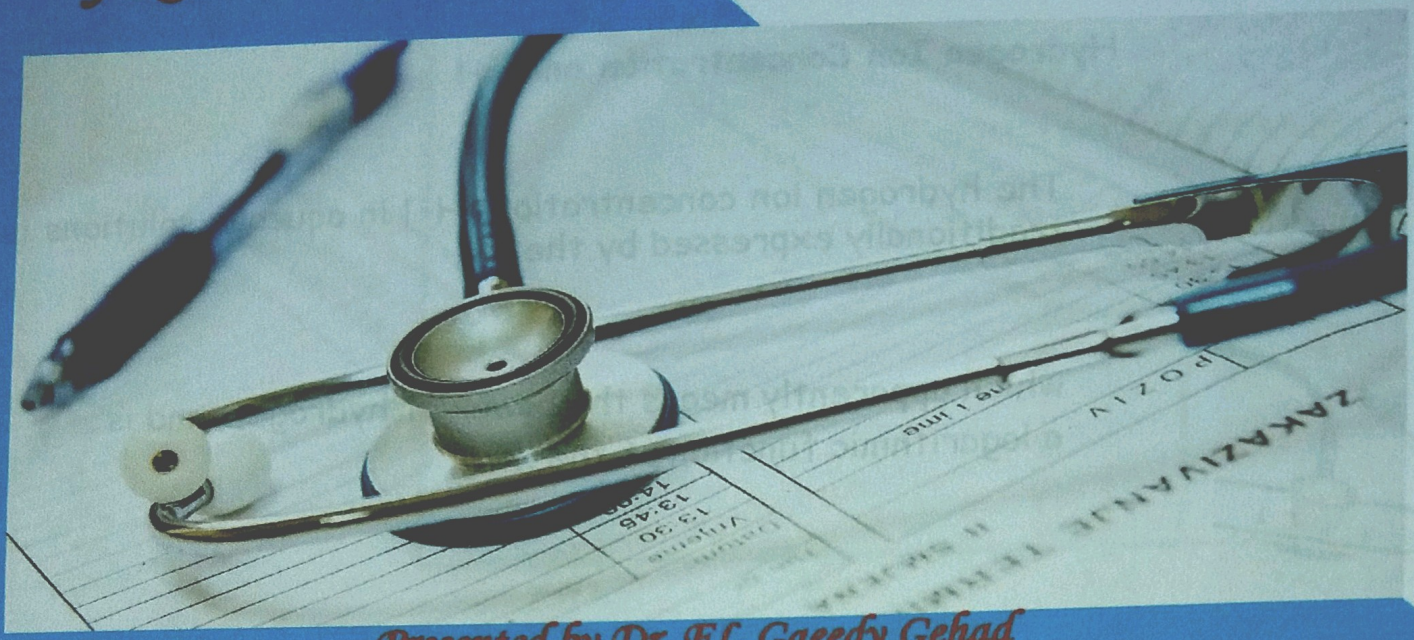
ACID-BASE DISORDERS

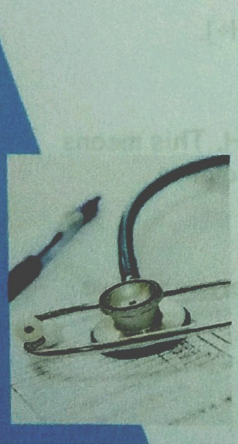
CRITICAL CARE MEDICINE



Presented by Dr. EL Gaeedy Gehad

Life is a struggle,
not against sin,
not against money power...
but against hydrogen ions.

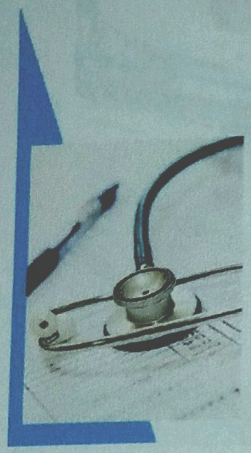
H.L. Mencken



Basic Concepts

Hydrogen Ion Concentration and pH

The hydrogen ion concentration [H+] in aqueous solutions is traditionally expressed by the pH,



which apparently means the power of hydrogen, and is a logarithmic function of the [H+]

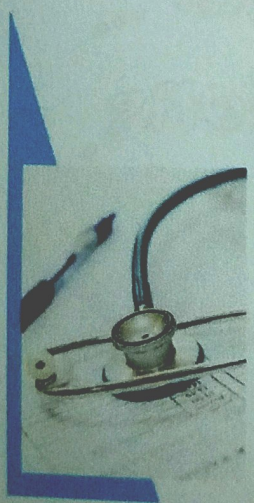
power = potencia
بالإسباني

pH
H+

The normal pH of plasma is indicated as 7.40, which corresponds to a [H+] of 40 nEq/L.

Features of the pH

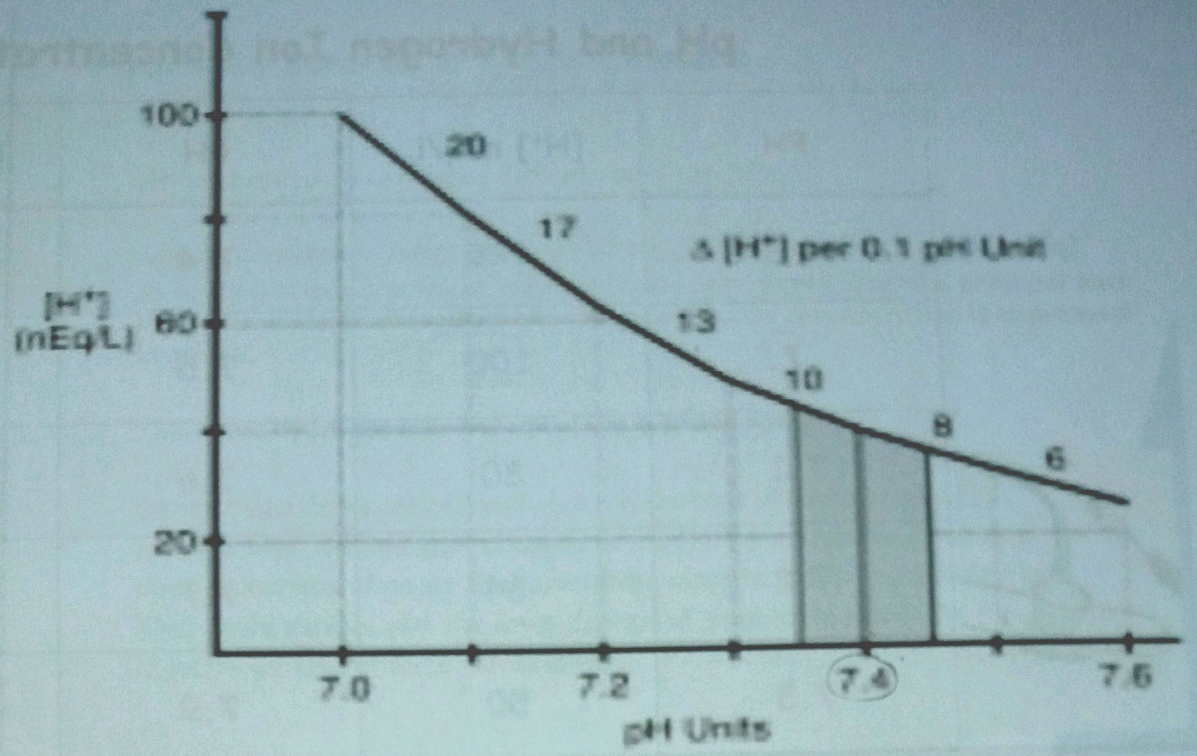
- it is a dimensionless number, which has no relevance in chemical or physiological events,
- it varies in the opposite direction to changes in [H+],
- changes in pH are not linearly related to changes in [H+].
  Note that as the pH decreases,



the changes in [H+] become gradually larger with each change in pH. This means that changes in pH will have different implications for acid-base balance At different points along the pH spectrum.

Although it is unlikely that the pH will be abandoned, it is not a representative measure of the acid-base events in the body.

The relationship between hydrogen ion concentration and pH. (not linear)



Inspection of the curve reveals that,

As the pH decreases from 7.60, the slope of the curve progressively increases, which means there is a progressively larger change in [H+] for a given change in pH.

The numbers above the curve indicate the change in [H+] associated with each change of 0.1 pH units.

At the acidotic end of the curve, the change in [H+] for a given change in pH is more than threefold greater than at the alkalotic end of the curve (20 nEq/L versus 6 nEq/L per 0.1 pH unit, respectively).

pH and Hydrogen Ion Concentration

PH	$[H^+]$ nEq/L	PH	$[H^+]$ nEq/L
6.9	126	7.4	40
7	100	7.5	32
7.1	80	7.6	25
7.2	64	7.7	20
7.3	50	7.9	16

100 يساوي pH 7 و ، (10) يزيد 7.3 إلى 7.4

32 يساوي (8) و يقل ، 7.5 إلى 7.4 يقل

[Non linear relationship].

The Henderson-Hasselbalch equation

The Henderson-Hasselbalch equation describes the relationship of pH as a measure of acidity with the acid dissociation constant (pKa), in biological and chemical systems.

The equation is especially useful for estimating the pH of a buffer solution and finding the equilibrium pH in acid-base reactions.

$$pH = 6.1 + \log (HCO3 / (0.03 \times PCO2))$$

$$= 6.1 + \text{Log} (24/(0.03 \times 40))$$

$$= 6.1 + \text{Log} (24/1.2)$$

$$= 6.1 + \text{Log} (20)$$

$$= 6.1 + 1.3 = 7.4$$

Log 20 = 1.3

Hydrogen Ions as a Trace Element

[H+] is expressed as nanoequivalents per liter (nEq/L).

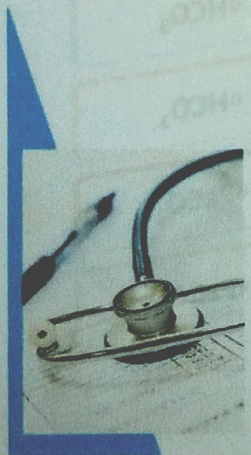
One nanoequivalent is one-millionth of a milliequivalent (1 nEq = 1×10^6 mEq), so hydrogen ions are about a million times less dense than the principal ions in extracellular fluid (sodium and chloride), whose concentration is expressed in mEq/L.



This gives hydrogen ions the status of a trace element.

Other trace elements certainly have important biological effects, but it is also possible that changes in the [H+] are just one of several physicochemical changes that are taking place in the extracellular fluid. This would explain why the same degree of acidosis is more life-threatening in lactic acidosis than in ketoacidosis.

The reference ranges for arterial pH, PCO 2, and HCO3



- PH · 7.36 - 7.44
- $PaCO_2$ · 36-44 mm Hg
- HCO_3 · 22-26 mEq/L

Classification of Acid-Base Disorders

The **[H+]** in extracellular fluid is determined by the balance between the partial pressure of **carbon dioxide (PCO_2)** and the **concentration of Bicarbonate (HCO_3)** in the fluid.

This relationship is expressed as follows

$$[H+] = 24 \times (PaCO_2/HCO_3)$$

The **PCO_2/HCO_3 ratio** identifies the primary acid-base disorders and secondary responses,

Primary Disorder	Primary Change	Secondary Response
Respiratory Acidosis	⇧$PaCO_2$	⇧HCO_3
Respiratory Alkalosis	⇩$PaCO_2$	⇩HCO_3
Metabolic Acidosis	⇩HCO_3	⇩$PaCO_2$
Metabolic Alkalosis	⇧HCO_3	⇩$PaCO_2$

$PaCO_2$
HCO_3 > القيمة/ دائماً لا يزيد واحد عن الثانية

الثاني يزيد زيه، ولما يقل واحد الثاني يقل.

Primary Acid-Base Disorders

A change in either the PCO_2 or the HCO_3 will cause a change in the [H+] of extracellular fluid.



When a **change in PCO_2 is responsible for a change in [H+]**, the condition is called a **respiratory acid-base disorder**:

- increase in PCO_2 is a respiratory acidosis
- decrease in PCO_2 is a respiratory alkalosis.

When a **change in HCO_3 is responsible for a change in [H+]**, the condition is called a **metabolic acid-base disorder**:

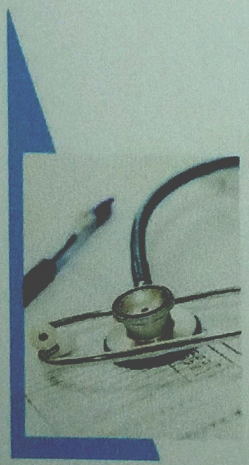
- decrease in HCO_3 is a metabolic acidosis
- increase in HCO_3 is a metabolic alkalosis.

resp. ← PCO_2 السبب المتغير هو

metabolic ← HCO_3 - - - -

Secondary Responses

Secondary responses are designed to limit the change in [H+] produced by the primary acid-base disorder, and this is accomplished by changing the other component of the $PaCO_2/HCO_3$ ratio in the same direction.



✓ **Secondary responses are always in the same direction as the primary change.**

For example, if the primary problem is an increase in $PaCO_2$ (respiratory acidosis), the secondary response will involve an increase in HCO_3, and this will limit the change in [H+] produced by the increase in $PaCO_2$.

Secondary responses should not be called "compensatory responses" because they do not completely correct the change in [H+] produced by the primary acid-base disorder.

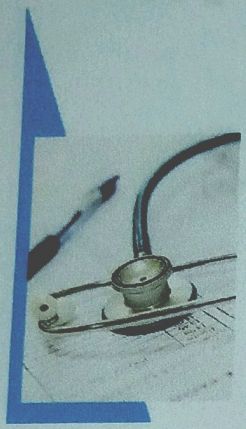
ال 2ry response ما بيعيد الأمور لطبيعي

هو فقط بيكون سبب لجميع ال pathology

Responses to Metabolic Acid-Base Disorders

The response to a metabolic acid-base disorder involves a change in minute ventilation that is mediated by peripheral chemoreceptors located in the carotid body at the carotid bifurcation in the neck.

Metabolic Acidosis



response appears in 30–120 minutes, and can take 12 to 24 hours to complete. The magnitude of the response is defined by the equation.

$$\Delta PaCO_2 = 1.2 \times \Delta HCO_3$$

Using a normal PaCO2 of 40 mm Hg and a normal HCO3 of 24 mEq/L, the above equation can be rewritten as follows:

$$\text{Expected } PaCO_2 = 40 - [1.2 \times (24 - \text{Current } HCO_3)]$$

Example

For a **metabolic acidosis** with a plasma **HCO_3 of 14 mEq/L**, the **HCO_3 is 24 – 14 = 10 mEq/L**, the **$PaCO_2$ is 1.2×10 = 12 mm Hg**, and the

Expected $PaCO_2$ is 40 – 12 = 28 mm Hg.



If the **$PaCO_2$ is >28 mm Hg**, there is a **secondary respiratory acidosis.**

If the **$PaCO_2$ is <28 mm Hg**, there is a **secondary respiratory alkalosis.**

Metabolic Alkalosis

The secondary response to metabolic alkalosis is a decrease in minute ventilation and a subsequent increase in $PaCO_2$.

This response is not as vigorous as the response to metabolic acidosis because the peripheral chemoreceptors are not very active under normal conditions, so they are easier to stimulate than inhibit.



The magnitude of the response to metabolic alkalosis is defined by

$$\Delta PaCO_2 = 0.7 \times \Delta HCO_3$$

Using a normal $PaCO_2$ of 40 mm Hg and a normal HCO_3 of 24 mEq/L, the above equation can be rewritten as follows:

$$\text{Expected } PaCO_2 = 40 + [0.7 \times (\text{Current } HCO_3 - 24)]$$

Example

For a **metabolic alkalosis** with a plasma
HCO_3 of 40 mEq/L,
HCO_3 is 40 – 24 = 16 mEq/L,
$PaCO_2$ is 0.7×16 = 11 mm Hg,

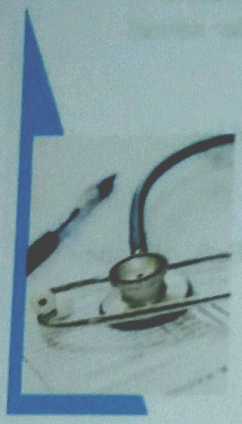


Expected $PaCO_2$ is 40 + 11 = 51 mm Hg.

This is only a borderline elevation in $PaCO_2$, and it demonstrates the relative weakness of the response to metabolic alkalosis.

Responses to Respiratory Acid-Base Disorders

The secondary response to changes in $PaCO_2$ occurs in the kidneys, where HCO_3 absorption in the proximal tubes is adjusted to produce the appropriate change in plasma HCO_3.



This renal response is relatively slow, and can take 2 or 3 days to reach completion.

Because of the delay in the secondary response, respiratory acid-base disorders are separated into acute and chronic disorders.

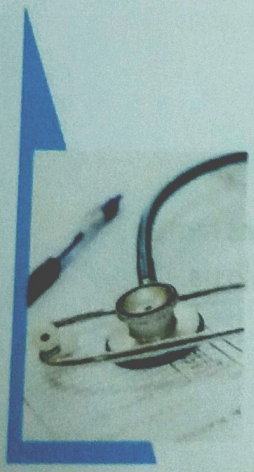
Acute Respiratory Disorders

Acute changes in $PaCO_2$ have a small effect on the plasma HCO_3, as indicated in the following two equations.

For acute respiratory acidosis:

$$\Delta HCO_3 = 0.1 \times \Delta PaCO_2$$

Expected HCO3 = 24 + [0.1 x (Current PaCO2 - 40)]



For acute respiratory alkalosis:

$$\Delta HCO_3 = 0.2 \times \Delta PaCO_2$$

Expected HCO3 = 24 - [0.2 x (40 -Current PaCO2)]

Example

For an acute increase in $PaCO_2$ to 60 mm Hg.

HCO_3 is 0.1 × 20 = 2 mEq/L for an acute respiratory acidosis

HCO_3 is 0.2×20 = 4 mEq/L for an acute respiratory alkalosis.

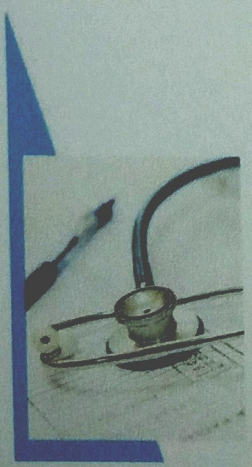


Neither of these changes would be recognized as significant.

Chronic Respiratory Disorders

The renal response to an increase in $PaCO_2$ is an increase in HCO_3 reabsorption in the proximal renal tubules, which raises the plasma HCO_3 concentration.

The response to a decrease in $PaCO_2$ is a decrease in renal HCO_3 reabsorption, which lowers the plasma HCO_3 concentration.



The magnitude of this response is similar, regardless of the directional change in $PaCO_2$,

so the equation below applies to both chronic respiratory acidosis and alkalosis.

$$\Delta HCO_3 = 0.4 \times \Delta PaCO_2$$

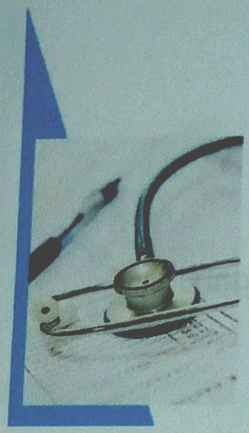
Using a normal $PaCO_2$ of 40 mm Hg and a normal HCO_3 of 24 mEq/L, the above equation can be rewritten as follows:

For chronic respiratory acidosis:

$$\text{Expected } HCO_3 = 24 + [0.4 \times (\text{Current } PaCO_2 - 40)]$$

For chronic respiratory alkalosis:

$$\text{Expected } HCO_3 = 24 - [0.4 \times (40 - \text{Current } PaCO_2)]$$



Example

For an increase in $PaCO_2$ to 60 mm Hg that persists for at least a few days,

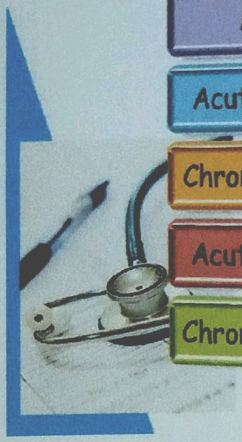
$PaCO_2$ is 60 – 40 = 20 mm Hg,
HCO_3 is 0.4×20 = 8 mEq/L,

the expected HCO_3 is 24 + 8 = 32 mEq/L.



Predictive equations for evaluating secondary responses to primary ABD

Primary Disorder	• Secondary Response
Metabolic Acidosis	• Expected $PaCO_2 = 40 - [1.2 \times (24 - \text{Current } HCO_3)]$
Metabolic Alkalosis	• Expected $PaCO_2 = 40 + [0.7 \times (\text{Current } HCO_3 - 24)]$
Acute Respiratory Acidosis	• Expected $HCO_3 = 24 + [0.1 \times (\text{Current } PaCO_2 - 40)]$
Chronic Respiratory Acidosis	• Expected $HCO_3 = 24 + [0.4 \times (\text{Current } PaCO_2 - 40)]$
Acute Respiratory Alkalosis	• Expected $HCO_3 = 24 - [0.2 \times (40 - \text{Current } PaCO_2)]$
Chronic Respiratory Alkalosis	• Expected $HCO_3 = 24 - [0.4 \times (40 - \text{Current } PaCO_2)]$



Stepwise Approach to Acid-base Analysis

Stage I: Identify the Primary Acid-Base Disorder

The **$PaCO_2$**
and
pH

are used to identify the

primary acid-base disorder.



Rule 1



If the $PaCO_2$

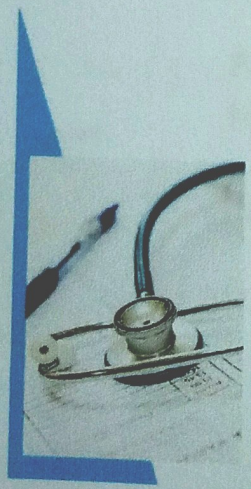
and/or the

pH

is outside the normal range,

there is an acid-base disorder.

Rule 2



If the $PaCO_2$

and

pH

are both abnormal,

compare the directional change.

Rule 2a.



If the $PaCO_2$
and
pH

change in the same direction,

there is a primary metabolic acid-base disorder.

Rule 2b.



If the $PaCO_2$
and
pH

change in opposite directions,

there is a primary respiratory acid-base disorder.

Example

Consider a case where the
↓ arterial **pH = 7.23** and the
↓ **$PaCO_2$ = 23** mm Hg.

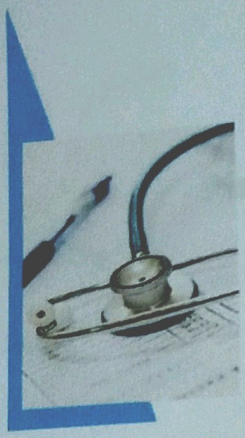
The **pH** and **$PaCO_2$** **are both reduced** indicating a

primary metabolic disorder and

the **pH is low** indicating an

acidosis,

so the diagnosis is a **primary metabolic acidosis.**



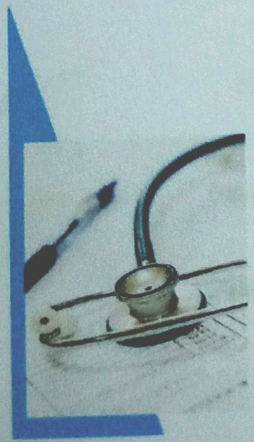
Rule 3

If only the **pH**
or
$PaCO_2$ is abnormal,

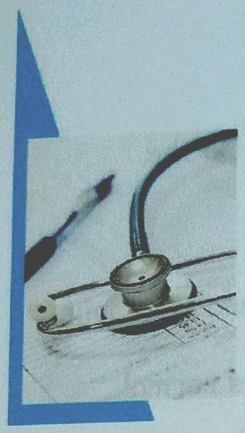
the condition is a

mixed metabolic and respiratory disorder

(i.e., equal and opposite disorders).



Rule 3a.



If the $PaCO_2$

is abnormal,

the directional change in $PaCO_2$

identifies the type of respiratory disorder

(e.g., high $PaCO_2$ indicates a respiratory acidosis),

and the opposing metabolic disorder.

Rule 3b.



If the pH

is abnormal,

the directional change in pH

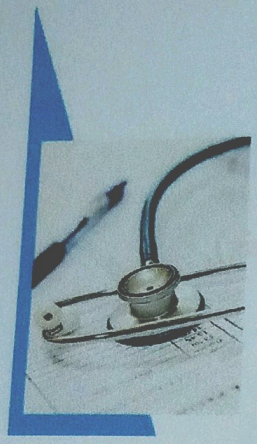
identifies the type of metabolic disorder

(e.g., low pH indicates a metabolic acidosis) and

the opposing respiratory disorder.

Example

Consider a case where the arterial **pH = 7.38** and the **$PaCO_2$ = 55** mm Hg.



Only the **$PaCO_2$ is abnormal**, so there is **a mixed metabolic and respiratory disorder.**

The **$PaCO_2$ is elevated, indicating a respiratory acidosis**, so the **metabolic disorder must be a metabolic alkalosis.**

Therefore, this condition is a mixed respiratory acidosis and metabolic alkalosis.
Both disorders are equivalent in severity because the pH is normal.

Stage II: Evaluate the Secondary Responses



The second stage of the approach is for cases where a primary acid-base disorder has been identified in Stage I.

If a mixed acid-base disorder was identified in Stage I, go directly to Stage III.

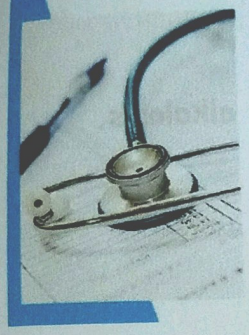
The goal in Stage II is to determine if there is an additional acid-base disorder.

Rule 4

For a **primary metabolic disorder**,

if the measured $PaCO_2$ is higher than expected,

there is a secondary respiratory acidosis,



and

if the measured $PaCO_2$ is less than expected,

there is a secondary respiratory alkalosis.

Example

Consider a case where the
$PaCO_2$ = 23 mm Hg, the
pH = 7.32, and the
HCO_3 = 16 mEq/L.

The **pH** and **PCO_2 change in the same direction**, indicating a

primary metabolic disorder,and the

pH is acidemic, so



the disorder is a **primary metabolic acidosis**.

The $PaCO_2$ is $1.2\times(24 - 16) = 10$ mm Hg (rounded off),

the expected $PaCO_2$ is 40 - 10 = 30 mm Hg.

The **measured $PaCO_2$** (23 mm Hg) is **lower than the expected $PaCO_2$**,

so there is an **additional respiratory alkalosis**.



Therefore, this condition is a

primary metabolic acidosis with a secondary respiratory alkalosis.

Rule 5

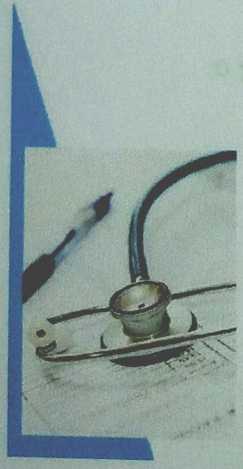
For a

primary respiratory disorder,

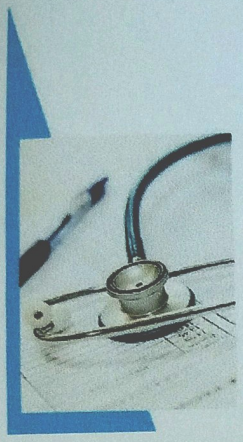
a normal or near-normal HCO_3

indicates that

the **disorder is acute.**



Rule 6



For a

primary respiratory disorder

where the **HCO_3 is abnormal**,

determine

the **expected HCO_3 for a chronic respiratory disorder.**

Rule 6a.



For a

chronic respiratory acidosis,

if the **HCO_3 is lower than expected**,

there is an **incomplete renal response**, and

if the **HCO_3 is higher than expected**,

there is a **secondary metabolic alkalosis.**

Rule 6b.



For a

chronic respiratory alkalosis,

if the **HCO_3 is higher than expected,**

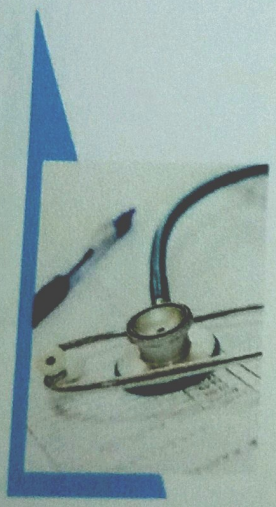
there is an **incomplete renal response**, and

if the **HCO_3 is lower than expected,**

there is a **secondary metabolic acidosis.**

Example

Consider a case where the
$PaCO_2$ = 23 mm Hg, the
pH = 7.54, and the
HCO_3 = 17 mEq/L.



The **$PaCO_2$** and **pH change in opposite directions**, indicating a

primary respiratory disorder, and the

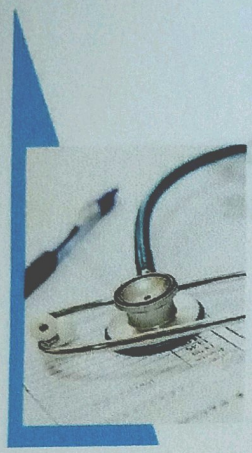
pH is alkaline,

so the disorder is a

primary respiratory alkalosis.

The HCO_3 is abnormal, indicating that this is not an acute respiratory alkalosis.

The PCO_2 is 40 – 23 = 17 mm Hg,
the HCO_3 is 0.4 × 17 = 7 mEq/L,
And the expected HCO_3 is 24 - 7 = 17 mEq/L.



The measured HCO_3 is the **same as expected** for

chronic respiratory alkalosis,

so this condition is a

chronic respiratory alkalosis
with an appropriate (completed) renal response.

If the measured HCO_3 was less than 17 mEq/L,

this condition would be a

chronic respiratory alkalosis
with a secondary metabolic acidosis, and



if the measured HCO_3 was higher than 17 mEq/L,

this would indicate an

incomplete renal response.

Stage III: Use The "Gaps" to Evaluate a Metabolic Acidosis

The final stage of this approach is for patients with a metabolic acidosis,



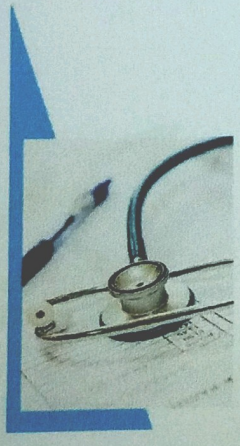
Where the use of gaps can help to uncover the underlying cause of the acidosis.

The Gaps

The Anion Gap

The anion gap is a rough estimate of the relative abundance of unmeasured anions.

Used to determine if a metabolic acidosis is due to an accumulation of non-volatile acids (lactic acid) or a primary loss of bicarbonate (diarrhea).



Determinants

To achieve electrochemical balance, the concentration of negatively charged anions must equal the concentration of positively charged cations.

This electrochemical balance is expressed in the equation using electrolytes that are routinely measured, including Na, CL, and HCO_3, as well as the unmeasured cations (UC) and unmeasured anions (UA).

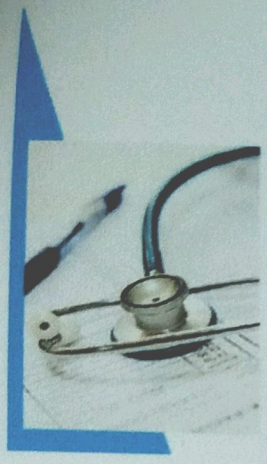
$$Na+UC = (Cl+HCO_3)+UA$$

Rearranging the terms in this equation yields the following relationships:

$$Na-(Cl+HCO_3) = UA-UC$$

The difference (UA - UC) is a measure of the relative abundance of unmeasured anions, and is called the anion gap (AG).

$$AG = Na-(Cl+HCO_3)$$



Reference Range:

The original reference range for the **AG** was **12±4 mEq/L** (8 to 16 mEq/L).

With subsequent improvements in automated systems that measure serum electrolytes, the reference range for the AG has decreased to 7±4 mEq/L (range = 3 to 11 mEq/L).

Influence of Albumin

Albumin is the principal unmeasured anion, and the principal determinant of the anion gap.

Albumin is a weak acid that contributes about 3 mEq/L to the AG for each 1 g/dL of albumin in plasma (at a normal pH).

A low albumin level in plasma will lower the AG, and this could mask the presence of an unmeasured anion (e.g., lactate) that is contributing to a metabolic acidosis.



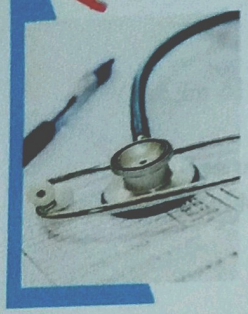
Since hypoalbuminemia is present in as many as 90% of ICU patients, the corrected AG" (AGc) to include the contribution of albumin:

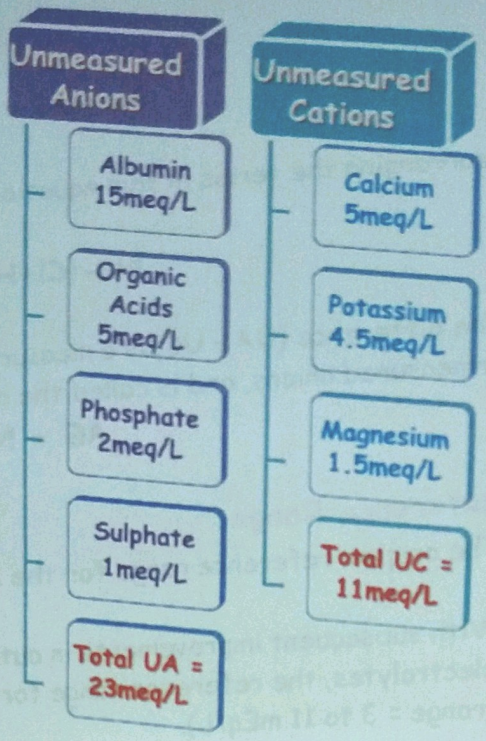
$$AGc = AG + (2.5 \times (4.5 - [\text{Albumin in g/dL}])$$

(4.5 represents the normal concentration of albumin in plasma).

For a patient with an AG of 10 mEq/L and a plasma albumin of 2 g/dL, the AGc is 10 + (2.5×2.5) = 16 mEq/L, which represents a 60% increase in the AG.

AG = UA - UC = 12 meq/L





Using the Anion Gap

The AG can be used to identify the underlying mechanism of a metabolic acidosis



Helps to identify the underlying clinical condition

Elevated AG



occurs when there is an accumulation of fixed or non-volatile acids (e.g., lactic acidosis),

There is loss of H+ secretion in the distal tubules of the kidneys.

Also included are toxic ingestions of
- Methanol (which produces formic acid),
- Ethylene glycol (which produces oxalic acid),
- Salicylates (which produce salicylic acid).

Normal AG



occurs when there is a primary loss of bicarbonate (e.g., diarrhea).

There is loss of bicarbonate reabsorption in the proximal tubules.

The loss of HCO_3 is counter balanced by a gain of chloride ions to maintain electrical charge neutrality; hence the term hyperchloremic metabolic acidosis is used for normal AG metabolic acidosis.

NB)

In high AG metabolic acidosis, the remaining anions from the dissociated acids balance the loss of HCO3, so there is no associated hyperchloremia.



High AG

- Lactic Acidosis
- Ketoacidosis
- ESRD
- Methanol Ingestion
- Ethylene Glycol Ingestion
- Salicylate Toxicity

Normal AG

- Diarrhea
- Isotonic Saline Infusion
- Early Renal Insufficiency
- Renal Tubular Acidosis
- Acetazolamide
- Ureteroenterostomy



Reliability

The AG has shown a limited ability to detect non-volatile acids, and there are several reports where the AG was normal in patients with lactic acidosis.

The poor performance of the AG may be due to the confounding influence of albumin, which was not considered in early studies of the AG.

Recent study shows that the albumin-corrected AG (AGc) provides a more accurate assessment of metabolic acidosis than the AG.

The Gap-Gap Ratio



In the presence of a high AG metabolic acidosis, it is possible to detect another metabolic acid-base disorder (a normal AG metabolic acidosis or a metabolic alkalosis)

$$\text{AG Excess/HCO}_3\text{ Deficit} = (\text{AG} - 12)/24 - \text{HCO}_3)$$

This ratio is sometimes called the gap-gap ratio because it involves two gaps (the AG excess and the HCO_3 deficit).

Mixed Metabolic Acidoses



In metabolic acidosis caused by non-volatile acids (high AG metabolic acidosis), the **decrease in serum HCO_3** is **equivalent to** the **increase in AG**, and the **gap-gap** (AG Excess/HCO_3 deficit) **ratio is unity or 1.**

However,
if there is a second acidosis that has a normal AG, the **decrease in HCO_3 is greater than the increase in AG,**
and the **gap-gap ratio falls below unity (<1).**

Therefore,
in the presence of a **high AG metabolic acidosis**, a **gap-gap ratio <1** indicates the **co-existence of a normal AG (hyperchloremic) Metabolic acidosis.**

Diabetic Ketoacidosis

A patient with diabetic ketoacidosis (DKA) is associated with improvement in the blood glucose and the clinical condition of the patient, but the acidosis persists, and you are asked what to do (more insulin, more fluids, etc).

The answer lies in the gap-gap ratio; i.e., DKA presents with a high AG metabolic acidosis, but the aggressive infusion of isotonic saline during the initial management creates a hyperchloremic (normal AG) metabolic acidosis, which replaces the high AG acidosis as the ketoacids are cleared.



In this situation,
the serum bicarbonate remains low, but the gap-gap ratio falls below 1 as the acidosis switches from a high AG to a normal AG acidosis.
Therefore, monitoring the serum HCO_3 alone will create a false impression that the DKA is not resolving, while the gap-gap ratio provides an accurate measure of the acid-base status of the patient.

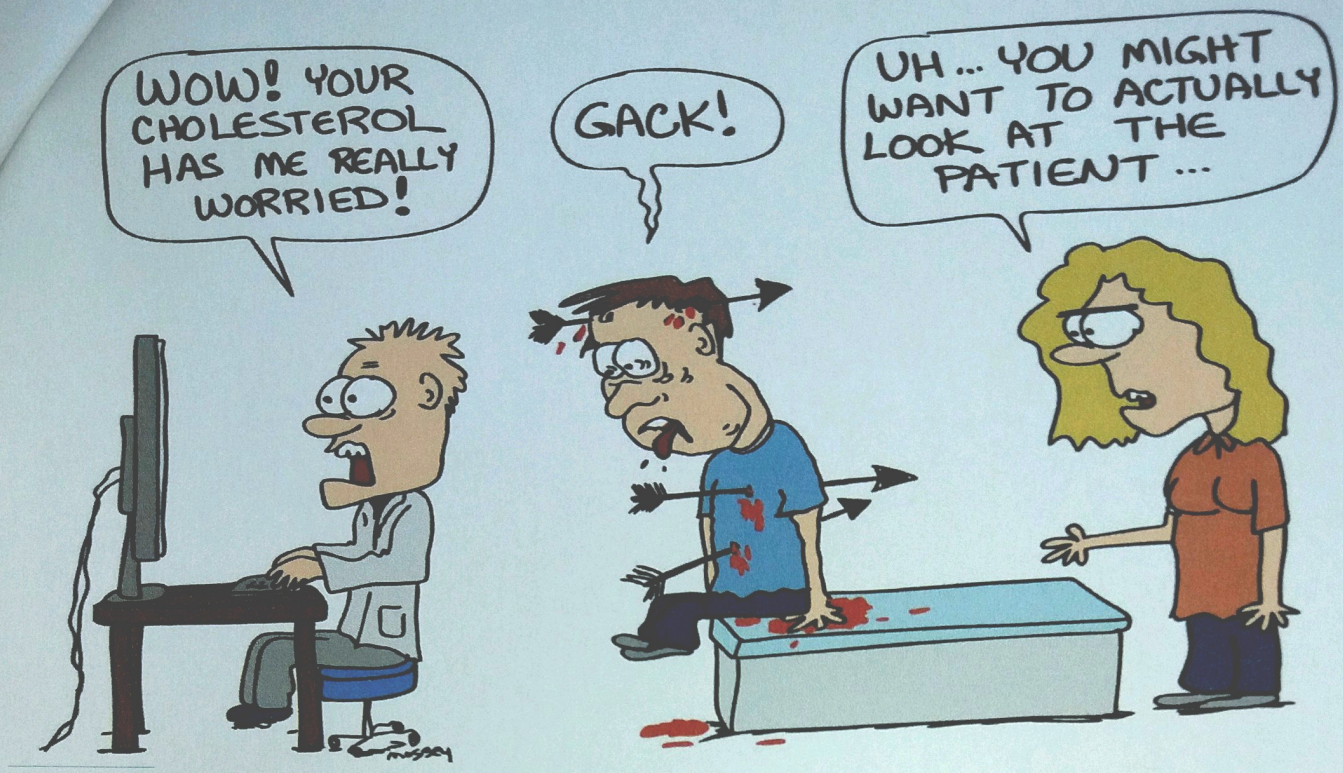
Metabolic Acidosis and Alkalosis

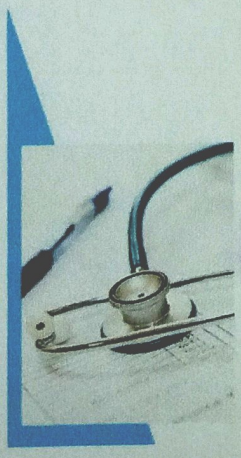
When alkali is added in the **presence of a high AG acidosis**, the **decrease in serum bicarbonate** **is less than the increase in AG**, and the **gap-gap is greater than unity (>1).**



Therefore,
in the presence of a **high AG metabolic acidosis**, a **gap-gap >1** indicate s the **co-existence of a metabolic alkalosis.**

This is an important consideration because metabolic alkalosis is common in ICU patients (from the frequent use of nasogastric suction and diuretics).


WOW! YOUR CHOLESTEROL HAS ME REALLY WORRIED!
GACK!
UH... YOU MIGHT WANT TO ACTUALLY LOOK AT THE PATIENT...



Thank you