General Physiology 2024

Lecture 33&34

Acid Base Balance

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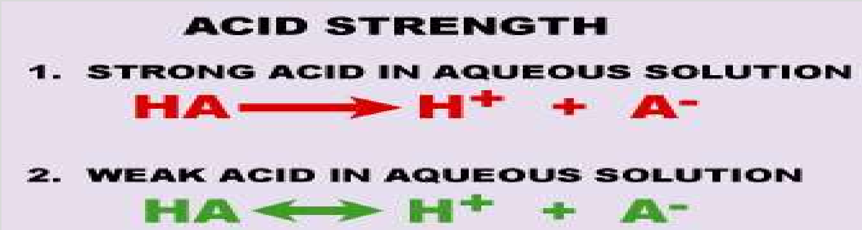
OBJECTIVES

- Define acids, bases, and buffers.
- Define fixed and volatile acid
- List the major sources of H ions in the body
- State the normal ranges of arterial pH, PCO2, and bicarbonate concentration.
- List the buffer systems in the ECF and ICF and outline their function
- Define alkalosis and acidosis
- Define alkalosis, acidosis, alkalemia and acidemia
- List the potential causes of respiratory acidosis and alkalosis and metabolic acidosis and alkalosis.
- Discuss the respiratory mechanisms that help compensate for acidosis and alkalosis.
- Discuss the renal mechanisms that help compensate for acidosis and alkalosis.

Evaluate blood gas data to determine acid-base status.

Acid: a molecule that contributes H+ to solution.

-May be strong or weak according to degree of dissociation.



Base : a molecule that combines with H+ to remove them from solution.

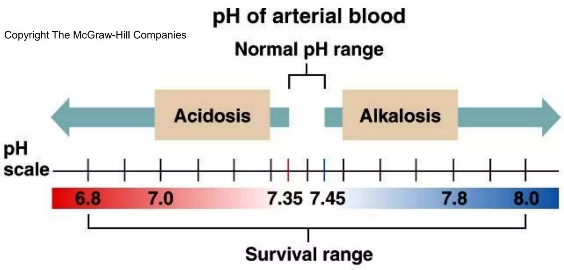
-It may be strong or weak

At equilibrium, the rate of dissociation of an acid to form $H^+ + A^-$ and the rate of association of H^+ and base A^- to form HA are equal. The equilibrium constant (K_a), which is also called the *ionization constant* or **acid dissociation constant,** is given by the expression:

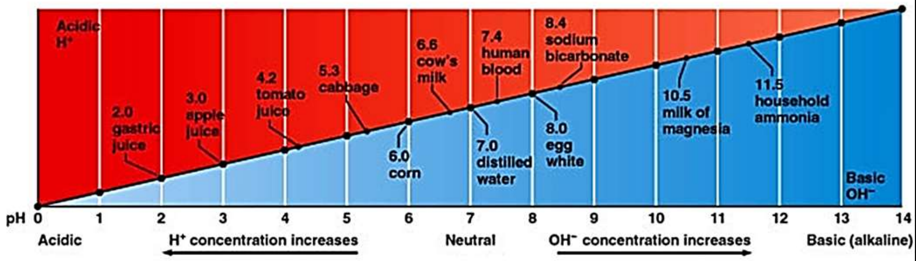
$$K_a = \frac{[H^+]\times[A^-]}{[HA]}$$

The higher the acid dissociation constant, the more an acid is ionized and the greater is its strength. Hydrochloric acid (HCl), for example, is a **strong acid**. It has a high K_a and is almost completely ionized in aqueous solutions. Other strong acids include sulfuric acid (H_2SO_4), phosphoric acid (H_3PO_4), and nitric acid (HNO_3).

An acid with a low K_a is a **weak acid**. For example, in a 0.1 M solution of acetic acid ($K_a = 1.8 \times 10^{-5}$) in water, most (99%) of the acid is nonionized, so that little (1%) is present as acetate$^-$ and H^+. The acidity (concentration of free H^+) of this solution is low. Other weak acids are lactic acid, carbonic acid (H_2CO_3), ammonium ion (NH_4^+), and dihydrogen phosphate ($H_2PO_4^-$).



pH = 7.35-7.45



***Free H+ concentration in ECF is very low (0.00004mmol/L).**
***The H+ concentration should be kept constant to keep the normal activity of many enzymes.**
***H+ concentration is kept constant by a <u>balance between gain and output.</u>**

<u>PH:</u> the H+ concentration is expressed by PH which is minus log to base 10 of H+ concentration

***pH= $-\log_{10}[H+]$**
pH of ECF = $-\log_{10} 0.00004 = 7.4$
***Life is compatible with narrow range of pH between 7.35-7.45.**
***Death occurs if pH<6.8 or > 8.0**

- *An **acid base disorder** is a change in the normal value of extracellular pH that may result when renal or respiratory function is abnormal or when an acid or base load overwhelms excretory capacity.*
- **Normal acid base values**

	pH	**pCO2**	**HCO_3^-**
Range	7.35- 7.45	36-44	22-26
Optimal Value	7.4	40	24

Acidemia: pH < 7.38
Alkalemia: pH > 7.42

Acidosis: process that decreases pH
Alkalosis: process that raises pH

Sources of H+

1-Ingested :

some free H+ in the food we eat.

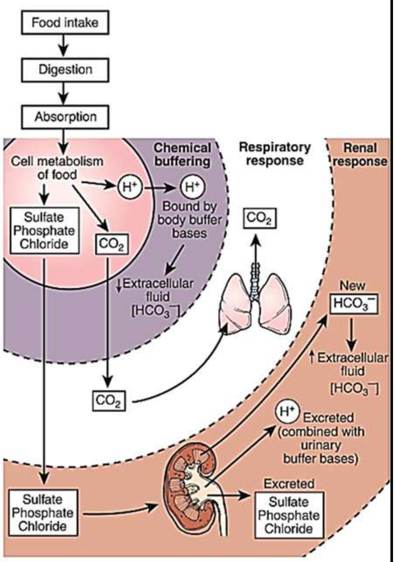
2-Metabolism of food:

a) Carbohydrate metabolism.

b) Proteins and lipid metabolism.

c) Lactic acid from muscles.

d) Ketoacids.



- Oxygen in the cell combines with carbohydrates to form energy and leads to generation of CO_2 and H_2O.
- The CO_2 and H_2O diffuse into the RBCs that supplied the oxygen. In presence of carbonic anhydrase (CA) the CO_2 and H_2O are reversibly converted to H^+ and HCO_3^-.

$$H_2O + CO_2 \xrightarrow{CA} H_2CO_3^+ \longrightarrow H^+ + HCO3^-$$

b) *Metabolism of proteins and lipids:* Many proteins and lipids contain sulphate and phosphate which are metabolized to H2S04 and H_3P04 (fixed acids). About 40 - 60 mmol of fixed acids may be produced from protein metabolism each day.

c) *Lactic acid accumulation in the muscle and ECF* when inadequate supplies of O_2 are delivered to muscle as in severe muscular exercise.

d) Ketoacids (aceto-acetic and β-hydroxy buteric acid) are produced when there is increased metabolism of fat with lack of insulin in diabetes mellitus.

Volatile acids (20,000 mEq/kg/day)

- Produced by oxidative metabolism of CHO, fat, protein.
- Excreted through the LUNGS as CO_2.

Fixed acids (1 mEq/kg/day)

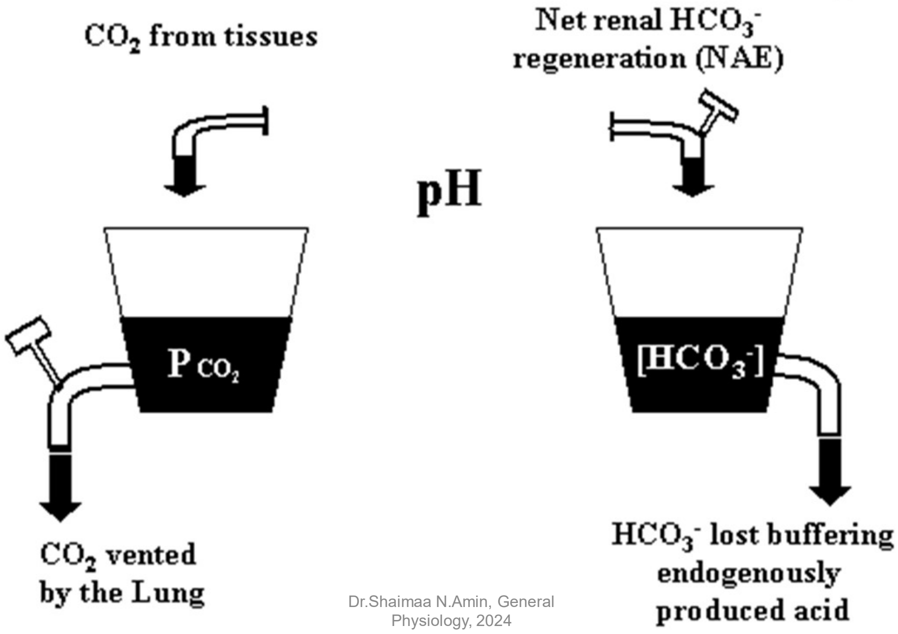
- Remain in body fluids until eliminated in the KIDNEYS.
- Examples: sulfuric, phosphoric, organic acids

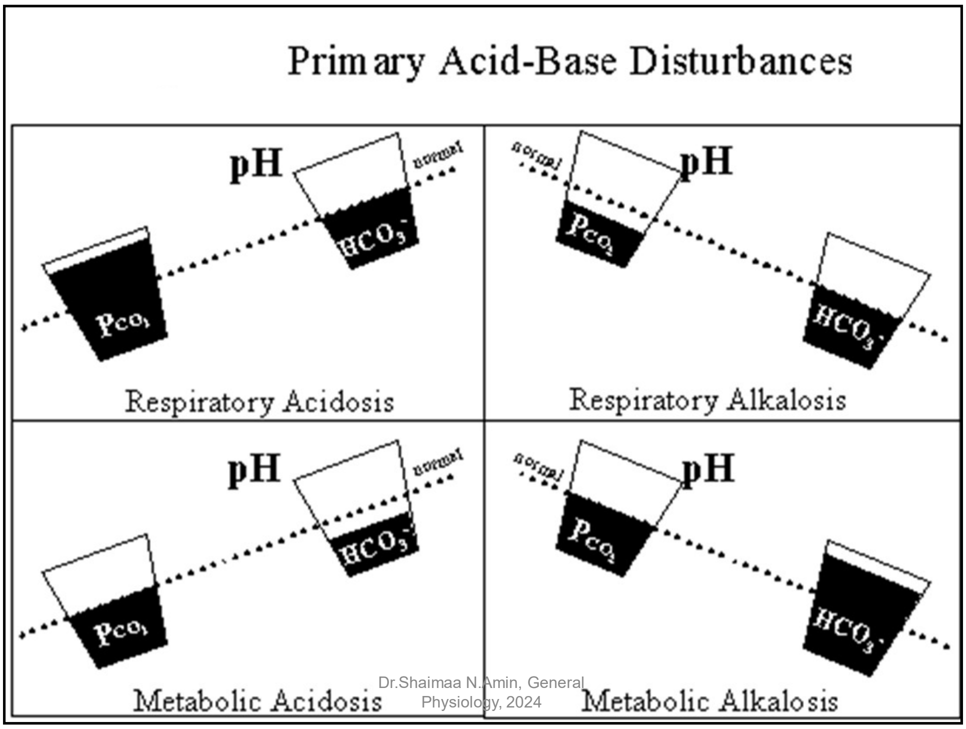
Acid base disorder

- ***Clinical disturbances of acid base metabolism classically are defined in terms of the HCO3- /CO2 buffer system.***
- **Acidosis –** process that increases [H+] by increasing PCO2 or by reducing [HCO3-]
  decrease in the blood pH below normal range

- **Alkalosis –** process that reduces [H+] by reducing PCO2 or by increasing [HCO3-]
  Elevation in blood pH above the normal range

Acid-Base Homeostasis-Concept





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***Acid-base disturbances caused primarily by one system results in compensation by the complementatory system**

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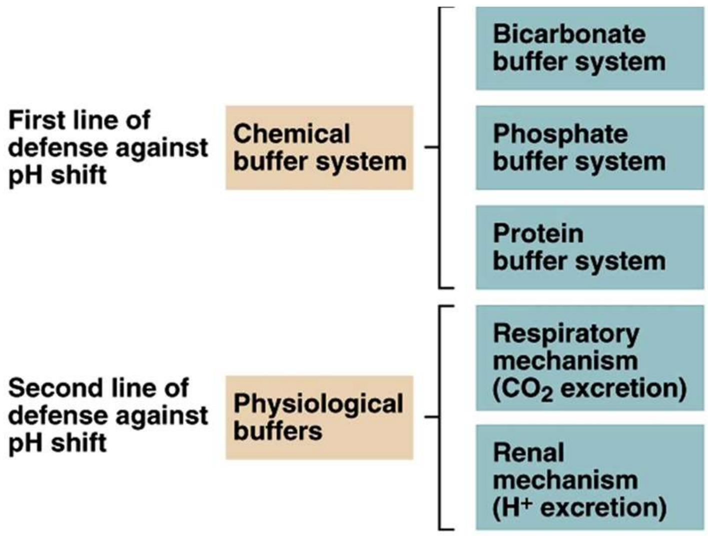
Regulation of Acid-Base imbalance



Buffer systems

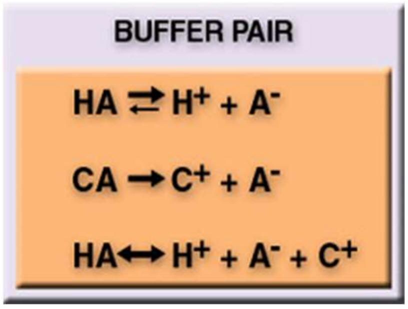
Buffer systems

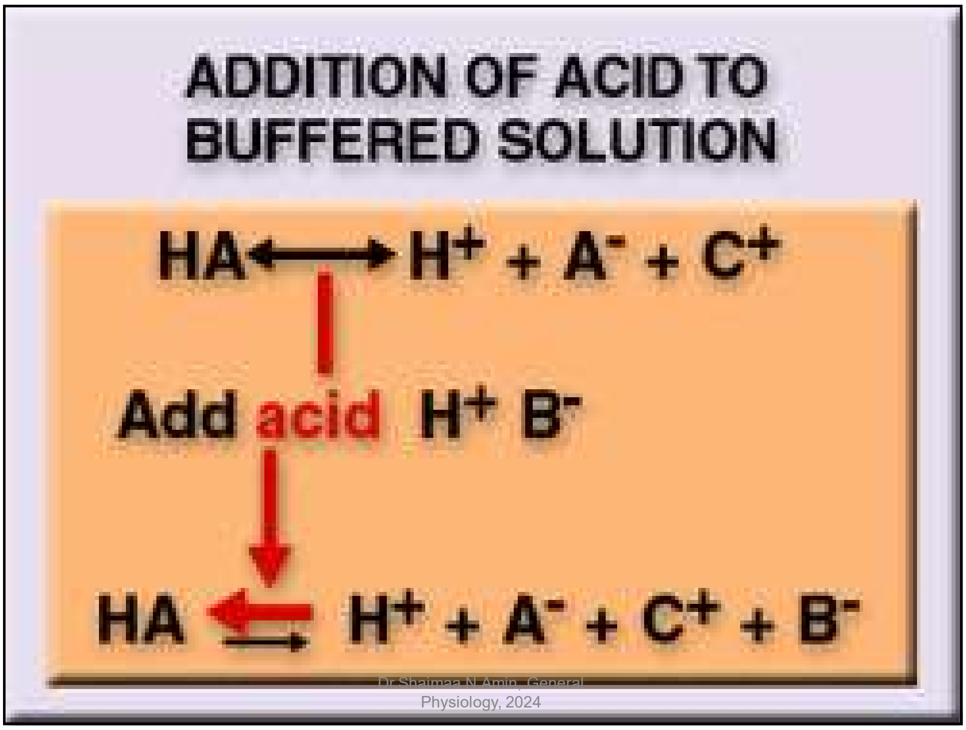
A buffer is a molecule that combines with or releases H+

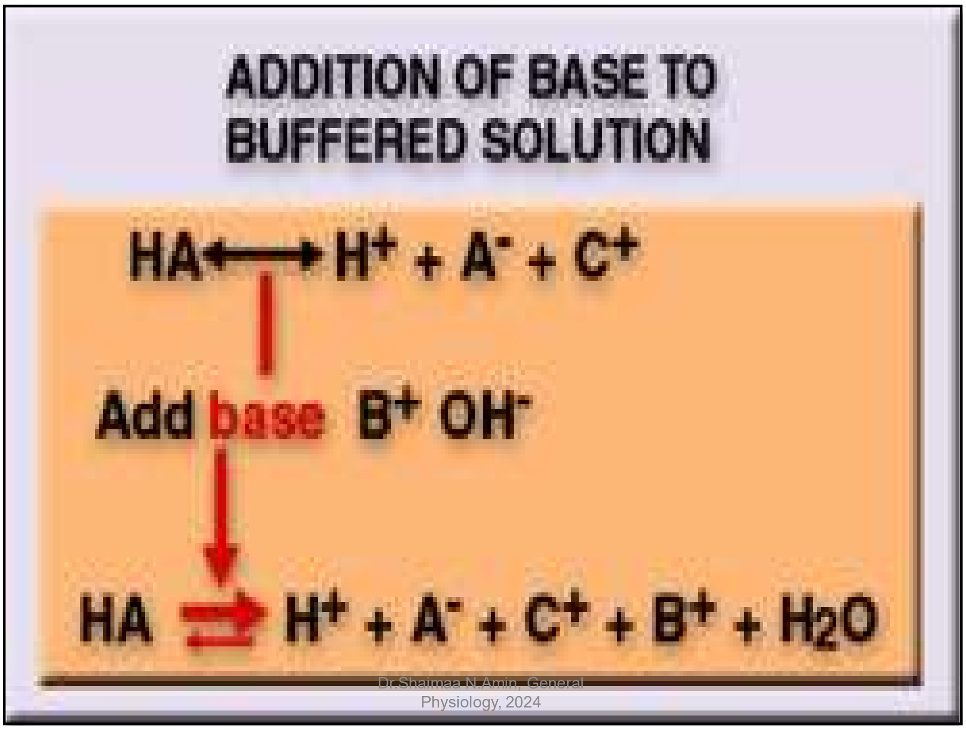
<u>It is composed of</u>

weak acid+ salt of its conjugate base.

*There are many buffers in the body the combination of all determine the free H+ concentration.







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Role of buffers in regulation of acid base balance

- They act immediately to trap H+ until respiratory and renal mechanisms act
- They only minimize the change in H+ concentration.

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Types of buffer systems

1- Bicarbonate buffer system

2-Phosphate buffer system

3-Protien buffer system:

a) Plasma proteins

b) Hemoglobin

C)Tissue proteins

Handerson-Hasselbalch equation

pH of a buffer = pK + $\log_{10}$ [Salt/acid]

pK = dissociation constant.

The effectiveness of the buffer depends on:

1-Amount of buffer pairs.

2-pK of the buffer system.

*The nearer the pK to pH of ECF the more the buffer is effective.

DISSOCIATION CONSTANT

$$K_A = \frac{[H^+][A^-]}{[HA]}$$

pK_A = The negative logarithm of K_A

Some examples of K_A and pK_A of acids of interest

Acid	K_A	pK_A
H_3PO_4	7.52×10^{-3}	2.12
$H_2PO_4^-$	6.23×10^{-8}	7.21
$HPO_4^=$	2.20×10^{-13}	12.67
H_2CO_3	4.30×10^{-7}	6.37
HCO_3^-	5.61×10^{-11}	10.65

Bicarbonate buffer system

$H_2CO_3/BHCO_3$ (B = Na+ or K+)

Physiological importanceof bicarbonate buffer:

1-Its components can be controlled

HCO_3^- regulated by the kidney.

H_2CO_3 regulated by the lung.

2-Its pK 6.1 is far from PH of the blood.

3-Its amount is not large (24mmol/L)

Physiological importanceof bicarbonate buffer:

1-Its components can be controlled: HCO_3^- regulated by the kidney. H_2CO_3 regulated by the lung.

2-Its pK 6.1 is far from PH of the blood.

3-Its amount is not large (24mmol/L)

4-Changes in PH that result from alternation in either HCO-3 concentration or PCO2 can be corrected by changing the other variable to preserve the buffer ratio

5-Factors affecting HCO-3 concentration →metabolic acidosis or alkalosis.

Factors affecting PCO2 →Respiratory acidosis or alkalosis.

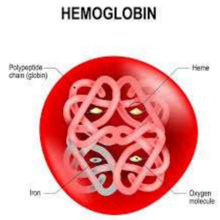
EXTRACELLULAR BUFFERING;
CO_2 - HCO_3^- SYSTEM

$$\underset{1.2}{CO_2} + H_2O \overset{CA}{\longleftrightarrow} \underset{0.0012}{H_2CO_3} \longleftrightarrow \underset{0.00004}{H^+} + \underset{24.0\ mM}{HCO_3^-}$$

$$pH = pK_A + \log \frac{[HCO_3^-]}{\alpha\ P_{aCO_2}}$$

$$pH = 6.1 + \log \frac{24.0}{0.03 \times 40} = 7.40$$

$$pH = pK_A + \log \frac{KIDNEY}{LUNG}$$



Hemoglobin Buffer

Physiological importance:

1-Play an important role in buffering CO_2.

2-High buffering capacity: it has 6 times the buffering capacity of all plasma proteins.

Phosphate Buffer

*It is a mixture of basic phosphate HPO_4^- and acid phosphate $H_2PO_4^-$

***Physiologic importance:**

1) It is not strong buffer extracellulay as its concentration is low(1mmol/L).

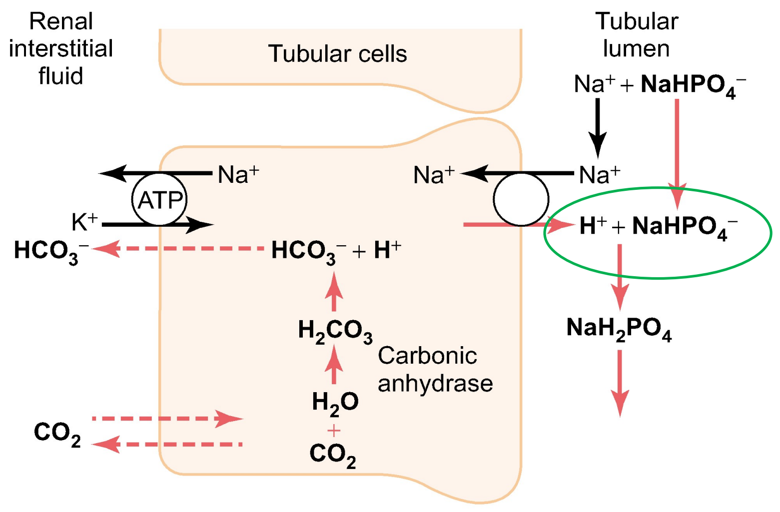
2) It is important buffer

a) intracellularly.

b) in the tubular fluid (in the kidney).

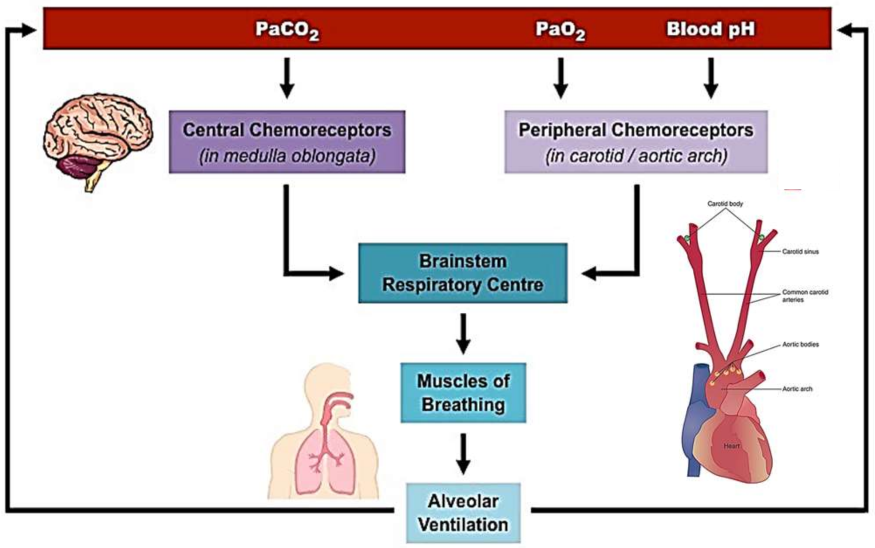
3)Its pK 6.8 is near to that of the plasma pH.

Intracellular buffers are mainly proteinate and organic phosphate.
***Prolonged metabolic acidosis depletes cells of K+ and bones of Ca++.**
***The capacity of intracellular buffers is similar to that of extracellular buffers but exchange between H+ and intracellular K+ or Na+ is much slower taking hours because of limited capacity of the membrane to H+.**

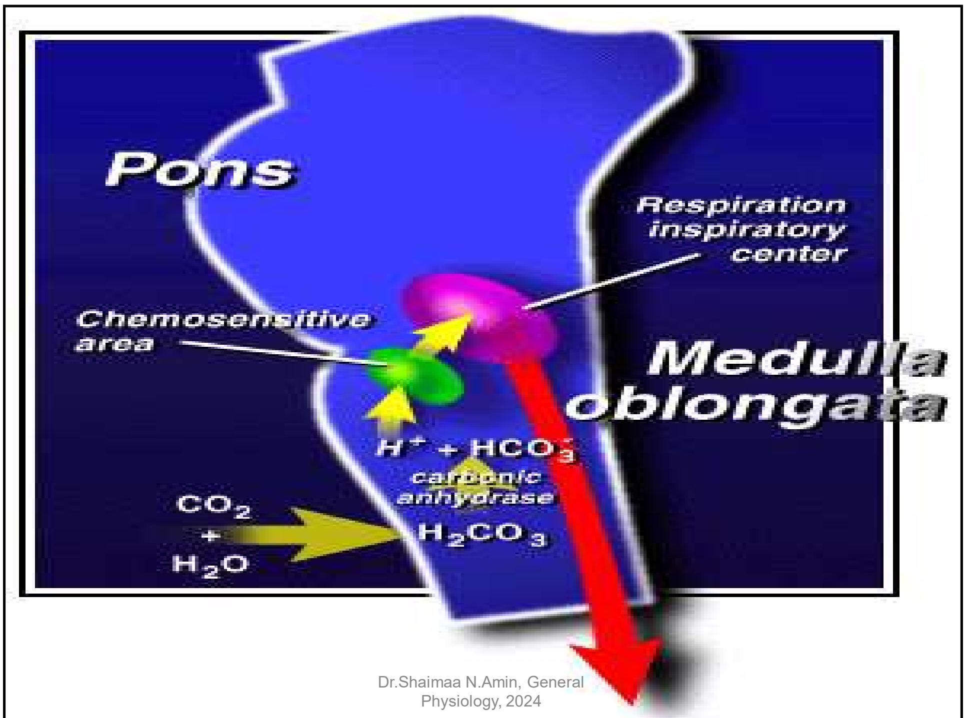


Respiratory Regulation of Body Fluids pH

-The respiratory control of pH is done through controlling of blood PCO_2.
-↓in PCO2 in rapid ventilation→↓H+ concentration and ↑pH according to Hasselbalch-equation for bicarbonate buffer.
-↓in pulmonary ventilation →↑PCO2 and H+ concentration and →↓pH.



$PaCO_2$
PaO_2
Blood pH
Central Chemoreceptors
(in medulla oblongata)
Peripheral Chemoreceptors
(in carotid / aortic arch)
Brainstem Respiratory Centre
Muscles of Breathing
Alveolar Ventilation
Carotid body
Carotid sinus
Common carotid arteries
Aortic bodies
Aortic arch
Heart



Pons
Respiration inspiratory center
Chemosensitive area
Medulla oblongata
$H^+ + HCO_3^-$
carbonic anhydrase
CO_2 + H_2O
H_2CO_3

Mechanism of respiratory control

1-↑in H+ concentration (in metabolic acidosis):

H+→peripheral chemoreceptors→ Respiratory centre →Hyperventilation →eliminate CO_2 and therefore the carbonic acid and H+ concentration↓.

2-A decrease in H+ concentration below normal (in metabolic alkalosis):

The respiratory center becomes depressed →CO_2 retention →↑H+ concentration toward normal.

Control effectiveness of the respiratory control

*The respiratory system can return the H+ and pH about two-thirds of the way toward normal within a few minutes after a sudden disturbance of acid base balance.

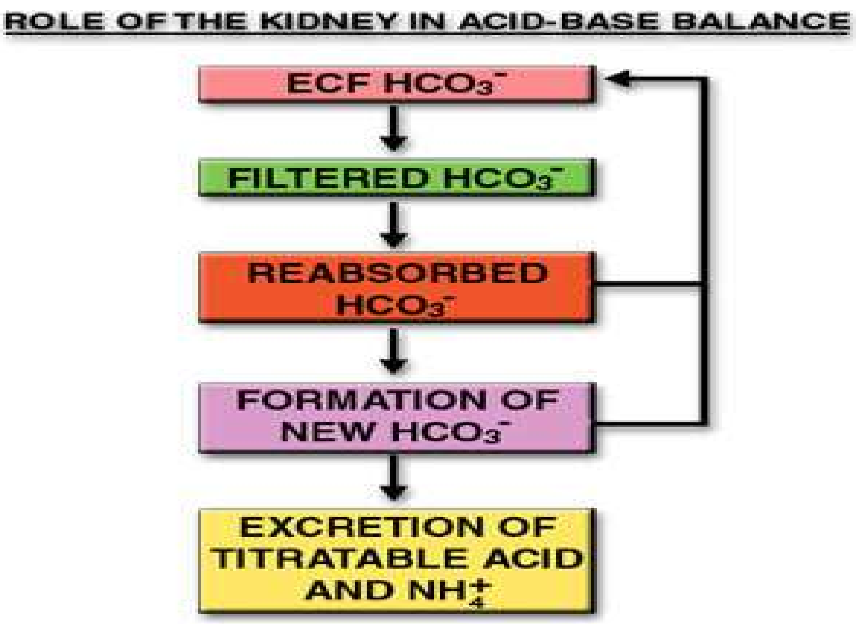
*It takes 1-12 minutes to make acute adjustments in pH.

*The buffering power of respiratory control=1-2 times as all the chemical buffers combined.

*It has limited ability because the changes in PCO2 have opposite effects on respiration.

Renal Control of Acid Base Balance

*When the respiratory system fails to completely restore H+ to normal the kidneys are capable of bringing it back to normal within 12-24 hours in most cases.
*The renal control of acid base is the most powerful and the most effective buffer mechanism.



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The secreted H+ is buffered by:

1-Bicarbonate buffer in the tubular fluid .

2-Phosphate buffer in the tubular fluid.

3-Ammonia synthesized by tubular epithelium.

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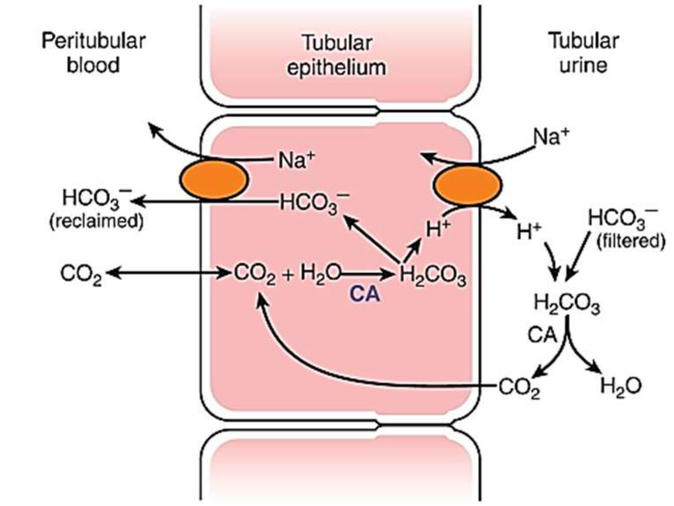


Figure 24.7 A cell model for HCO_3^- reabsorption. Filtered HCO_3^- combines with secreted H^+ and is reabsorbed indirectly. Carbonic anhydrase (CA) is present in the cells and, in the proximal tubule, on the brush border.

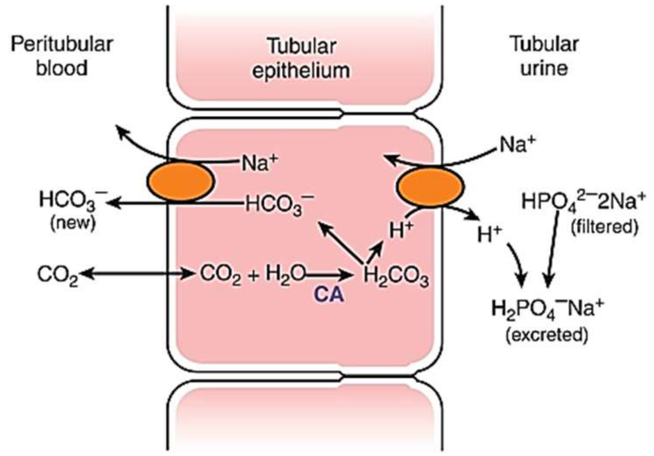
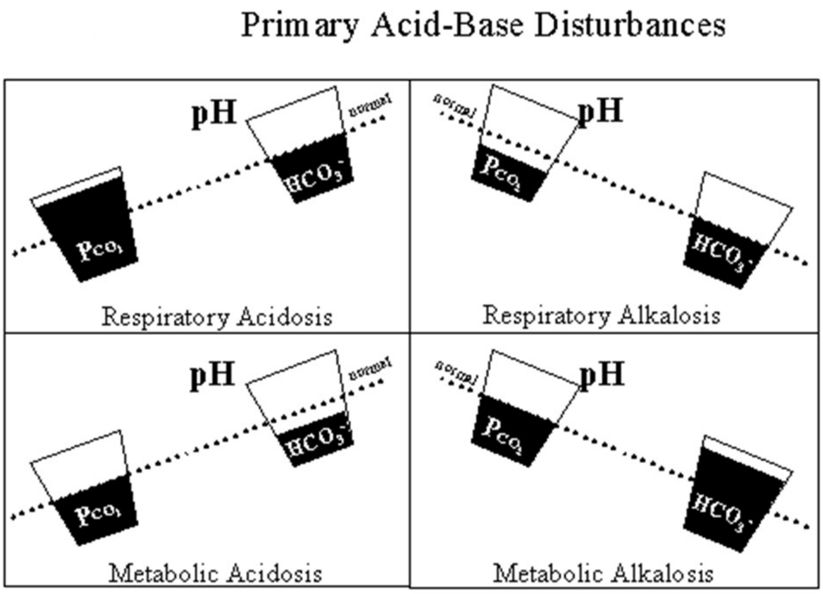


Figure 24.8 A cell model for the formation of titratable acid. Titratable acid (e.g., $H_2PO_4^-$) is formed when secreted H^+ is bound to a buffer base (e.g., HPO_4^{2-}) in the tubular urine. For each milliequivalent of titratable acid excreted, a milliequivalent of new HCO_3^- is added to the peritubular capillary blood. CA, carbonic anhydrase.



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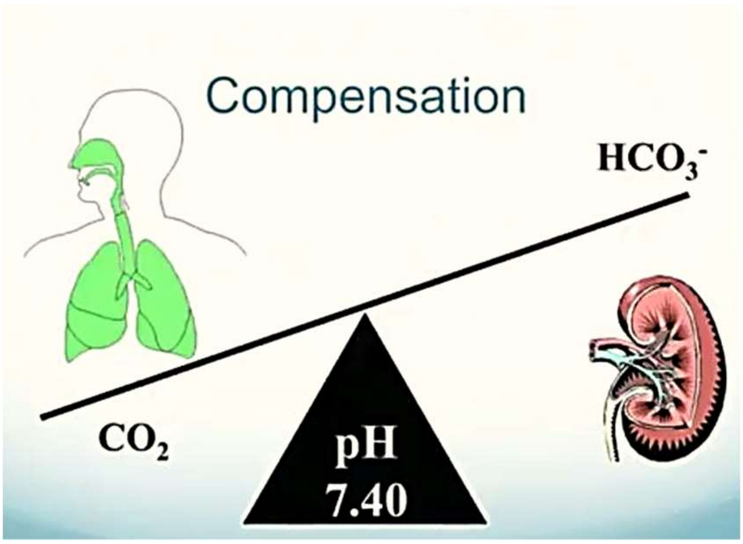

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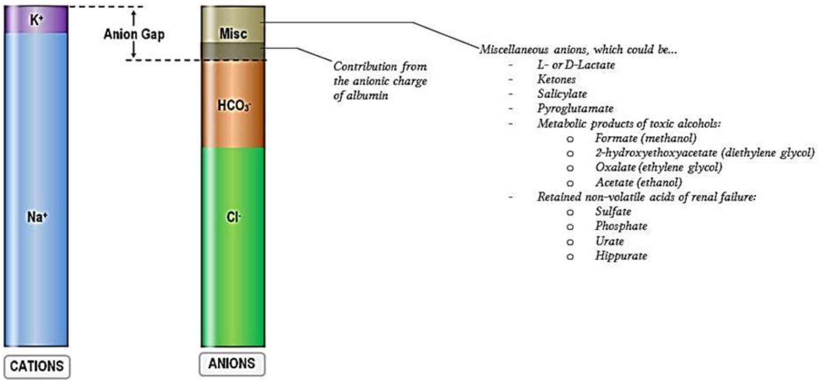
Anion Gap (AG)

- Normally, the concentrations of cations and anions in the plasma are equivalent. Some anions, such as protein, sulfates, phosphates, and organic acids, however, are not measured in the common laboratory evaluations of the blood. Therefore, the normal anion gap represents these unmeasured negative ions (sulfate, phosphate, lactate, keto acids, albumin). A convenient measure of the anion gap is the difference between the sum of Na+ and K+ concentrations and the sum of and Cl− concentrations, or about 10 to 12 mEq/L:

$$\text{Anion gap} = [Na^+ \ (140) + K^+ \ (4.0)] - [HCO_3^- \ (24) + Cl^- \ (110)] = 10 - 12 \text{ mEq/L}$$



Two types of Metabolic Acidosis

- **High Anion Gap** = net gain of acid
- **Normal anion gap** = loss of bicarbonate

BE (base excess)

The base excess indicates the amount of excess or insufficient level of bicarbonate in the system. (A negative base excess indicates a base deficit in the blood.) A negative base excess is equivalent to an acid excess.

Normal: -3 to +3 mmol/L

Metabolic acidosis: < -3 mmol/L

Metabolic alkalosis: > +3 mmol/L

RESPIRATORY DISTURBANCES OF ACID-BASE BALANCE

NORMAL CONDITIONS

$$pH = pK_A + \log \frac{[HCO_3^-]}{\alpha\ P_aCO_2}$$

$$pH = 6.1 + \log \frac{24.0}{0.03 \times 40} = 6.1 + \log \frac{24.0}{1.2} = 7.40$$

$$pH = pK_A + \log \frac{KIDNEY}{LUNG}$$

RESPIRATORY DISTURBANCE

$$pH = pK_A + \log \frac{KIDNEY}{LUNG} \rightarrow \uparrow PCO_2 \text{ or } \downarrow PCO_2$$

Respiratory acidosis

Characterized by :

*Arterial blood pH < 7.35

*↑arterial PCO2 > 45 mmHg

HCO3-/↑PCO2

Causes of respiratory acidosis:

1- Depression of the respiratory center by drugs.

2-Air way obstruction.

3-Pralysis of respiratory muscles.

Respiratory alkalosis

Characterized by:

1- Arterial pH > 7.45

2-Decreased arterial PCO2

{HCO3-/↓PCO2}

Causes of respiratory alkalosis:

1- Respiratory response to high altitude.

2-Psychological dyspnea and anxiety.

3-Fevers.

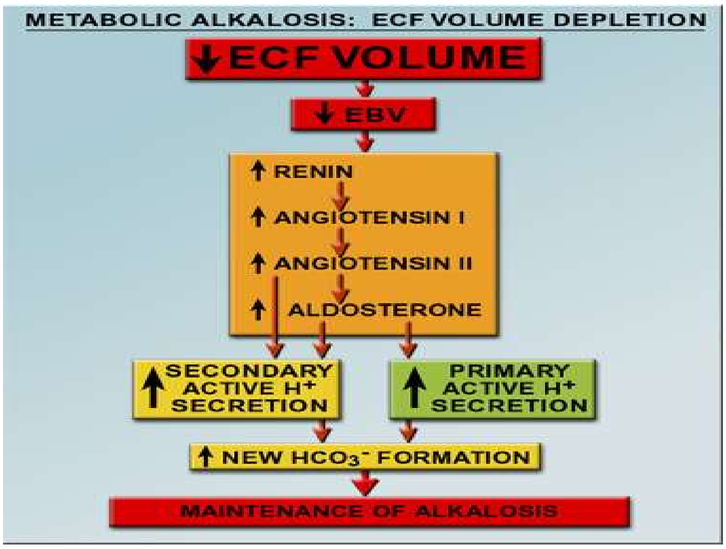
4-Early in exercise .

Metabolic acidosis

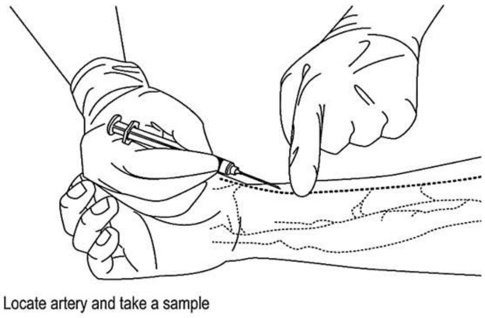
Characterized by:
1-Arterial blood PH <7.35
2-↓ Plasma HCO_3^-
Causes :
1-Excess production of fixed acids :
a) Diabetic ketoacidosis.
b) Shock.
2-Decreased elimination of fixed acids as in renal failure
3-Loss of HCO_3^-:
a) Severe diarrhea.
b) Addison's disease.

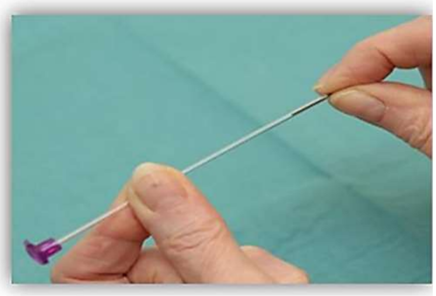
Metabolic alkalosis

Characterized by:
1-Arterial blood pH > 7.45
2-Increased plasma HCO_3^-
Causes:
1-Persisting vomiting.
2-Diet rich in fruits and vegetables.
3-Excess intake of alkalies to treat peptic ulcer.
4-Con's syndrome.
6-Diuretics except carbonic anhydrase inhibitors



ARTERIAL BLOOD GASES

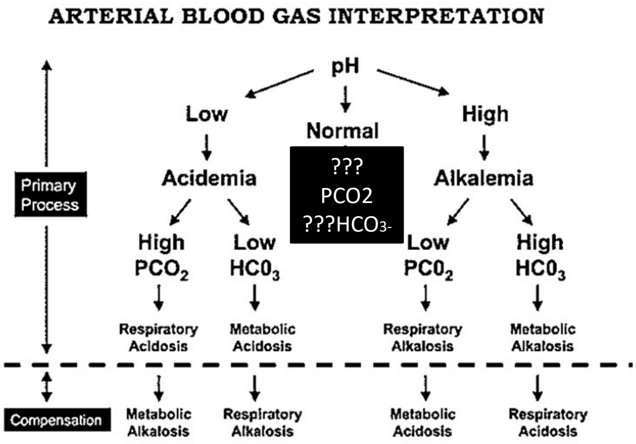




Normal Values

pH	7.35-7.45
CO_2	35-45
pO_2	80-100
HCO_3	22-26
O_2 Sat.	95-100%

AG ???
- Base Excess???



AG ???
- Base Excess???

Arterial Blood Gases (Example)

pH	6.98
pCO2	62
HCO3-	14
pO2 80	
O2 Sat.	89%
BE	-11
AG	18

Great things never come from comfort zones

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