OF pH:

The term pH (p stands for Potenz or Power) was introduced by Sorensen to express the molar $\text{H}^+$ ion concentrations. The pH of water is 7.0 and is called the "Universal neutral point". The H$^+$ ion concentration of pure water is $10^{-7}$ mmol/Litre, which contains 100 nanomoles of H$^+$ ions.

Similarly the pH of blood is 7.4 which contains 40 nanomoles of H$^+$ ions.

The pH and H$^+$ ion concentration are inversely related and pH is the negative logarithm of hydrogen ion concentration. The normal range of pH is 7.35 – 7.45 which contains 44 to 36 nanomoles of H$^+$ ions. *Clinically a pH of 8.0 and a sustained pH of 7.0 are incompatible with life. In fact a pH < 7.20 or > 7.7 is considered life threatening.*
HENDERSON – HASSELBALCH EQUATION

The law of mass action states that “the rate of a chemical reaction is directly proportional to the concentration of the reacting components”

Applied to the dissociation of carbonic acid

1. $\text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$
2. At equilibrium $K = \frac{(\text{H}^+) + (\text{HCO}_3^-)}{(\text{H}_2\text{CO}_3)}$
3. $\log K = \log \frac{(\text{H}^+) + (\text{HCO}_3^-)}{(\text{H}_2\text{CO}_3)}$
4. $\log K = \log (\text{H}^+) + \log \frac{(\text{HCO}_3^-)}{(\text{H}_2\text{CO}_3)}$
5. $-\log \text{H}^+ = -\log K + \log \frac{(\text{HCO}_3^-)}{(\text{H}_2\text{CO}_3)}$
6. $\text{pH} = \text{pK} + \log \frac{(\text{HCO}_3^-)}{(\text{H}_2\text{CO}_3)}$ → Henderson Hasselbalch Equation

$pK$ is the pH of the reaction mixture when 50% of the reaction is completed. All reversible chemical reactions have a characteristic constant $pK$ value and $pK$ value for the reaction $\text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$, has a constant value of 6.1.

7. Calculation of pH
   i) The normal arterial $\text{HCO}_3^-$ is 24 meq/litre,
   ii) The normal $\text{H}_2\text{CO}_3$ is calculated by $\text{PCO}_2 \times 0.03$, since dissolution of CO$_2$ in water promotes formation of $\text{H}_2\text{CO}_3$. The normal carbonic acid level in blood is $\text{PaCO}_2 \times 0.03$ = 40x0.03 = 1.2 meq/litre

8. Substituting the values in Henderson – Hasalbalch equation
   $\text{pH} = \text{pK} + \log \frac{(\text{HCO}_3^-)}{(\text{H}_2\text{CO}_3)}$
   = 6.1 + log 24/1.2
   = 6.1 + log 20/1
   = 6.1 + 1.3 = 7.4

9. Significance Of The Henderson Hasselbalch Equation
   a) It is based on the law of mass action
   b) pH varies directly with ratio of $\text{HCO}_3^-$/H$_2$CO$_3$
   c) $\text{HCO}_3^-$/H$_2$CO$_3$ ratio is normally 20:1
   d) As $\text{HCO}_3^-$/H$_2$CO$_3$ increases; pH increases
   e) As $\text{HCO}_3^-$/H$_2$CO$_3$ decreases; pH decreases
   f) When $\text{HCO}_3^-$ is constant, as $\text{PaCO}_2$ increases; pH decreases
   g) When $\text{PaCO}_2$ is constant, as $\text{HCO}_3^-$ increases; pH increases
PRINCIPLE OF ELECTRONEUTRALITY

ANION GAP

The principle of electroneutrality states that the total serum cations should be equal to the total serum anions. Cations include Na, K, Ca and Mg. (Ca and Mg are considered to be unmeasurable cations and the value of K is small). Anions include Cl, HCO$_3^-$, PO$_4^{3-}$, SO$_4^{2-}$, proteins and organic acid anions. (Phosphates, Sulfates, Proteins and organic acid anions are considered to be unmeasurable anions)

Measurable Cations + Unmeasurable Cations = Measurable Anions + Unmeasurable Anions

MC + UMC = MA + UMA

Na+K + UMC = Cl + HCO$_3^-$ + UMA

UMA – UMC = (Na+K) – (Cl+HCO$_3^-$)

This is the anion gap and the normal value is 12+4 meq/litre. The anion gap exists simply because, not all the electrolytes are measured routinely and more anions are left unmeasured than cations. Therefore the “Anion Gap” is an artifact of measurement and not a physiologic reality.

Increase in the “Anion Gap” may be either due ↑ UMA or ↓ UMC or both (or ↑ MC or ↓ MA). In hypoalbuminemia, there is a decrease in the UMA. Therefore the “Anion gap” decreases, but the measured ”Anion Gap” is normal because proteins are not normally measured. For every 1gm/dl decline in serum albumin level, a 2.5 – 3.0 meq/litre decrease in”Anion Gap” occurs.

Electrolyte estimation is a part of ABG analysis and calculation of the “Anion Gap” is very much useful in the diagnosis of the cause of “Metabolic Acidosis”

DELTA GAP

If the ‘anion gap is high’ calculation of the delta gap (Excess anion gap/ HCO$_3^-$ gap/Corrected HCO$_3^-$) must be done, to determine the presence or absence of associated metabolic alkalosis. Delta gap measures the original concentration of plasma HCO$_3^-$.

Delta Gap= Measured HCO$_3^-$ +(Measured Anion Gap-Normal Anion Gap)

The difference between the measured anion gap and normal anion gap refers to the ↓ HCO$_3^-$ levels, which has been utilized to neutralize the acids added to the blood. Therefore the sum of the measured HCO$_3^-$ and the increase in the gap reflects the original HCO$_3^-$ concentration.

PHYSIOLOGICAL PROCESSES REFLECTED IN ABG

The ABG analysis provides information on three physiologic processes.

1. ALVEOLAR VENTILATION:

PaCO$_2$ depends on CO$_2$ produced in the body and its excretion through alveolar ventilation ($V_A$). Alveolar ventilation is that part of the minute ventilation that takes part in gas exchange. [$V_A$ = ($V_T$ – $V_D$ phys) x f] Hence PaCO$_2$ becomes the best index for assessment of $V_A$. High PaCO$_2$ >45 mm of Hg, indicates alveolar hypoventilation and low PaCO$_2$ <35mm of Hg indicates alveolar hyperventilation.
2. OXYGNATION STATUS:

The ultimate aim of oxygenation is to provide adequate delivery of oxygen to the tissues and this is a function of the cardiopulmonary system and various factors like PaCO₂, Hb, saturation and cardiac output. The PaO₂ and SaO₂ are primarily used to assess the oxygenation status.

“Hypoxaemia” is defined as PaO₂ of less than 80mm of Hg at sea level in an adult patient breathing room air, while "Hypoxia” is the similar decrease in cells / tissues. The arterial oxygen tension decreases with age and can be calculated from PaO₂ =104 - (0.27 x age).

Tissue hypoxia is unlikely in mild hypoxaemia (PaO₂ = 60 -80 mm of Hg) and is always present in severe hypoxaemia (PaO₂ <45 mm of Hg).

Normal PaO₂ in an adult breathing room air with FiO₂ of 0.2 is 80 -100 mm of Hg. The normal value of PaO₂/FiO₂ ratio is 400 – 500 mm of Hg and the normal oxygenation ratio is 4 -5. PaO₂/FiO₂ ratio of less than 200, most often indicates a shunt fraction greater than 20%, the normal being 5% of cardiac output. (Shunt is that part of the cardiac output that returns to the left side of the heart without picking up oxygen from the alveoli.)

The normal alveolar to arterial PO₂ difference (PAO₂ – PaO₂) is due to true shunt and low V/Q ratio. The PAO₂-PaO₂ predicts the degree of shunt and gives an idea about how well the oxygen is moving from the alveoli to the arterial blood.

The PAO₂ can be calculated from the alveolar gas equation: PAO₂=760– 47 xFiO₂ – PaCO₂ /0.8. The PaO₂ can be obtained from the ABG analysis. The increase in A-a gradient is seen in abnormal shunts which may be extrapulmonary or intrapulmonary and lowV/Q ratios. The normal range for A-a gradient is 5-20 mm of Hg.

**Significance of the A-a Oxygen Gradient**

If the PAO₂ is low but the transfer of oxygen from the alveolus to arterial blood is normal the A-a O₂ gradient will remain normal e.g. hypoventilation. If the PAO₂ is normal but structural problems limit the transfer of oxygen from the alveolus to arterial blood the A-a O₂ gradient will increase e.g. ARDS, pulmonary embolus.
3. **ACID – BASE STATUS** :

**TIMING OF ABG SAMPLE**

Blood sampling should be done during a “Steady State”. Whenever there is initiation or change in oxygen therapy in spontaneously breathing patients or change in ventilator parameters with patients or mechanical ventilation, sampling should be done only when the “Steady State” is reached.

In patients without pulmonary disease a “Steady State” is reached between 3-10 minutes and in patients with chronic airway obstruction, it takes about 20-30 minutes after changes have been made.

As a general rule, if changes in FiO₂ have been made, the blood sample should be obtained after 20 minutes and in mechanically ventilated patients it should be obtained 30 minutes after changes have been made.

**HEPARIN AND ITS EFFECT**

Heparin must be added to the syringe as an anticoagulant. 0.05 – 0.1ml of 1 in 1000 solution of heparin will anticoagulate 1 ml of blood. This sufficient amount of heparin remains in the dead space of the syringe, after it has been flushed.

Heparin has a pH of 7.0 and PO₂ and PCO₂ values near room air values. If excess heparin is added, it alters all three ABG values.

**AIR BUBBLES**

Air bubbles that mix with blood sample will equilibrate with the blood. Room air has a PO₂ of 150mm of Hg and PCO₂ of “O”. Thus mixing of air bubbles will cause

↑PaO₂

↓PaCO₂

↑PH

**HANDLING OF SAMPLE**

Blood contains leucocytes and platelets which are living cells. They continue to consume oxygen and liberate carbon dioxide. If the blood sample is not analyzed immediately PaO₂ decreases; PaCO₂ increases and pH decreases.

Therefore uncooled blood samples should be analyzed within 15 minutes. If it is not possible, the sample should be placed in a container of crushed ice and this cooled sample should be analyzed within one hour.
NORMAL ABG VALUES

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Absolutely Normal</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.4</td>
<td>7.35 – 7.45</td>
</tr>
<tr>
<td>PaO₂</td>
<td>100 mm of Hg</td>
<td>80–100 mm of Hg</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>40 mm of Hg</td>
<td>35–45 mm of Hg</td>
</tr>
<tr>
<td>HCO₃</td>
<td>24 meq /Litre</td>
<td>22 –26 meq / Litre</td>
</tr>
<tr>
<td>BE</td>
<td>0</td>
<td>± 2 meq /Litre</td>
</tr>
<tr>
<td>SPO₂</td>
<td>&gt;97%</td>
<td>90 -100</td>
</tr>
<tr>
<td>Hb</td>
<td>14 gms</td>
<td>12-14 gms</td>
</tr>
<tr>
<td>Anion Gap</td>
<td>12 mmol /Litre</td>
<td>12 ± 4 mmol/ Litre</td>
</tr>
<tr>
<td>PaO₂/FiO₂</td>
<td>5</td>
<td>4 -5</td>
</tr>
</tbody>
</table>

METHOD OF INTERPRETATION OF ABG

The classic method that is routinely followed is called the “Bicarbonate Centric Approach”

Another analytic method proposed by Stuart, based on the strong ion difference is called “Stuaris approach”

COMPENSATORY MECHANISMS

As previously stated buffers are the first line of defense against changes in H⁺ ion concentration. The goal of the compensation is to maintain the HCO₃⁻/H₂CO₃ ratio in the normal range of 20:1 and return the pH to the acceptable range. When there is an imbalance in one parameter the other tries to compensate for it by causing the opposite imbalance.

After initial buffering, the remaining H⁺ ions are excreted by the lungs in the form of CO₂ and by the kidneys which also reabsorb HCO₃⁻.

RULES OF COMPENSATION:

1. The compensatory response depends upon the proper functioning of the organ system involved in the response (lungs or kidneys) and how severe is the primary disturbance.
2. Acute compensation by the kidneys occurs within 6-24 hours and chronic within 1-4 days.
3. There is no acute and chronic compensation in respiratory compensation.
4. In clinical practice it is uncommon to see complete compensation. The maximum compensatory response is only 50-75%.

EXPECTED COMPENSATION:

1. pH&PaCO₂:
   - Acute conditions - For every 10 mm of Hg change in PaCO₂, pH changes by 0.08 UNITS.
   - Chronic conditions - For every 10 mm of Hg change in PaCO₂, pH changes by 0.03 UNITS.
2. **Respiratory Acidosis:**

<table>
<thead>
<tr>
<th>pH</th>
<th>PaCO₂</th>
<th>Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓</td>
<td>↑</td>
<td>Metabolic alkalosis</td>
</tr>
</tbody>
</table>

**Acute conditions:**
- For every 10 mm of Hg change in PaCO₂,
  \[ \text{HCO}_3^- \text{↑} \text{ses by 1 meq/Litre.} \]

**Chronic conditions:**
- For every 10 mm of Hg change in PaCO₂,
  \[ \text{HCO}_3^- \text{↑} \text{ses by 3.5-4 meq/Litre.} \]

3. **Respiratory Alkalosis:**

<table>
<thead>
<tr>
<th>pH</th>
<th>PaCO₂</th>
<th>Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑</td>
<td>↓</td>
<td>Metabolic acidosis</td>
</tr>
</tbody>
</table>

**Acute conditions:**
- For every 10 mm of Hg ↓ in PaCO₂,
  \[ \text{HCO}_3^- \text{↓} \text{ses by 2 meq/Litre.} \]

**Chronic conditions:**
- For every 10 mm of Hg ↓ in PaCO₂,
  \[ \text{HCO}_3^- \text{↓} \text{ses by 5 meq/Litre.} \]

4. **Metabolic Acidosis:**

<table>
<thead>
<tr>
<th>pH</th>
<th>HCO₃⁻</th>
<th>Base deficit/ve Base Excess/Low Std HCO₃⁻</th>
<th>Tot.CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓</td>
<td>↑</td>
<td></td>
<td>↑</td>
</tr>
</tbody>
</table>

The expected compensation is respiratory alkalosis.

Expected PaCO₂ = \( (1.5 \times \text{HCO}_3^-) + (8 \pm 2) \) – *Winter’s Formula* (Or)

Expected PaCO₂ = the last two digits of pH

5. **Metabolic Alkalosis:**

<table>
<thead>
<tr>
<th>pH</th>
<th>HCO₃⁻</th>
<th>Base Excess</th>
<th>High Std HCO₃⁻</th>
<th>Tot.CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑</td>
<td>↓</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The expected compensation is respiratory acidosis.

For every 1 meq/L ↑ in HCO₃⁻ ; PaCO₂ ↑ by 0.5-0.7 mm of Hg

Expected PaCO₂ = Last two digits of pH

[** The equation that predicts the respiratory response to a “Metabolic acidosis” is called the *Winter’s Formula*. Expected PaCO₂ = \( (1.5 \times \text{HCO}_3^-) + (8 \pm 2) \) ]

**Acidosis and Alkalosis**

a) **Respiratory Acidosis:**  pH < 7.35; PaCO₂ > 45 mm of Hg

The causes of respiratory acidosis include,

i) Alveolar hypoventilation (Due to ventilatory failure or advanced cases of oxygenation failure)

ii) ↑CO₂ Production

iii) ↑Fi CO₂ or rebreathing

i) **Oxygenation Failure / Hypoxaemic Failure/Type I Failure:**  PaO₂ ↓ ; PaCO₂ – Normal

The structural problems in the airway or the pulmonary parenchyma limit the transfer of oxygen from the alveolus to arterial blood; the A-a O₂ gradient is increased.

The causes include atelectasis, pulmonary edema, pneumonia, pleural effusion, ARDS, haemopneumothorax, upper and lower airway obstruction.

In this type of failure, ventilation is low when compared to perfusion or FiO₂ is low. The PAO₂ is normal, PACO₂ is normal, but the PaO₂ is decreased, hence *A-a gradient is increased.*
ii) **Ventilatory Failure / Hypercapnic / Type II Failure:** PaO\textsubscript{2} ↓; PaCO\textsubscript{2} ↑

In this type the airway and the pulmonary parenchyma are normal. The causes include

i) CNS depression – Drugs/sleep/Head injury

ii) Phrenic nerve lesions

iii) COPD

iv) Type I causes in advanced states.

The compensatory mechanism is by the kidneys, which increases the excretion of H\textsuperscript{+} ions and retains HCO\textsubscript{3}\textsuperscript{-} ions. This is a slow process and may take days for full compensation to occur. The PAO\textsubscript{2} is low but the transfer of oxygen from the alveolus to arterial blood is normal. Hence the A-a O\textsubscript{2} gradient is normal

b) **Respiratory alkalosis:** pH > 7.45, PaCO\textsubscript{2} < 35 mm of Hg

Any condition which causes hypoventilation can result in respiratory alkalosis. These conditions include

i) CNS stimulation -Fever, Pain, Thyrotoxicosis, Cerebrovascular Accident

ii) Hypoxaemia - Pneumonia, pulmonary edema, anaemia

iii) Sepsis

iv) Pregnancy

v) Psychological

c) **Metabolic Acidosis:** PH < 7.35; HCO\textsubscript{3} \textsuperscript{-} < 22 meq/l; Base deficit; Low Std HCO\textsubscript{3} \textsuperscript{-}; Low Tot CO\textsubscript{2}

Metabolic acidosis is produced when

i) Acid production is in excess of kidney’s ability to excrete acid and regenerate HCO\textsubscript{3} \textsuperscript{-} (lactic acid, Aceto acetic acid)

ii) Loss of HCO\textsubscript{3} \textsuperscript{-} from ECF - GIT or Renal

iii) Renal pathology causing reduction in ability to excrete acid and regenerate bicarbonate.

1. **High Anion Gap Metabolic Acidosis**

Here acid production is in excess and the bicarbonate is consumed in buffering of the H\textsuperscript{+} ions. Hence there is decreased level of HCO\textsubscript{3} \textsuperscript{-}, which leads to “↑Anion Gap” (High anion gap metabolic acidosis)

The causes include

i) Lactic acidosis - Shock, Sepsis, Hypoxia, Seizures

ii) Ketoacidosis - Diabetes, Starvation

iii) Uraemic acidosis

iv) Toxins - Methanol, Ethanol

2. **Normal Anion Gap Metabolic Acidosis**

When bicarbonate is lost through urine or enteric drainage, compensatory increase in serum chloride concentration occurs. This produces a “Hyperchloremic, Normal Anion Gap Metabolic Acidosis”.

i) **Hypokalemic Normal Anion Gap Metabolic Acidosis.**

Renal and GIT losses of HCO\textsubscript{3} result in this type of metabolic acidosis: Along with HCO\textsubscript{3} \textsuperscript{-}, K\textsuperscript{+} is also lost.
i) GIT Losses of HCO₃⁻
   Ureteral diversion, Diarrhoea, Ileostomy, Pancreatic fistula

ii) Renal loss of HCO₃⁻
   Proximal Renal Tubular Acidosis, Carbonic anhydrase inhibitors

**ii). Normokalemic/Hyperkalemic Normal Anion Gap, Metabolic Acidosis.**

The kidney tries to excrete the H⁺ ions in exchange for Na⁺ at the distal convoluted tubules. This selectivity promotes the accumulation of K⁺ (hyperkalemia).

i) Renal Tubular disease
   ATN, Distal RTA, Hypoaldostreonism

ii) Pharmacological
   Ammonium chloride, Hyperalimentation.

d) **Metabolic Alkalosis:** pH > 7.45 ; HCO₃⁻ > 26 meq /L; Base excess ;High std HCO₃⁻

The causes of metabolic alkalosis includes

i) Loss of H⁺ ions – vomiting, NG suctioning

ii) Reabsorption of HCO₃⁻ – low intravascular volume

iii) Hypokalemia

iv) Administration of Alkali

v) Massive dose of steroids – Reabsorb Na⁺ in exchange for H⁺

vi) Diuretics.

**DETERMINATION OF THE PRIMARY DISORDER**

*Single acid base disorders do not lead to normal blood pH, though the pH can end up in the normal range (7.35-7.45). A truly normal pH, but with abnormal HCO₃⁻ and PaCO₂ invariably suggests a mixed disorder.*

When there are two imbalances, the pH provides the clue to determine the primary disorder. *Whichever side the pH is leaning* even if it is in the normal range, the parameter with the matching imbalance would be the primary problem.

(e.g)  
PpH - 7.43  
PaCO₂ - 20 mm of Hg  
HCO₃⁻ - 15 mmol / L

Is it “metabolic acidosis” compensated by respiratory alkalosis or “respiratory alkalosis” compensated by metabolic acidosis. The clue is in the pH. Though it is in the normal range, still it is alkaline. The matching alkaline parameter is PaCO₂. Therefore the primary problem is **respiratory alkalosis** with nearly complete compensation by kidneys.

In addition to the clue in the pH, the clinical history and physical examination provides valuable clues to arrive at a diagnosis.

**Mixed Acid -Base disorders**

To diagnose mixed acid-base abnormalities, the expected compensation for a primary disorder should be compared with the available data.
1) **Respiratory Acidosis:** ↑ in \( HCO_3^- \) is expected. If ↑ in \( HCO_3^- \) is
   i) < than expected – Complicating Metabolic Acidosis
      – Less time for the kidney to compensate
   ii) > than expected – Super imposed Metabolic Alkalosis
   iii) As expected – Appropriate compensation ; implies a simple disorder

2) **Respiratory Alkalosis:** ↓ in \( HCO_3^- \) is expected. If ↓ in \( HCO_3^- \) is
   i) < than expected – complicating Metabolic Alkalosis
   ii) > than expected – Super imposed Metabolic Acidosis
      – Insufficient time for compensation
   iii) As expected – Appropriate compensation ; implies a simple disorder

3) **Metabolic Acidosis:** ↓ \( PaCO_2 \) is expected. If ↓ in \( PaCO_2 \) is
   i) < than expected – Associated Respiratory Acidosis
   ii) > than expected – Associated Respiratory Alkalosis
   iii) As expected – Appropriate compensation ; simple disorder.

4) **Metabolic Alkalosis:** ↑ \( PaCO_2 \) is expected. If ↑ in \( PaCO_2 \) is
   i) < than expected – Associated Respiratory Alkalosis
   ii) > than expected – Associated Respiratory Acidosis
   iii) Normal \( PaCO_2 \) when \( HCO_3^- \) is ↑ – Less than expected compensation (or) Relative hyperventilation

**ABG ANALYSIS**

An ABG value can have many explanations. A diagnosis cannot be made on the basis of the numbers alone. A thorough history, physical findings and other investigations are to be considered while interpreting ABG values.

The respiratory parameters include the pH & \( PaCO_2 \) while the metabolic parameters include pH, standard \( HCO_3^- \), Actual \( HCO_3^- \), Base Excess and total CO₂.

Therefore the ventilatory and acid–base status is provided by pH ,\( PaCO_2 \),\( HCO_3^- \) and BE. The oxygenation status is provided by \( PaO_2 \),\( SPO_2 \) and Hb.

*For precise interpretation of blood gases, the following concepts must be understood*

i) Any acid–base abnormality is secondary to a respiratory or a metabolic disorder.

ii) A respiratory abnormality is identified from \( PaCO_2 \) level, whereas abnormal \( HCO_3^- \) level indicates a metabolic disturbance.

iii) \( PaCO_2 \) & pH relationship
   - ↑\( PaCO_2 \) – ↓pH – Acidosis
   - ↓\( PaCO_2 \) – ↑pH – Alkalosis

iv) \( HCO_3^- \) and pH relationship
   - ↑\( HCO_3^- \) – ↑pH – Alkalosis
   - ↓\( HCO_3^- \) – ↓pH – Acidosis

v) Base excess provides an index for quantifying the metabolic contribution to the acid–base imbalance
   - Metabolic alkalosis – Positive BE
   - Metabolic acidosis – Negative BE / Base deficit
**STEPS IN THE INTERPRETATION OF ABG**

**STEP 1** Electrolyte estimation

Serum electrolytes are part of ABG analysis. The blood gas data should not be interpreted for acid-base diagnosis, without examining the serum electrolytes. In metabolic acidosis, electrolyte values are needed to calculate ‘Anion Gap’ and to arrive at a diagnosis.

**STEP 2** Validity of Report

Ensure that the machine has been calibrated properly.

**STEP 3** Ensure that the sample is from an artery.

It is best known to the person who has done the arterial puncture. A free flowing plunger confirms this. If PaO$_2$ > 40mm of Hg and SPO$_2$ > 75% it is unlikely to be a venous sample.

**STEP 4** Steady state, Heparin, Immediate analysis, Preservation in ice, Air bubbles

Adequate heparin must be added as an anticoagulant and air bubbles should be removed. The uncooled sample should be analyzed within 15 minutes and the cooled sample should be analyzed within an hour. The patient must be in a steady state in terms of oxygenation and ventilation while the sample is obtained.

As a general rule wait for 20 minutes after any change in FiO$_2$ in a spontaneously breathing patient and 30 minutes in mechanically ventilated patients to reach steady state.

**STEP 5** Look at pH

Only three possibilities exist
i) Normal pH
   - Normal acid-base status
   - Completely compensated status (very rare)
   - Mixed acid-base disorder

ii) Acidosis – pH < 7.35
   - Respiratory
   - Metabolic

iii) Alkalosis – pH > 7.45
   - Respiratory
   - Metabolic

**STEP 6** Determine the primary disorder using the following parameters.

<table>
<thead>
<tr>
<th></th>
<th>pH</th>
<th>PaCO$_2$</th>
<th>BE</th>
<th>STD HCO$_3^-$</th>
<th>TOTAL HCO$_3^-$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory acidosis</td>
<td>↓</td>
<td>↑</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>↑</td>
<td>↓</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>↓</td>
<td>-</td>
<td>Negative BE</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>↑</td>
<td>-</td>
<td>Positive BE</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>
STEP 7 Determine whether the primary disorder has been fully compensated, partially compensated or uncompensated.

STEP 7a Uncompensated States
An abnormality is precipitated by one parameter, while the other parameter is within the normal range and the pH is not restored to the normal range.

<table>
<thead>
<tr>
<th>pH</th>
<th>PaCO₂ mm of Hg</th>
<th>HCO₃⁻ meq/Litre</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.10</td>
<td>80</td>
<td>24</td>
<td>Uncompensated Respiratory Acidosis</td>
</tr>
<tr>
<td>7.52</td>
<td>30</td>
<td>23</td>
<td>Uncompensated Respiratory Alkalosis</td>
</tr>
<tr>
<td>7.20</td>
<td>37</td>
<td>13</td>
<td>Uncompensated Metabolic Acidosis</td>
</tr>
<tr>
<td>7.55</td>
<td>42</td>
<td>40</td>
<td>Uncompensated Metabolic Alkalosis</td>
</tr>
</tbody>
</table>

STEP 7b Partially Compensated States
Any underlying acid-base abnormality in time promotes compensatory action by the complementary system ie, respiratory or renal. In a partially compensated state both the parameters PaCO₂ & HCO₃⁻ are abnormal and the pH is not restored to the normal range.

<table>
<thead>
<tr>
<th>pH</th>
<th>PaCO₂ mm of Hg</th>
<th>HCO₃⁻ meq/Litre</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.32</td>
<td>60</td>
<td>29</td>
<td>Partially compensated Respiratory Acidosis</td>
</tr>
<tr>
<td>7.51</td>
<td>20</td>
<td>17</td>
<td>Partially compensated Respiratory Alkalosis</td>
</tr>
<tr>
<td>7.25</td>
<td>24</td>
<td>9</td>
<td>Partially compensated Metabolic Acidosis</td>
</tr>
<tr>
<td>7.55</td>
<td>50</td>
<td>4</td>
<td>Partially compensated Metabolic Alkalosis</td>
</tr>
</tbody>
</table>

STEP 7c Totally Compensated States
In total compensation, pH has been restored to the normal range, but both the parameters, PaCO₂ & HCO₃⁻ will be abnormal.

<table>
<thead>
<tr>
<th>pH</th>
<th>PaCO₂ mm of Hg</th>
<th>HCO₃⁻ meq/Litre</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.37</td>
<td>59</td>
<td>35</td>
<td>Compensated Respiratory Acidosis</td>
</tr>
<tr>
<td>7.43</td>
<td>27</td>
<td>16</td>
<td>Compensated Respiratory Alkalosis</td>
</tr>
<tr>
<td>7.37</td>
<td>27</td>
<td>18</td>
<td>Compensated Metabolic Acidosis</td>
</tr>
<tr>
<td>7.42</td>
<td>49</td>
<td>30</td>
<td>Compensated Metabolic Alkalosis</td>
</tr>
</tbody>
</table>

STEP 8 compare the measured data and expected compensation to diagnose mixed disorders.

STEP 9 If it is a “metabolic acidosis” calculate the “Anion gap”
**STEP 10** If ‘Anion gap’ is increased calculate the ‘delta gap’ / excess anion gap to detect additional metabolic disturbance. Delta Gap = (Measured HCO₃⁻) + (Measured Anion gap– Normal Anion gap)

**STEP 11** Asses the oxygenation status by

i)PaO₂ / FiO₂ ratio
ii)SPO₂
iii)A-a gradient
iv)a/A ratio

PaO₂ / FiO₂ ratio should normally be 400 – 500 and > 300 is acceptable. The normal A – a is 5 -20 mm of Hg. It is increased in oxygenation failure due to venous admixture (True shunt & low v/Q). But the A-a gradient is normally maintained in ventilatory failure.

a/A ratio is normally >80% .If the ratio is <40% it indicates a shunt fraction of >20%.

**STEP 12 Never interpret ABG based on numbers to treat patients -Golden Step**

A thorough clinical history and examination is very valuable. The aim should not be to correct a number but the underlying abnormality represented by the abnormal number.

(eg) ↑Anion Gap Acidosis

a) Lactic acidosis suggests a hypoperfusive state. So treatment should be directed towards improving perfusion, by optimizing the fluid status, and using inotropes and oxygen therapy, rather than giving bicarbonate.

b) DKA – The treatment should be with saline and insulin infusion to correct acidosis. Administration of NaHCO₃ has no role in this situation.

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