Renal Block

Physiology Team

9th Lecture

Basics of Acid-Base Balance

this lecture is done by:

Ahmad BoGari

10th Lecture

Buffer System

this lecture is done by:

Reem Aljurayyed

Akeel Al- Mahdaly

Organized By : Suliman AL-Shammari & Layan Akkielah

What is Acid-base balance?

• Acid-base balance is a balance of H+ concentration in ECF.
• To achieve homeostasis a balance should be kept between the intake or production of hydrogen ions and the net removal of hydrogen ions from the body.

- **Definition:**

pH is defined as potential of H^+ Ion concentration in body fluid. The amount of H^+ ion concentration is so low in the body hence it is expressed as negative logarithm to base of the H^+ ion concentration in mEq/lit.

$$pH = \log 1/[H^+] = -\log [H^+]$$

- **Arterial blood pH = 7.35 – 7.45**

Can be explained as follows;
Normal value of H^+ ion conc. is about 40nEq/lit.
40 nEq/lit = 0.00000004 Eq/lit.
Therefore pH = - log [0.00000004]
= 7.4

pH and H^+ ion concentration

pH	H^+ ion in nmol/lit
6.0	1000
7.0	100
8.0	10
9.0	1

Note: one point drop in pH results in a ten fold decrease in H^+ ion conc.

	H^+ Concentration (mEq/L)	pH
Extracellular fluid		
Arterial blood	4.0×10^{-5}	7.40
Venous blood	4.5×10^{-5}	7.35
Interstitial fluid	4.5×10^{-5}	7.35
Intracellular fluid	1×10^{-3} to 4×10^{-5}	6.0 to 7.4
Urine	3×10^{-2} to 1×10^{-5}	4.5 to 8.0
Gastric HCl	160	0.8

pH Review :

- **pH = -log [H+]**
- **If [H+] is high, the solution is acidic; pH < 7**
- **If [H+] is low, the solution is basic or alkaline; pH > 7**

pH is the log of the reciprocal of the H+ ion concentration

pH = log (1 / [H+])

OR

pH = - log([H+])

The normal H ion concentration in blood is 40 nmol/l or 0.00004 mmol/l

- For Na it is 140 mmol/l

40 nmol/l or 0.00004 mmol/l is equal to pH 7.4

An Acid :

- Molecules containing hydrogen atoms that can release (donate) hydrogen ions in solutions are referred to as an acid.
- Strong acids: completely dissociate (HCL, H2SO4)
- Weak acid: partially dissociate (H2CO3)

A Base :

- A base is an ion that can accept a hydrogen ion.
- Bases are ions or molecules that bind free H+ and remove it from a solution.
- An example of a base is bicarbonate ion (HCO3)
- Alkali is a molecule formed by one of the alkaline metals. (Na, K, Li) with a highly basic ion such as a hydroxyl ion (OH–).

Extracellular pH (blood pH)

•Homeostasis of pH is important for the function of body enzymes
•Acid-base balance can also affect electrolytes concentration (Na^+, K^+, and Cl^-)
•Can also affect certain hormones
•Blood pH = 7.35 –7.45 (normal pH: around 7.4)
•Blood pH can be calculated by Henderson-Hasselbach equation
•PH = pKa+ log10 [Base]

Note: Arterial blood pH = Blood pH = Extracellular fluid pH

[Acid]

•Acidosis= decrease in arterial pH (< 7.4) due to excess H^+
•Alkalosis= an elevation in arterial PH (>7.4) due to excess base
•pH < 6.8 or > 8.0 death occurs

Henderson-Hasselbalch Equation :

- It is essential for measurement of pH.
- $H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
- According to law of mass action

HENDERSON-HASSELBACH EQUATION

Relates pH to the Ratio of the Conc. of Conjugate Base and Acid	$pH = pK \times \log \frac{\text{Base}}{\text{Acid}}$

The ratio of dissociated to undissociated forms of an acid is CONSTANT (K) and shows the Strength of an Acid

$$K = [H^+][A^-] / [HA]$$

$$\text{eg: } K = [H^+][HCO_3^-] / [H_2CO_3]$$

$$\frac{[H^+]x\,[HCo_3^-]}{[H2Co_3]}$$

$$\left(pH = 6.1 + \log \frac{(HCo_3)Kidney\ (20)}{(Co_2)Lungs\ (1)} \right)$$

$$pH = 7.4 = \frac{Alkali(HCo_3)}{Acid\ (H_2Co_3)\ or\ Co_2} \quad Is\ then\ \frac{20}{1}$$

$$K_A = \frac{[H^+]\ X\,[HCo_3^-]}{[Co_2]}$$

K_A = dissociation constant of carbonic acid

$$K_A = \frac{[H^+]\ X\,[HCo_3^-]}{[Co_2]}$$

K_A = dissociation constant of carbonic acid

According to log

$$Log\ K_A = \log(H^+) + \log \frac{[HCo_3^-]}{[Co_2]}$$

$$-Log\ (H^+) = -\log(K_A) + \log \frac{[HCo_3^-]}{[Co_2]}$$

Because pH is – log hence

$$pH = pK + \log \frac{[HCo_3^-]}{[Co_2]}$$

$$pH = 6.1 + \log \frac{24}{0.03X\,40} \qquad \left(pH = 6.1 + \log \frac{(HCo_3)Kidney\ (20)}{(Co_2)Lungs\ (1)} \right)$$

$$pH = 6.1 + \log 20$$
$$pH = 6.1 +\ 1.3$$
$$pH = 7.4$$

Explanation

The Henderson-Hasselbalch Equation Relates pH to the ratio of the Concentrations of Conjugate Base and Acid

pK :

pK (also a log) is where concentration of both components of the buffer are equal.

REMEMBER to maintain plasma pH at 7.4, there needs to be much more HCO3- than H2CO3

pH = pK

pK

- **pH = pK x Base/Acid**
- **pH = pK x 50/50**
- **pH = pK**

Acid-Base Imbalances :

•pH< 7.35 acidosis

•pH > 7.45 alkalosis

•The body response to acid-base imbalance is called compensation

•Is complete if pH brought back within normal limits

•Partial compensation if range is still outside norms.

System Compensation :

•If underlying problem is metabolic, hyperventilation or hypoventilation can help: respiratory compensation.

•If problem is respiratory, renal mechanisms can bring about metabolic compensation.

Body produces more acids than bases :

- Acids take in with foods
- Acids produced by metabolism of lipids and proteins

Cellular metabolism produces CO_2. (Volatile acid)

- $CO_2 + H_20 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$

Volatile acids: (e.g. carbonic acid, H_2CO_3; formation catalyzed by carbonic anhydrase)
Non-volatile acids: ingested acids and products of fat, amino acid, and sugar metabolism:
- e.g. phosphoric acid, lactic acid, butyric acid
- Incomplete Carbohydrate and Fat

Metabolism Produces Nonvolatile Acids (strenuous exercise, hemorrhagic or cardiogenic shock, uncontrolled diabetes mellitus, starvation, and alcoholism)

- Amino Acid Metabolism yields about 50 meq/day for example: (H_2SO_4, HCl, and H_3PO_4)
- CO_2 production yields 12,500 meq/day300 L of CO_2
- Normal daily diet yields 80 meq/day

The basics

- An acid is an ion donor which increase H ion concentration of the solution e.g. lower the ph.(acidic)
- Base is Ion accepter e.g. increase the pH (alkaline)
- Buffer is an agent that minimizes the change in pH when an acid or base is added.
- Base excess (BE= -2to 2)= is a calculation of the amount of base that needs to be added to or removed from a sample of blood to achieve a neutral pH at 37 degree. A positive BE indicates that there is more base than normal (metabolic alkalosis) and a negative BE less base than normal (metabolic acidosis).

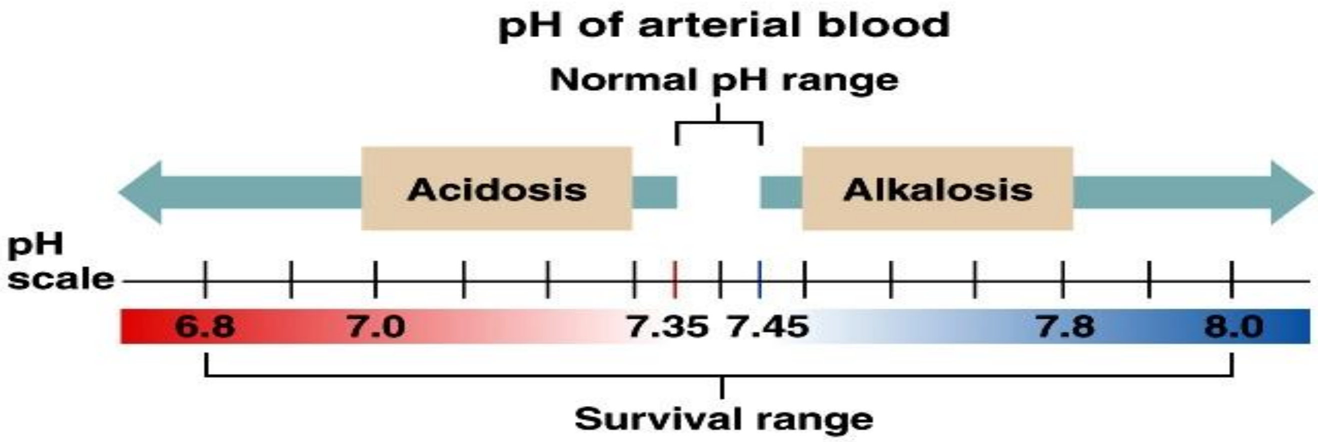
About H+

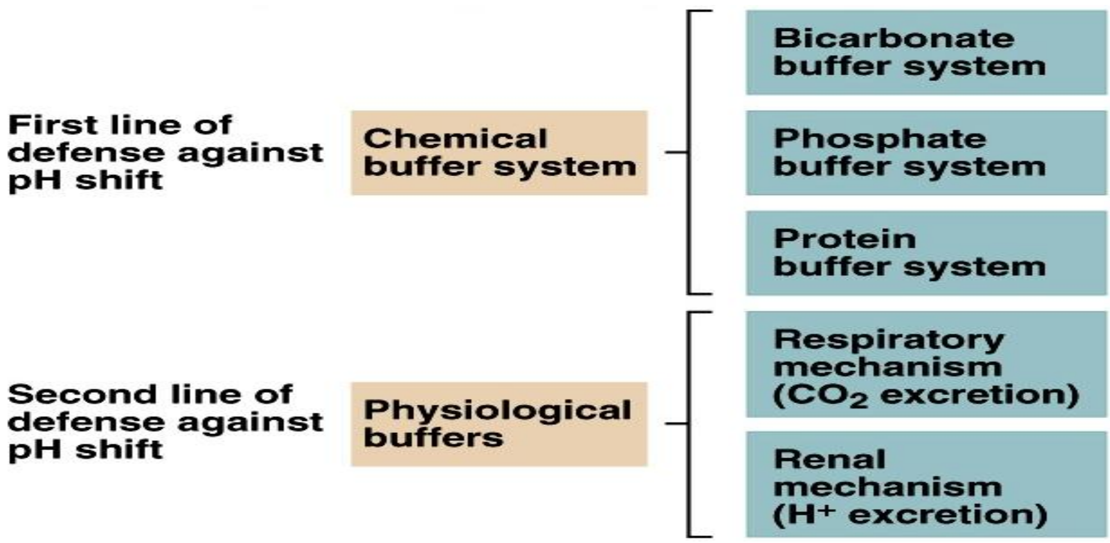
H^+ ions are derived from hydrogen atoms. Hydrogen atom has proton, a positive electrical charge with a negative charge electron which is revolving around it. The hydrogen ion is formed when negative ion (electron) is lost and it contains only proton. The H^+ is the smallest ionic particle, highly reactive with a very short life and unable to survive on its own.
Hydrogen ions are the toxic end product of metabolism and they adversely affect all physical and biochemical cellular process in our body.

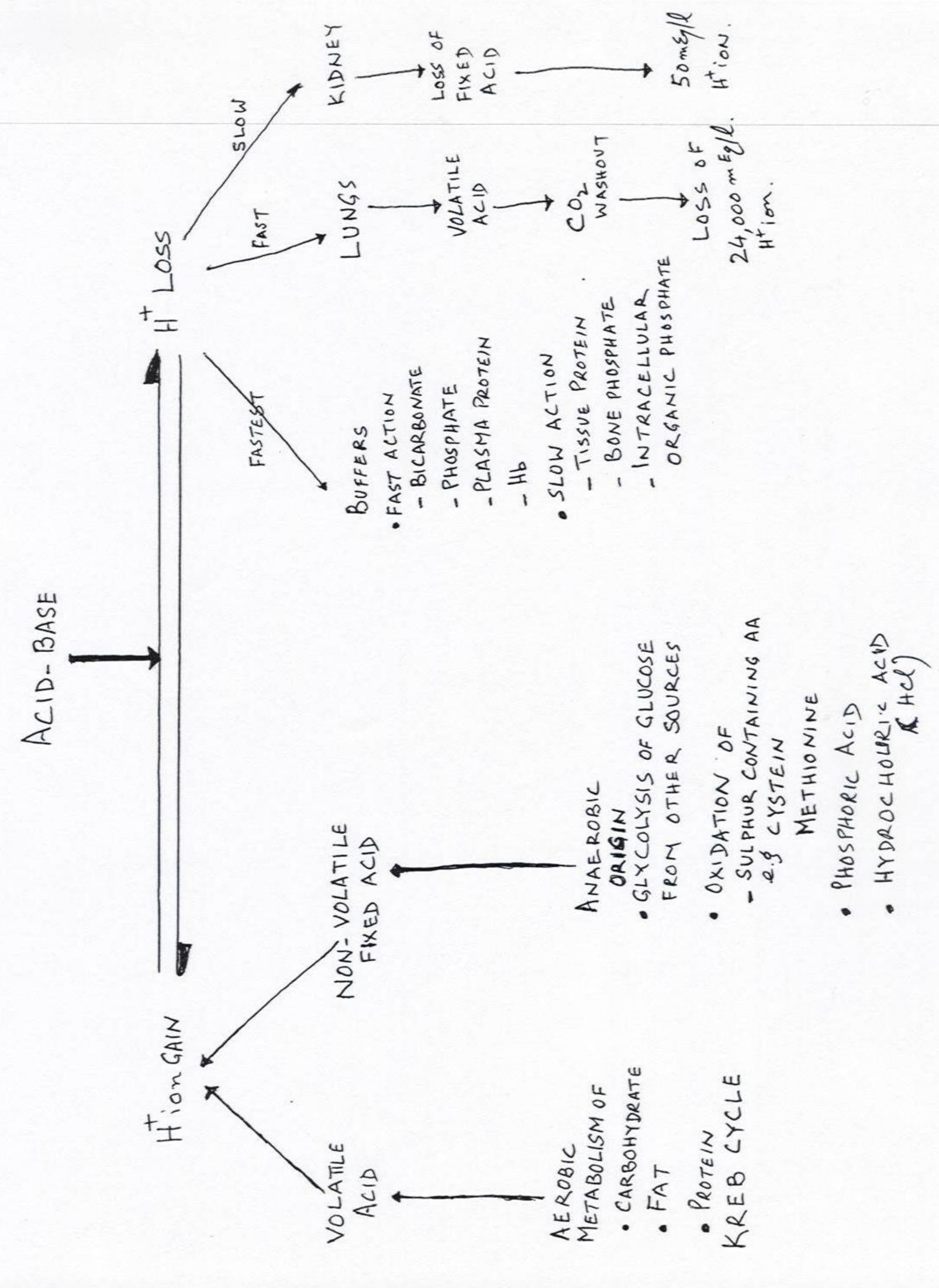
Scale of pH measurement :

- The pH scale is between 0 – 14.

Zero onwards below 7 is acidic.
After 7 up to 14 the solution is alkaline.
At 7 (neutral e.g. water) where the amount of H+ and Hydroxyl ion are equal at 23^{o}






ACID- BASE
H+ ion GAIN
VOLATILE ACID
NON- VOLATILE FIXED ACID
AEROBIC METABOLISM OF
• CARBOHYDRATE
• FAT
• PROTEIN
KREB CYCLE
ANAEROBIC ORIGIN
• GLYCOLYSIS OF GLUCOSE FROM OTHER SOURCES
• OXIDATION OF
- SULPHUR CONTAINING AA e.g CYSTEIN
METHIONINE
• PHOSPHORIC ACID
• HYDROCHOLRIC ACID (HCl)
H+ LOSS
FASTEST
FAST
SLOW
BUFFERS
• FAST ACTION
- BICARBONATE
- PHOSPHATE
- PLASMA PROTEIN
- Hb
• SLOW ACTION
- TISSUE PROTEIN
- BONE PHOSPHATE
- INTRACELLULAR ORGANIC PHOSPHATE
LUNGS
VOLATILE ACID
CO2 WASHOUT
LOSS OF 24,000 mEq/l. H+ ion.
KIDNEY
LOSS OF FIXED ACID
50 mEq/l H+ ion.

Buffers :

- Buffers are substances that neutralize acids or bases
- Consist of a WEAK ACID and its conjugate base (or a weak base and its conjugate acid)

- يعني تخلي المحلول متساوي في الحمضية والقاعدية. ممكن تكون من مواد أو تفاعل كيميائي.

- (to prevent acidosis or alkalosis)

Just read: **Acid-base homeostasis** is the part of human homeostasis concerning the proper balance between acids and bases, in other words, the pH.

- The body's acid-base balance is tightly regulated.

- Several **buffering agents** that reversibly bind hydrogen ions and impede any change in pH exist.

- **Extracellular** buffers include bicarbonate and ammonia.

- Whereas proteins and phosphate act as **intracellular** buffers.

For example in Bicarbonate buffer system
H_2CO_3 is the weak acid and $NaHCO_3$ is its salt.

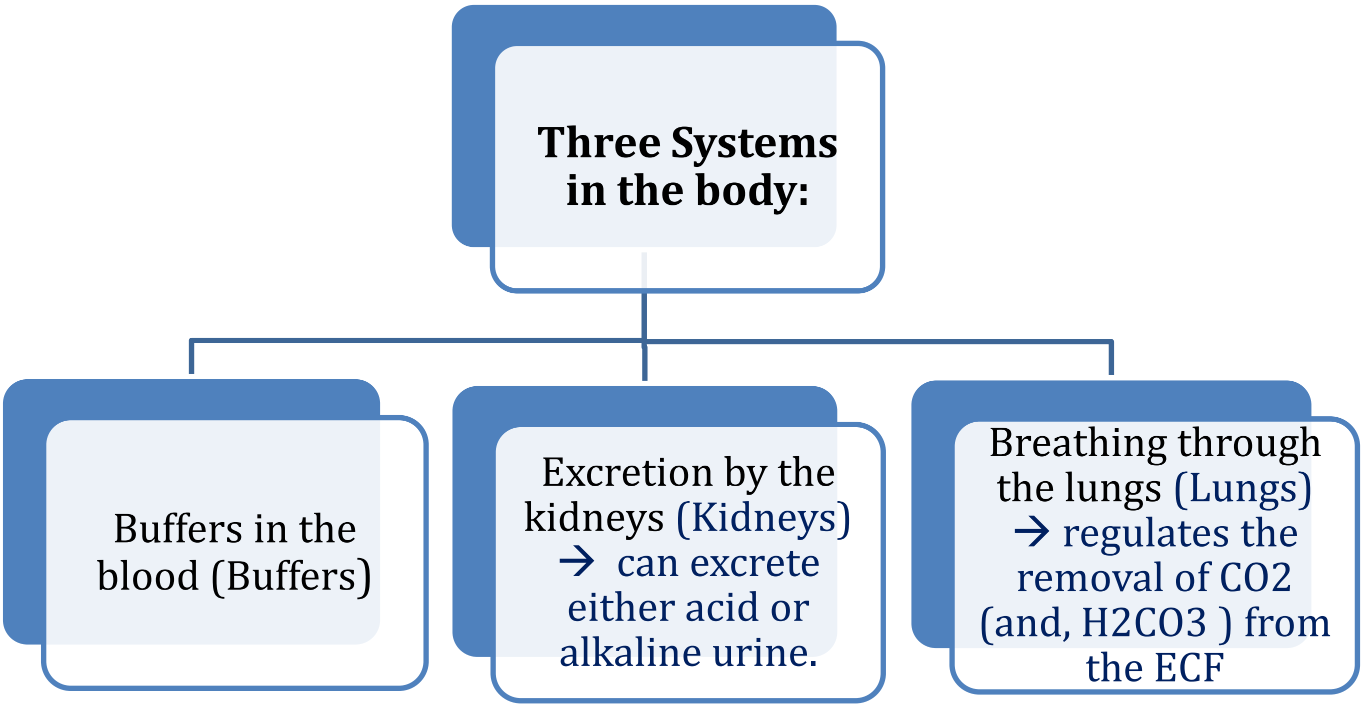
Buffer power :

- Depends on relative amount of acid and base in a buffer solution
- It is maximum when both are in equal amounts
- Absolute concentration of Buffers in body fluids is also important
- If the pH of medium is near pK of buffer system it becomes more effective
- Buffers Promote the Stability of pH
- Chemical reactions which reduce the effect of adding acid or base to a solution PH.
  - Buffers take up H+ or release H+ as conditions change
  - Buffer pairs a weak acid and a base
  - Exchange a strong acid or base for a weak one

Results in a much smaller pH change :

- Buffer reacts with hydrogen ion within seconds to minimize the injurious consequences on body
- Buffers do not eliminate H ion but it soaks H ion as sponge soaks water.
- A weak acid dissociate their ions slowly therefore releases H^+ with a slow speed and this reaction is reversible. E.g. Buffer + H^+ = H Buffer (weak acid) this weak acid keeps H^+ with it for some time.
- Buffer + ↑↑ H^+ ↔ H Buffer

Note: A pKa of 6.8 Makes Phosphate a Good Buffer in ECF however, its plasma conc. is low (about 1 mmol/L) unlike HCO3- which is 24 mmol/L



DEFENCE MECHANISMS IN THE BODY :

- Chemical buffering (First Line) Acid-Base buffer systems of the body fluids
- Respiratory response (Second Line) respiratory center
- Renal response (Third Line) Kidneys [slow to respond & powerful]

- **Extracellular Buffer**
  - Bicarbonate buffer system (Blood)
  - Phosphate buffer (Kidney)

- **Intracellular Buffer**
    - Proteins (all the cellular elements which contains protein)

– Proteins (Amphoteric) : Prot / H Prot

• important in ICF

- Hemoglobin

– Hemoglobin: Hb / HHb

- • important in ICF

    - AMP, ADP, ATP
- Bone Matrix also acts a buffer.

- Blood Buffer :

These buffer systems serve as a first line of defense against changes in the acid-base balance

•Bicarbonate
•Protein
•Phosphate
•Hemoglobin

Buffers systems do not eliminate H from or add them to the body but only keep them tied up until balance can be reestablished

Bicarbonate Buffer

• Important extracellular buffer	• HCO_3 = 24-28 mEq/ml
• Present in larger quantities	• Water solution consists of: weak acid H_2CO_3 and Bicarbonate salt $NaHCO_3$
• Can be regulated by respiratory and renal	• HCO_3^-:H_2CO_3 Maintain at a ratio of 20:1
• $pH = 6.1 + \log \frac{HCO3}{0.03 \times Pco2}$	
• If Acid is added – $H^+ + HCO_3 \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$ (And excess CO_2 greatly stimulate respiration, which eliminates the CO_2 from the ECF)	• If Base is added – $NaOH + H_2CO_3 \leftrightarrow NaHCO_3 + H_2O$

- ↓ CO_2 → the decreased CO_2 in the blood inhibits respiration and decreases the rate of CO_2 expiration.

- The rise in blood HCO_3 that occurs is compensated for by increased renal excretion of HCO_3.

- Phosphates & Intracellular Buffers

Note: Phosphate is an intra and extracellular buffer

- Minor role compare to HCO_3 or HB
- Intracellular buffers (proteins & phosphate) are needed because H does not cross PM.
- Intracellular pH is more acidic (7.2)

The phosphate buffer system has a pK of 6.8, which in not far from the normal pH of ***7.4*** *in the body fluids; this allows it to operate near its "Max. Buffering Power".*

■ Proteins :

- Includes hemoglobin and plasma protein
- Acidic and basic amino acids in plasma and cell protein act as buffers
  - Carboxyl group gives up H+
  - Amino Group accepts H+
- Side chains that can buffer H+ are present on 27 amino acids.
- Cannot be regulated physiologically
  - 60 – 70 % of total buffering capacity of protein of the body fluid is inside the cell (intracellular).

$H^+ + Hb \leftrightarrow HHb$

- Desoxygenated Hb (deoxygenated)

- **Respiratory regulation of pH :**

•Maintain normal ECF pH by changing the rate and depth of breathing to maintain constant PCO2 (volatile acid) (سريع الزوال , متقلب)
•Controlled by chemoreceptors
•Respiratory doesn't affect fixed acids like lactic acid
• Rise in PCO2 leads to decrease in pH

- The transport of CO_2 has a profound effect on acid base status of the body.
- Lung excretes over 10000meq. of carbonic acids per day compared to less than 100meq of fixed acids by the kidney. Therefore alveolar ventilation thus eliminates Co_2 from the body and has a greater impact over the acid base balance.
- Co_2 is mostly evolved aerobically by metabolism of carbohydrate fat and proteins.
- Co_2 stimulates the respiratory center directly (present over the ventral surface of medulla oblongata) with increased respiration causing washing out of Co_2.

- ↑ H^+ → stimulates respiratory center→↑Alveolar ventilation → washing out of Co2 → ↓H^+

Kidney excretion :

•Can eliminate large amounts of acid by tubular secretion of H+
•Can also excrete base by adjusting tubular reabsorption of HCO3
•Can conserve and produce bicarbonate ions
•Kidney is the most effective regulator of pH
•If kidneys fail, pH balance fails

(Very Important)
Tubular secretion of H+

1. In all parts of nephron except thin part of loop
2. In PCT, thick loop and early DCT H+ is secreted in exchange for Na+
3. Secreted H+ is used for HCO3 reabsorption
4. In late DCT H+ is secreted by active transport by intercalated cells acidifying Urine to pH 4.5

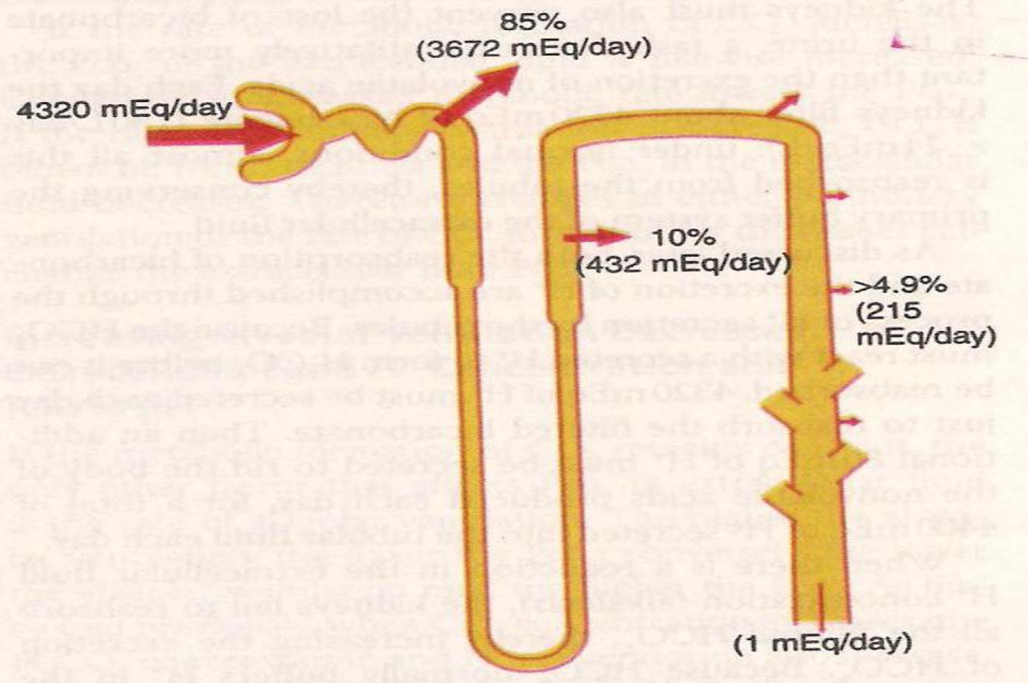


Figure 30-4 Reabsorption of bicarbonate in different segments of the renal tubule. The percentages of the filtered load of HCO_3^- absorbed by the various tubular segments are shown, as well as the number of milliequivalents reabsorbed per day under normal conditions.

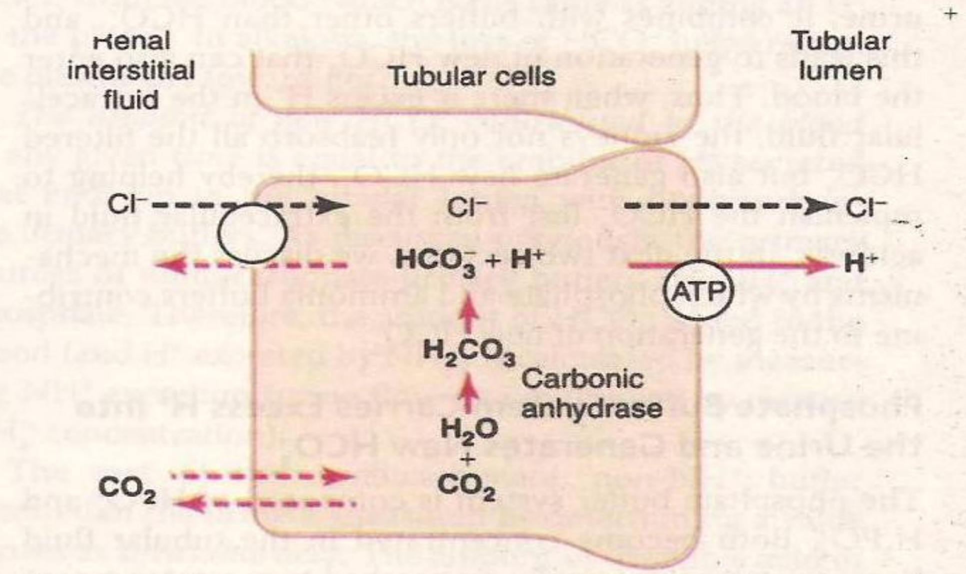
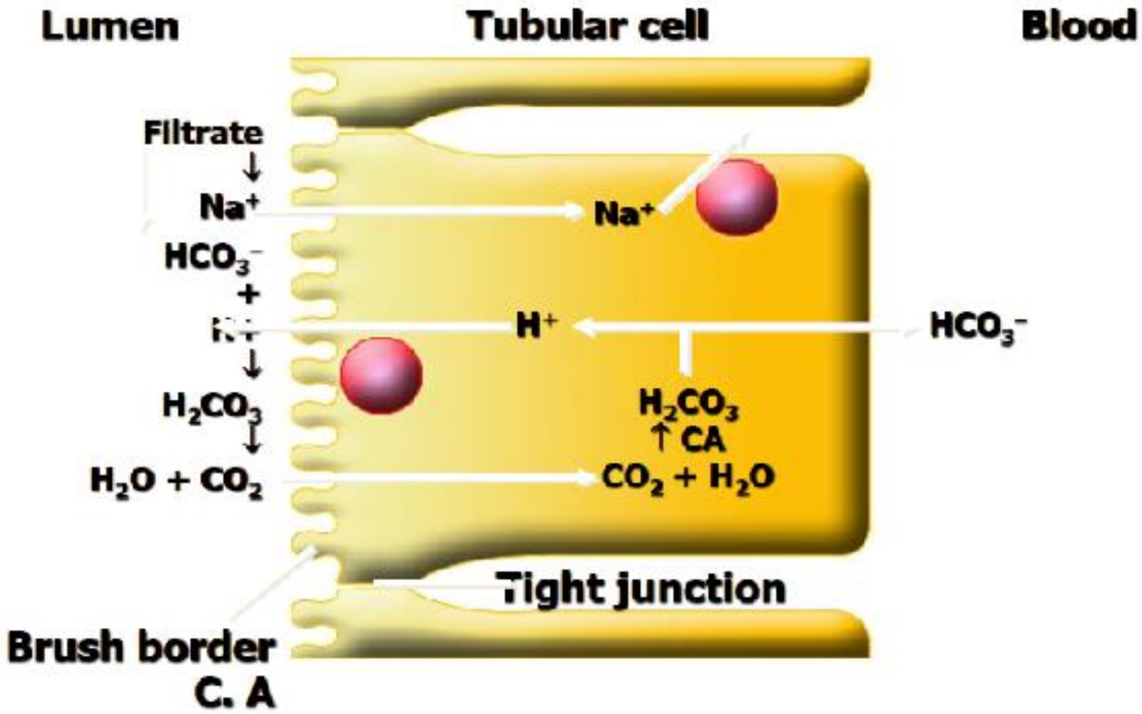


Figure 30-6 Primary active secretion of H^+ through the luminal membrane of the intercalated epithelial cells of the late distal and collecting tubules. Note that one HCO_3^- is absorbed for each H^+ secreted, and a chloride ion is passively secreted along with the H^+.

Buffering of Secreted H^+ and Bicarbonate reabsorption



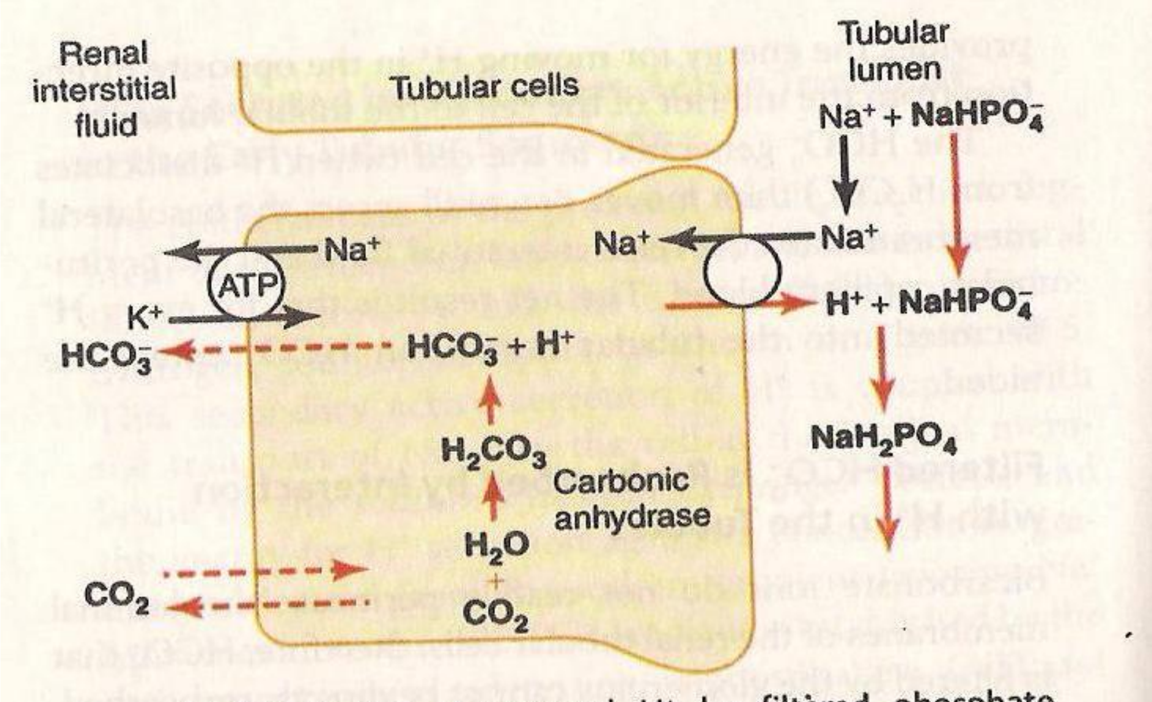
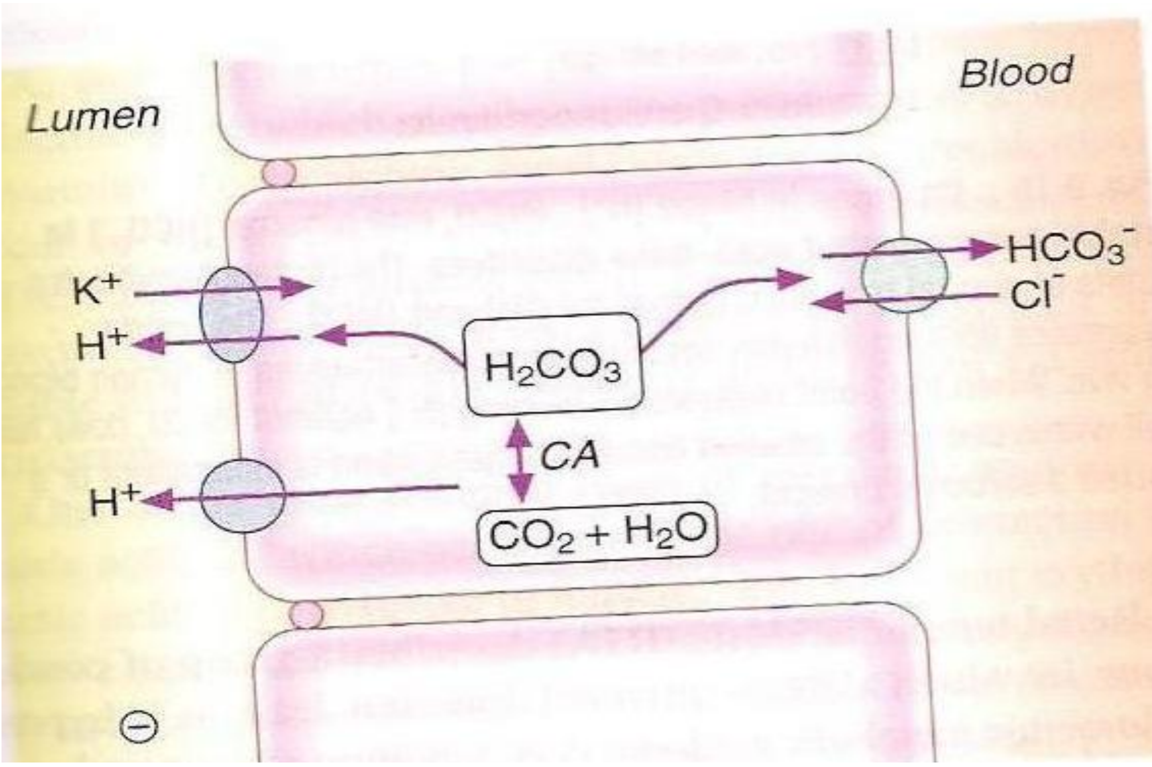


Figure 30-7 Buffering of secreted H^+ by filtered phosphate ($NaHPO_4^-$). Note that a new HCO_3^- is returned to the blood for each $NaHPO_4^-$ that reacts with a secreted H^+.



-- Buffering of Secreted H+ and phosphate absorption :

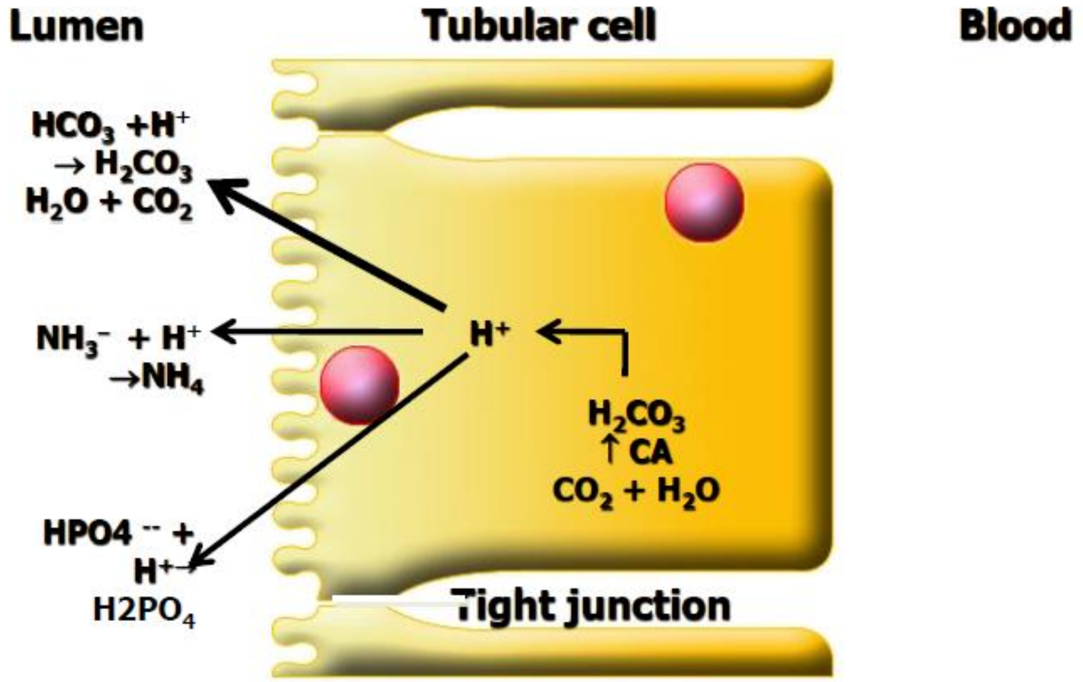
1. Excess secreted H+ will be neutralize by phosphate buffer
2. HPO4+ H+= H2PO4+ Na= Na H2PO4 (salt)

-- Buffering of Secreted H+ with ammonia buffer

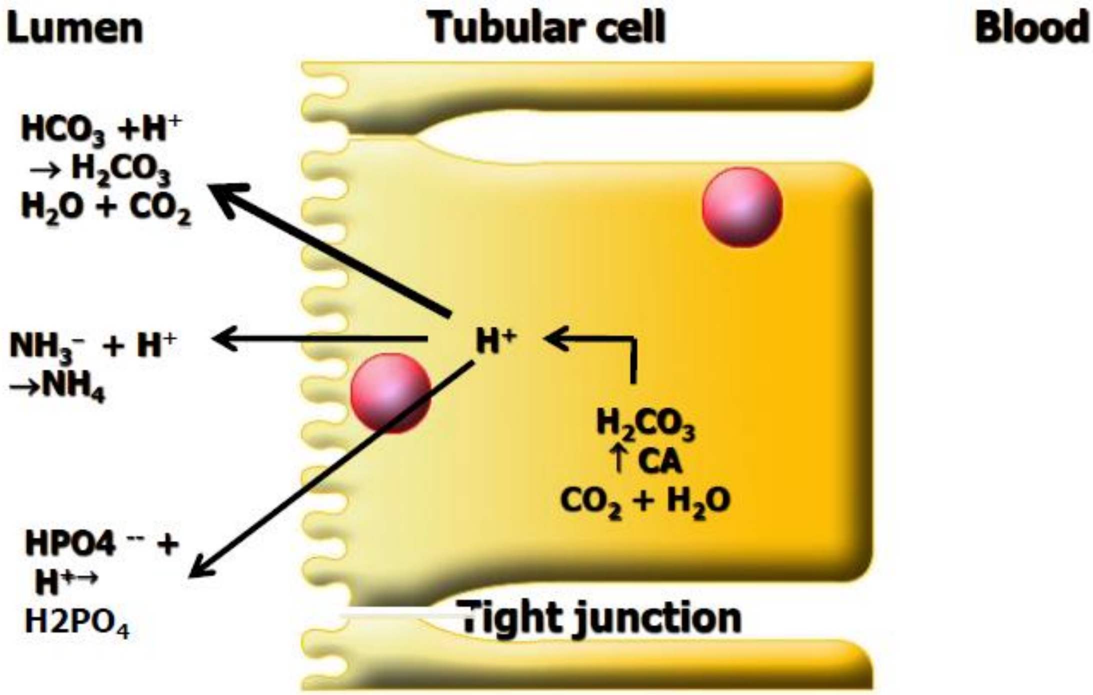
Filtered ammonia NH3 + H+= NH4 (ammonium) not acidic excreted in urine
Ammonia: NH3 / NH4+

- **pK = 9.0**
- **used to buffer the urine**

Buffering of secreted Hydrogen in urine



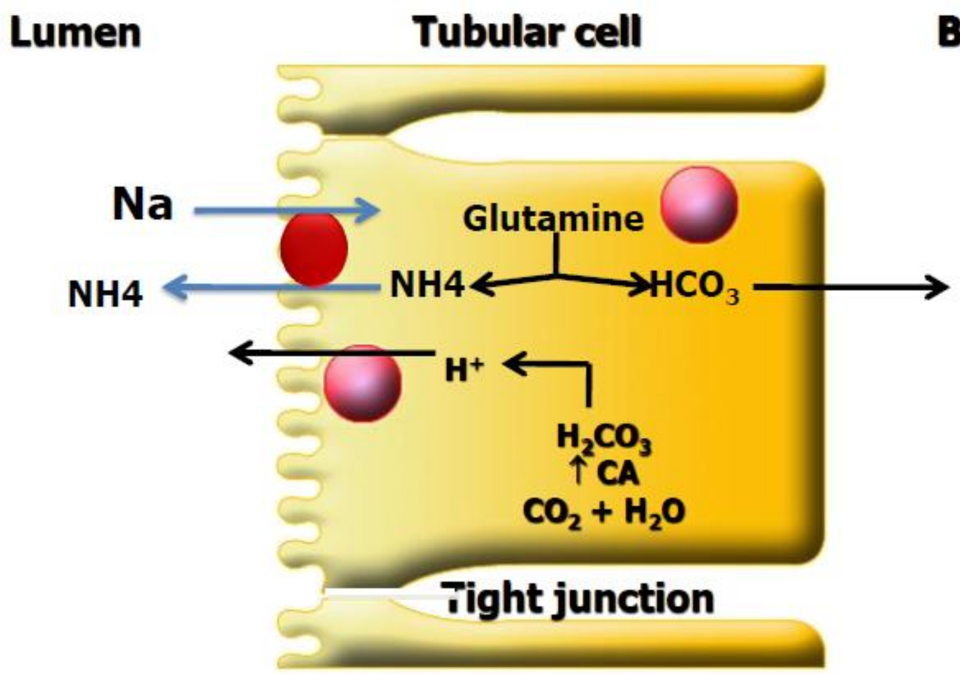
Buffering of the excreted Hydrogen



Formation of new bicarbonate by renal cells :

1. Glutamine molecule is metabolized inside renal cell -> 2NH4+ 2HCO3 stimulated by acidosis
2. NH4 is secreted in exchange for Na+

Formation of new Bicarbonate



Diagnosis of Acid-Base Imbalances :

- pH low (acidosis) or high (alkalosis)

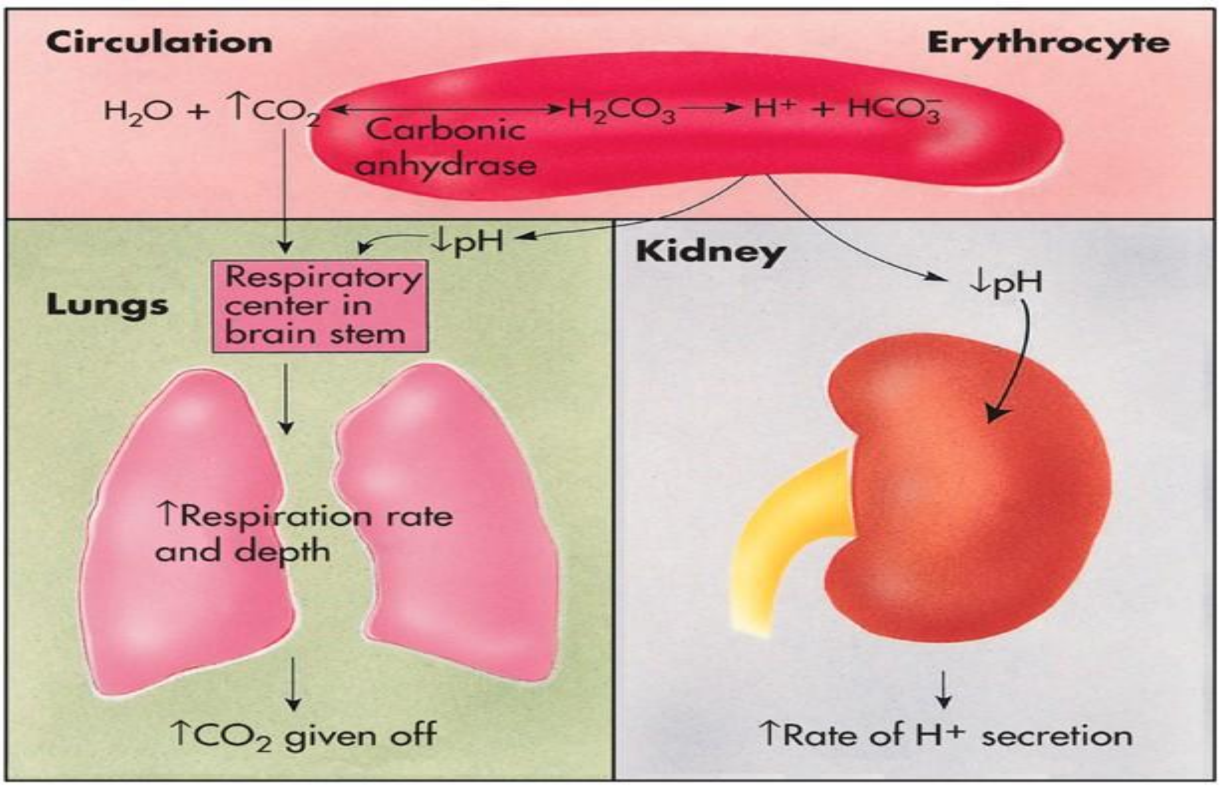
- If PCO2, is abnormal the problem is respiratory, renal mechanisms can bring about metabolic compensation.

- If HCO3- is abnormal the problem is metabolic hyperventilation or hypoventilation can help; respiratory compensation.

> - **Respiratory problem = Abnormal PCO2 = Renal metabolic compensation.**
>
> - **Metabolic problem = Abnormal HCO3- = Respiratory compensation.**

- If pH is within the normal range, there is full compensation.
- If it is outside the normal range, the body is partially compensating for the problem.

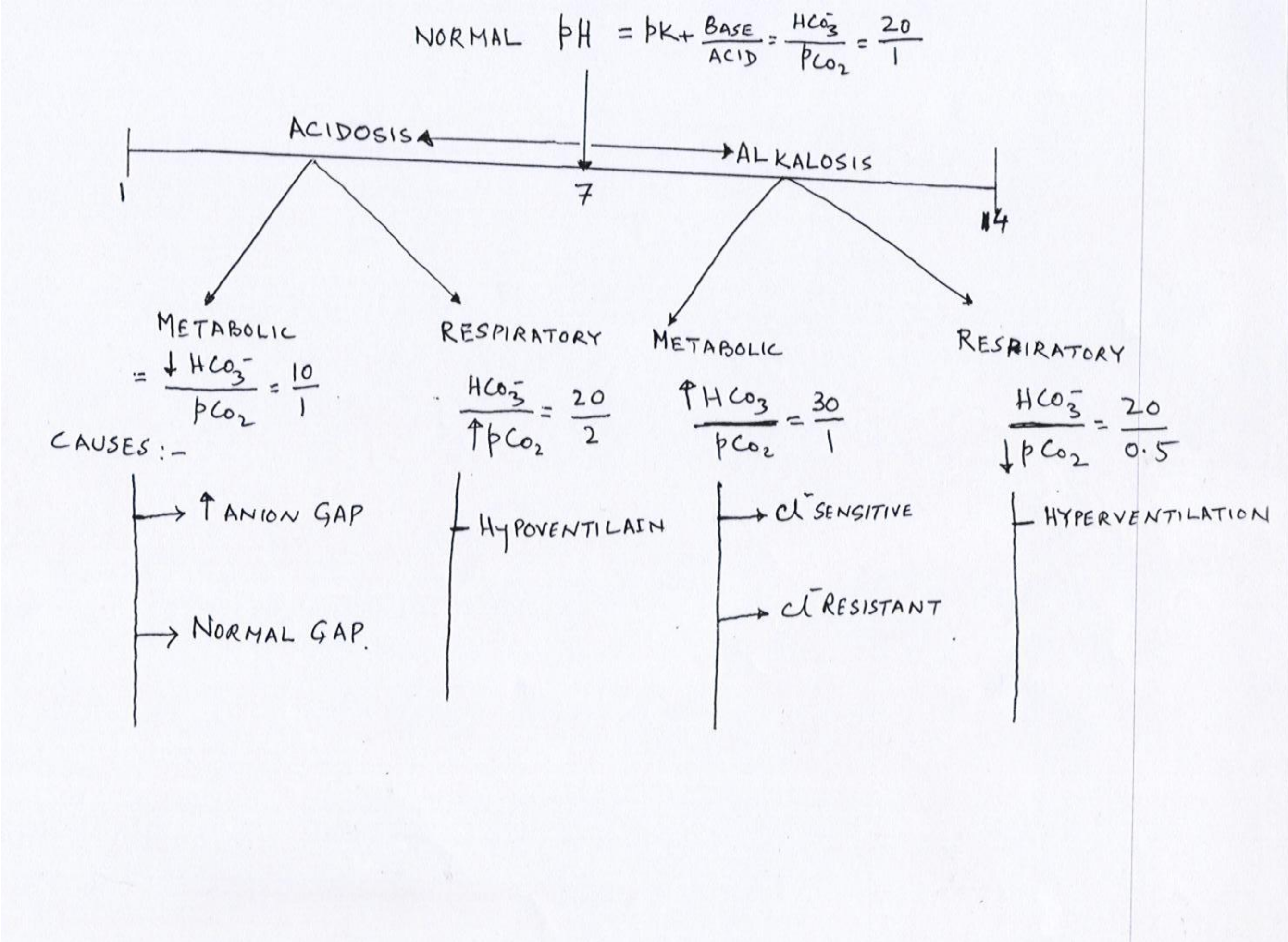
- pH< 7.35 acidosis
- pH > 7.45 alkalosis
- The body response to acid-base imbalance is called **compensation**



From Thibodeau GA, Patton KT: *Anatomy & physiology*, ed 5, St Louis, 2003, Mosby.

Rates of correction

- Buffers function almost instantaneously
- Respiratory mechanisms take several minutes to hours
- Renal mechanisms may take several hours to days



Acid Base Imbalance

1. Acidosis

- Low pH
- Metabolic causes
- Respiratory causes

2. Alkalosis

- High pH
- Metabolic causes
- Respiratory causes

There are 4 Types of Acid-base Imbalances

1. Respiratory Alkalosis
2. Respiratory Acidosis
3. Metabolic Alkalosis
4. Metabolic Acidosis

Acidosis

- Principal effect of acidosis is depression of the CNS through ↓in synaptic transmission.
- Generalized weakness
- Severe acidosis causes
  - Disorientation
  - Coma
  - Death

Alkalosis

•Alkalosis causes over excitability of the central and peripheral nervous systems.

•Numbness

•Lightheadedness

•It can cause :

- Nervousness
- muscle spasms or tetany
- Convulsions
- Loss of consciousness
- Death