Lecture 18
How to read and interpret arterial blood gases??

Objectives:

1. Interpret scenarios on buffering systems
2. Explain information related to formulating a diagnosis
3. Explain information related to 3-question method
4. Solve problems concerning the 4 primary disturbances
5. Use knowledge of compensation
6. Solve problems concerning plasma anion gap diagnosis

Buffers:

They are ionic compounds that resist changes in pH when acid or base is either added or removed.

- **Buffer solution is formed of either:**

i. Weak acid and its salt with strong base, e.g., carbonic acid and sodium bicarbonate, or sodium acid phosphate (NaH_2PO_4) and sodium alkaline phosphate (Na_2HPO_4).

ii. Weak base and its salt with strong acid, e.g., ammonium hydroxide and ammonium chloride.

-Importance of buffers:

The body maintains blood pH within a tight range (approximately 7.40 ± 0.05) via a complex system of buffers. This is very essential for body health because most enzymes in the body function optimally within a very small pH range. Consequently they are very sensitive to any change in the pH. These physiological buffers strictly guard this narrow pH range.

-The important physiological buffer widely distributed in tissues and body fluids are:

These are categorized based on their location in relation to the cellular membrane: **intracellular (**mainly of proteins and phosphates)and **extracellular (**mainly of bicarbonate and phosphates)

1. Bicarbonate buffer:

- It is one of the major buffer systems of the blood because it is the alkali reserve and is linked to respiration. It is formed of carbonic acid and sodium or potassium bicarbonate. The base/acid ratio of this buffer is 20/1 at pH 7.4, $H_2CO_3/NaHCO_3$ and $H_2CO_3/KHCO_3$. Consequently, bicarbonate is a good buffer when blood is being acidified but very poor

if the blood is alkalinized. It acts mainly extracellularly (sodium salts) but also intracellularly particularly in RBCs (potassium salts).

To demonstrate the changes in the major variables during acid-base disturbances, bicarbonate buffer system is main focus of this lecture:

The CO_2 produced then reacts with H_2O via the enzyme carbonic anhydrase to produce carbonic acid as shown:

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

It can be simplified to the following:

$$CO_2 \leftrightarrow H^+ + HCO_3^-$$

pH of the blood is maintained by preserving the HCO_3^-/ CO_2 ratio nearly constant.

Alkali Reserve:

- This is represented by the bicarbonate (sodium or potassium) present in the blood. It is a measure for alkali available for neutralization of any added acid to the blood.

2. Phosphate buffer:

- This buffer has a base/acid ratio of 4/1 in plasma and is controlled by kidney. It is the chief buffer in urine.

3. Protein buffer:

- 20% of the buffer capacity of blood depends on the plasma proteins

4. Hemoglobin and oxyhemoglobin buffer:

- This accounts for 60% of the buffer capacity of blood as hemoglobin concentration lies around 14 g/dl. It is responsible for buffering of most CO_2 added to the blood by tissues.

Acid Production in human body

Acid production within the body is of two types: **volatile** and **nonvolatile.** Most of the acids in the body are weak acids, with the exception of hydrochloric acid (HCl), which is secreted in the form of gastric acid.

Volatile Acid

They are produced in the form of CO_2 via cellular metabolism.

Nonvolatile Acid

Protein catabolism generates sulfuric acid, and phospholipid catabolism creates phosphoric acid. Other nonvolatile acids produced by the body

include lactic acid and ketones. They are normally buffered in the blood by the alkali reserve.

Acid-base disturbances:

- From the above-mentioned facts, it can be noticed that the buffer systems present in the blood are so efficient to keep the pH of blood within a very limited range (7.35 – 7.45).
- Recall that the respiratory system plays the key role in regulating CO_2, while the kidneys serve as the long-term regulators of H^+ and HCO_3^-. Thus, the kidneys and lungs are the principal organs responsible for regulation of acid–base homeostasis.
- However, excessive addition of acids or alkalis might disturb such buffer systems by exhausting the alkali reserve leading to acidosis or by exhausting acid reserve leading to alkalosis, both are fatal. If the pH in such conditions is kept on the lower or upper extremes of the physiological range of the pH, it will result in a quite serious condition called acidemia or alkalemia. Values outside the range of 6.8–8.0 are typically incompatible with life due to changes in enzymatic function and protein denaturation. These disturbances are caused by either respiratory or metabolic causes. These causes are discussed in details by physiology department.

There are 4 primary acid- base disturbances, each of which results in altered concentration of H+. The basic deviations from normal can be an acidosis (excess H+) or an alkalosis (deficiency of H+), either may be caused by a respiratory or metabolic problem.

	pH	**PCO_2**	**HCO_3^-**	**Compensatory response**
Metabolic acidosis	↓	↓	⇓	Hyperventilation (immediate)
Metabolic alkalosis	↑	↑	⇑	Hypoventilation (immediate)
Respiratory acidosis	↓	⇑	↑	↑ renal reabsorption of HCO_3^-
Respiratory alkalosis	↑	⇓	↓	↓ renal reabsorption of HCO_3^-

Key: ⇑⇓ = Primary disturbance ↑↓ = Effect or compensation

Normal values:

Normal pH= 7.35- 7.45

Normal PCO_2 = 36- 44 mmHg (In calculations = 40 mmHg)

Normal HCO_3^- = 22- 28 mEq/L (In calculations = 24 mmHg)

Formulating a Diagnosis:
Acid base disturbances can be diagnosed from arterial blood gases (ABGs) using a 3-question method:
Question 1: What is the abnormality acidosis or alkalosis?
Question 2: What is the cause of the abnormality metabolic or respiratory?
Question 3: Was there compensation?

Question 1: What is the abnormality (acidosis or alkalosis)?
Normal pH= 7.35- 7.45
If pH < 7.35, it is acidosis
If pH > 7.45, it is alkalosis
However, one can in fact have an underlying acid-base disorder even though pH is in the normal range.

Question 2: What is the cause of the abnormality (metabolic or respiratory)?
To answer this, look at the bicarbonate concentration and remember the basic CO_2 – bicarbonate reaction.

$$CO_2 \longleftrightarrow H^+ + HCO_3^-$$

Acute changes in pH/ HCO_3^-

	pH	**HCO_3^-**
Respiratory acidosis	↓	↑ For every 1 mmHg rise in PCO_2, there is a 0.1 mEq/L increase in HCO_3^-, as a result of the chemical reaction (not compensation). Thus, There is a 1: 0.1 ratio of CO_2 increase to HCO_3^- increase for an acute (uncompensated) respiratory acidosis.
Metabolic acidosis	↓	↓↓ Caused by: 1- the addition of H^+ consumes bicarbonate and drives the reaction to the left 2- Direct loss of bicarbonate.

Respiratory alkalosis	↑	↓ Reduced CO_2 drives the reaction to the left, thereby reducing bicarbonate, for every 1mmHg fall in PCO_2 there is a 0.2 mEq/L decrease in HCO_3^- as a result of the chemical reaction (not compensation) Thus, There is a 1: 0.2 ratio of CO_2 decrease to bicarbonate decrease for an acute (uncompensated) respiratory alkalosis.
Metabolic alkalosis	↑	↑↑ Caused by: 1- Loss of H^+ that drives the reaction to the right. 2- Direct addition of base (bicarbonate) to the body.

Question 3: Was there compensation?

Respiratory acidosis:

- The kidneys compensate by increasing bicarbonate and eliminating H^+, but the kidneys take days to fully compensate. For every 1 mmHg increase in P CO_2, HCO_3^- increases 0.35 mEq/L as a result of kidney compensation. Thus, there is a 1:0.35 ratio CO2 increase to HCO_3^- increase in a chronic (compensated) respiratory acidosis.
- It is important to distinguish between acute (uncompensated) (1: 0.1 ratio) and chronic (compensated) (1: 0.35 ratio) respiratory disturbances.

For example, a patient has a respiratory acidosis (determined by steps 1 and 2) with P CO_2 60 mm Hg, which is 20 mm Hg greater than the normal of 40 mmHg.

If acute, then bicarbonate will be ~26 (20 × 0.1 = 2; 24 + 2 = 26).

If chronic, then bicarbonate will be ~31 (20 × 0.35 = 24 + 7 =31).

Metabolic acidosis:

- The drop in pH stimulates ventilation via peripheral chemoreceptors.
- **Winter's formula** gives the expected PCO_2 based on a measured HCO_3^- and is used to determine if the respiratory compensation for a metabolic acidosis is appropriate:

$$\text{Predicted } PCO_2 = [(1.5 \times HCO_3^-) + 8]$$

The patient's PCO_2 should be within 2 (±) of this predicted value, with 3 probable conditions:

- If the patient's PCO_2 is within 2, then the patient has **metabolic acidosis with respiratory compensation.**
- If it is higher than 2, then the respiratory response is inadequate and the patient has **metabolic and respiratory acidosis**.
- If the patient's PCO_2 is too low, then the patient has a **metabolic acidosis with a respiratory alkalosis**.

For example, a patient has a metabolic acidosis with a HCO_3^- of 10 mEq/L and a PCO_2 of 23 mm Hg. Expected PCO_2 is (1.5 × 10) + 8 = 23 mm Hg, which is what the patient has, thus respiratory compensation is adequate.

Respiratory alkalosis:

- The kidneys compensate by eliminating bicarbonate and conserving H^+, but the kidneys take days to fully compensate.
- For every 1 mmHg drop in P CO_2, HCO_3^- decreases 0.5 mEq/L as a result of kidney compensation. Thus, there is a 1:0.5 ratio of CO_2 decrease to HCO_3^- decrease in a chronic (compensated) respiratory alkalosis.
- Again, it is important to distinguish between acute (uncompensated) (1:0.2 ratio) and chronic (compensated) (1:0.5 ratio) respiratory disturbances.

For example, a patient has a respiratory alkalosis (determined by steps 1 and 2) with a PCO_2 of 25 mm Hg, which is 15 mm Hg less than the normal of 40 mmHg. If acute, then bicarbonate will be about 21 (15 × 0.2 = 3; 24 – 3 = 21), but if chronic it will be around 16 (15 × 0.5 = 7.5; 24 – 7.5 = 16.5).

Metabolic alkalosis:

- Ventilation decreases to retain CO_2.
- The following equation is used to determine if compensation occurred. It computes the PCO_2, which denotes appropriate compensation.

Expected PCO_2 = (0.7 x rise in HCO_3^-) + 40

The patient's PCO_2 should be within 2 (±) of the expected value, but should not exceed 55 mmHg. There are 3 probable conditions:

• If the patient's PCO_2 is within 2, the patient has metabolic alkalosis with respiratory compensation.

• If it is higher than 2, then the patient has metabolic alkalosis and respiratory acidosis.

• If the patient's PCO_2 is too low, then the patient has a metabolic and respiratory alkalosis.

For example, a patient has a metabolic alkalosis with HCO_3^- 34 mEq/L (10 greater than normal) and PCO_2 47 mm Hg. Expected PCO_2 is (10 × 0.7) + 40 = 47 mm Hg, which is what the patient has, thus respiratory compensation is adequate.

Additional important points:

- The body never overcompensates. If it appears that a patient overcompensated for a primary disorder, there is likely a second disorder.
- If CO_2 and HCO_3^- go in opposite directions, there is a combined disturbance – either a combined (mixed) respiratory and metabolic acidosis or a combined (mixed) respiratory and metabolic alkalosis.

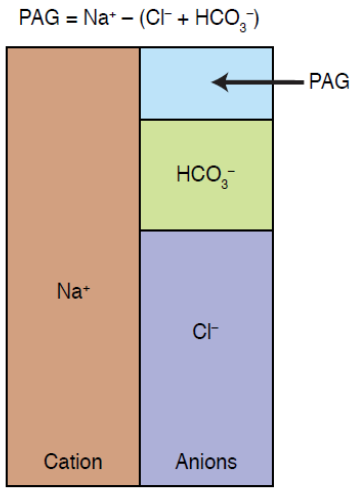
Plasma Anion gap (PAG):

The total cation charges in the plasma are always equal the total anion charges present. However, only major ions are typically measured in a blood sample.

Cations are estimated as the plasma concentration of the major cation, Na+. Anions are estimated as the plasma Cl- and HCO3-.

Unmeasured serum anions = $[Na^+] – ([HCO3^-] + [Cl^-])$(normal = 10–12 mEq/L)

Normal values:
Na+: 140 mEq/L
Cl-: 104 mEq/L
HCO_3^-: 24 mEq/L
PAG: 12 ± 2



Metabolic acidosis occurs secondary to either a loss of HCO_3^- or an excess of H^+. Conditions that lead to metabolic acidosis can be differentiated based on the **anion gap.**

An anion gap greater than the normal range indicates the presence of an unexpected, unmeasured serum anion (eg, lactate in lactic acidosis). In

elevated anion-gap acidosis, the concentration of an unmeasured anion is increased to replace lost $HCO3^{-}$.

In contrast, in normal anion-gap (hyperchloremic) acidosis, the concentration of Cl^{-} is typically increased to replace lost HCO_3^{-} resulting in no change in the anion gap.

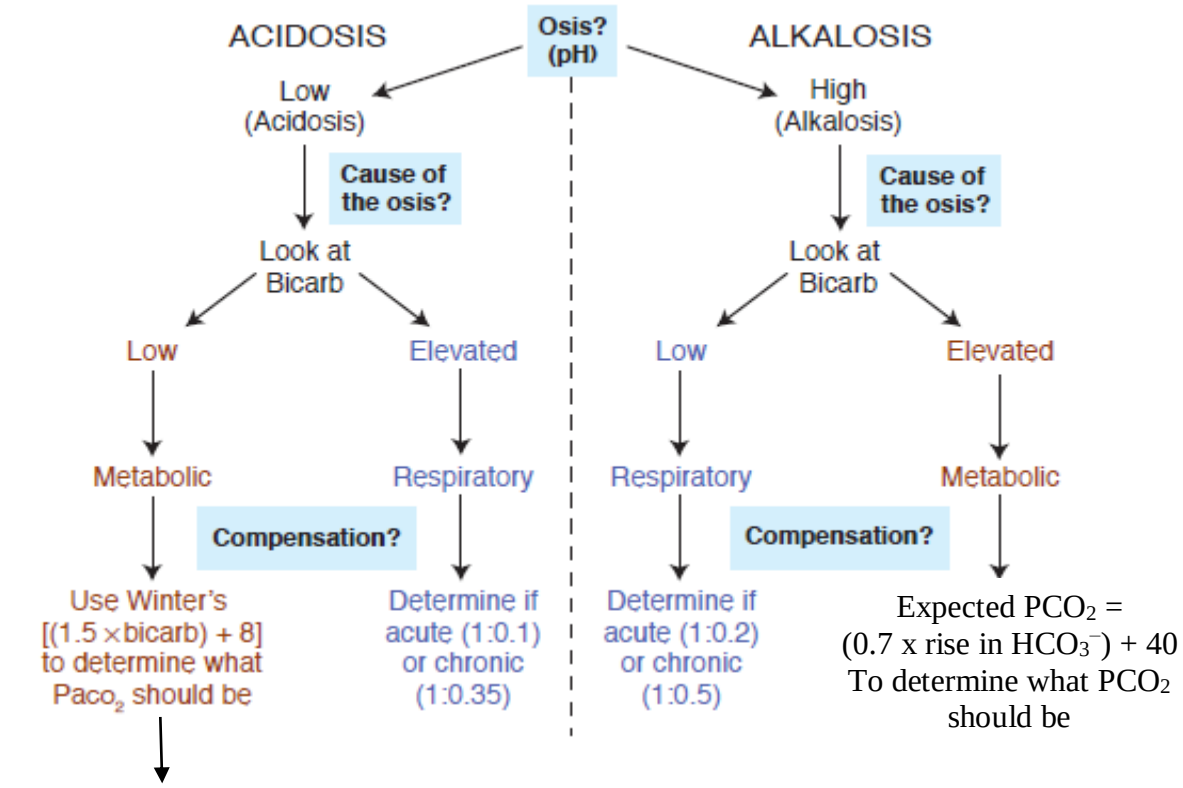
Causes of metabolic acidosis with increased anion gap (>20):

1. Methanol toxicity (formic acid)
2. Uremia
3. Diabetic ketoacidosis
4. Iron tablets or INH
5. Lactic acidosis
6. Salicylates toxicity (late)

Causes of metabolic acidosis with normal anion gap (Hyperchloremic acidosis):

1. Hyperalimentation
2. Addison disease
3. Renal tubular acidosis
4. Diarrhea
5. acetazolamide
6. Spironolactone

A simplified scheme for analyzing an ABG



Example: pH 7.3, HCO3– 14 mEq/L, PCO2 30 mm Hg, PO2 95 mmHg

Answer:
What is the osis? pH is low, so acidosis.
Cause of the osis? HCO3– is low, so metabolic acidosis.
Compensation? Use Winter's to compute predicted PCO2: (14 × 1.5) + 8 = 29. Patient's is 30, which is within 2, thus this is a metabolic acidosis with respiratory compensation.