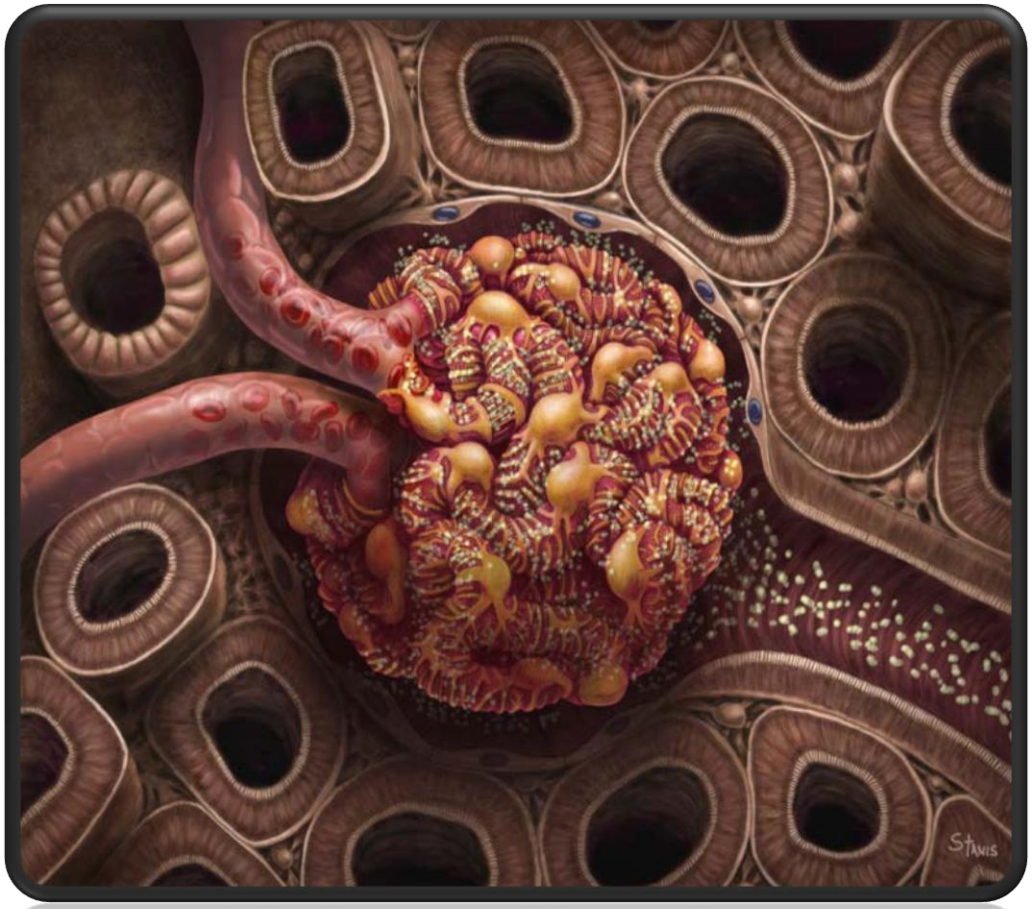
Physiology Team 431



Acid Base System

- Dr.Sitelbanat/Dr. Syed Shahid Habib

Mentioned in the girls' slides

Mentioned in the boys' slides

Explained by the Dr.

Important

Objectives:

- At the end of this lecture student should be able to describe:

1. **Acid-Base balance.**
2. **Normal range of Extracellular pH.**
3. **Identify the body systems that control against Acid-Base Imbalance.**
4. **Identify types of Acid-Base Imbalance.**
5. **Symptoms and signs of Acid-Base Imbalances.**
6. **Treatments for Acid-Base imbalances.**

What is Acid-base balance?

Acid-base balance is a balance of H+ concentration in ECF.

To achieve homeostasis a balance between the intake or production of hydrogen ions and the net removal of hydrogen ions from the body.

PH Review

- pH = - log [H+]

- Mathematically we use the Henderson-Hasselbach equation; because we don't have a constant here (Pka).
- [H^+] represents hydrogen concentration.
- Why we express – log [H^+] as PH ??

Because H ion concentration in blood is low that it is expressed in negative log to the base 10 of H ion conc. " Normal H ion conc. In blood is 40 nmol/L or 0.00004 mmol/L = PH 7.4 "

- If [H+] is high, the solution is acidic; pH < 7

- If [H+] is low, the solution is basic or alkaline ; pH > 7

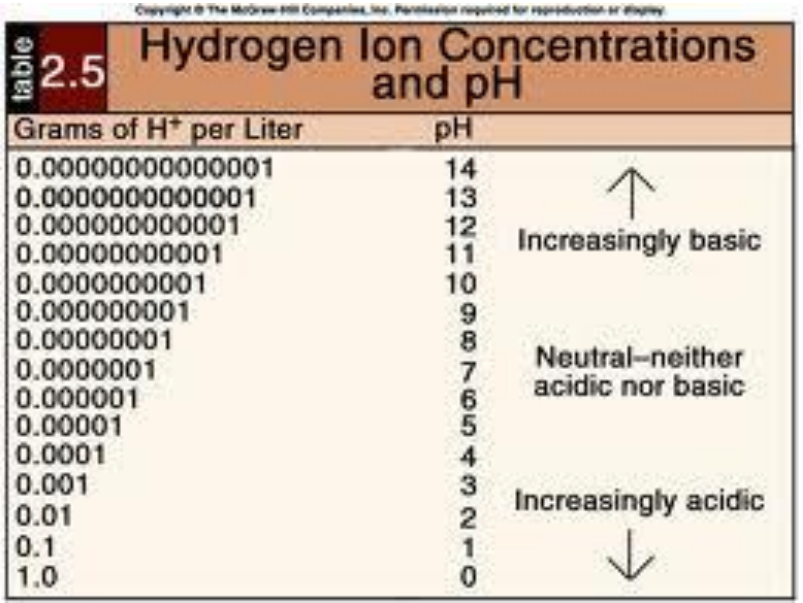


table 2.5 Hydrogen Ion Concentrations and pH

Grams of H^+ per Liter	pH	
0.00000000000001	14	↑ Increasingly basic
0.0000000000001	13	
0.000000000001	12	
0.00000000001	11	
0.0000000001	10	
0.000000001	9	
0.00000001	8	Neutral–neither acidic nor basic
0.0000001	7	
0.000001	6	
0.00001	5	
0.0001	4	
0.001	3	Increasingly acidic ↓
0.01	2	
0.1	1	
1.0	0	

An Acid :

Molecules containing hydrogen atoms that can be released (donate) , hydrogen ions in solutions are referred to as an acid.

Strong acids: completely dissociate in water (HCL, H2SO4). **$HCL \longrightarrow H^{+}+cl^{-}$ (it ionizes completely in an aqueous solution by losing one proton) .**

Weak acid: partially dissociate in water (H2CO3). **" carbonic acid" (partially ionized in their solutions).**

- **A Base:**

is an ion that can accept a hydrogen ion.

An example of a base is is bicarbonate ion (HCO3).

" $HCO_3 + H \longrightarrow H_2CO_3$ "

Extra cellular pH

Extra-cellular PH =7.4 (7.3 to 7.5).

Homeostasis of pH is important for the function of body enzymes.

Acid-base balance can also affect electrolytes. concentration (Na+,K+,Cl-).

Can also affect the function of certain hormones.

Importance of Acid-base balance :

- Having a natural PH balance in the body will enable enzymes to speed up chemical reaction (to function).
- Acid-base balance can also affect electrolyte concentration .. How??

As we know K+ gets secreted in the kidney in exchange for Na reabsorption [Na reabsorbed , K secreted / NA reabsorbed, H secreted] but ,if we have high amounts of H^+ (acidosis) >> K will not be secreted >> Hyperkalemia

- **Blood pH**

Blood pH = 7.35 – 7.45.

Blood pH can be calculated by Henderson-Hasselbach equation

$$PH = pKa + \log_{10} \frac{[Base]}{[Acid]}$$

PKA = constant of Acid.

Relates pH to the Ratio of the Conc. of Conjugate Base and Acid

Acidosis= decrease in arterial pH (< 7.4) due to excess H+.

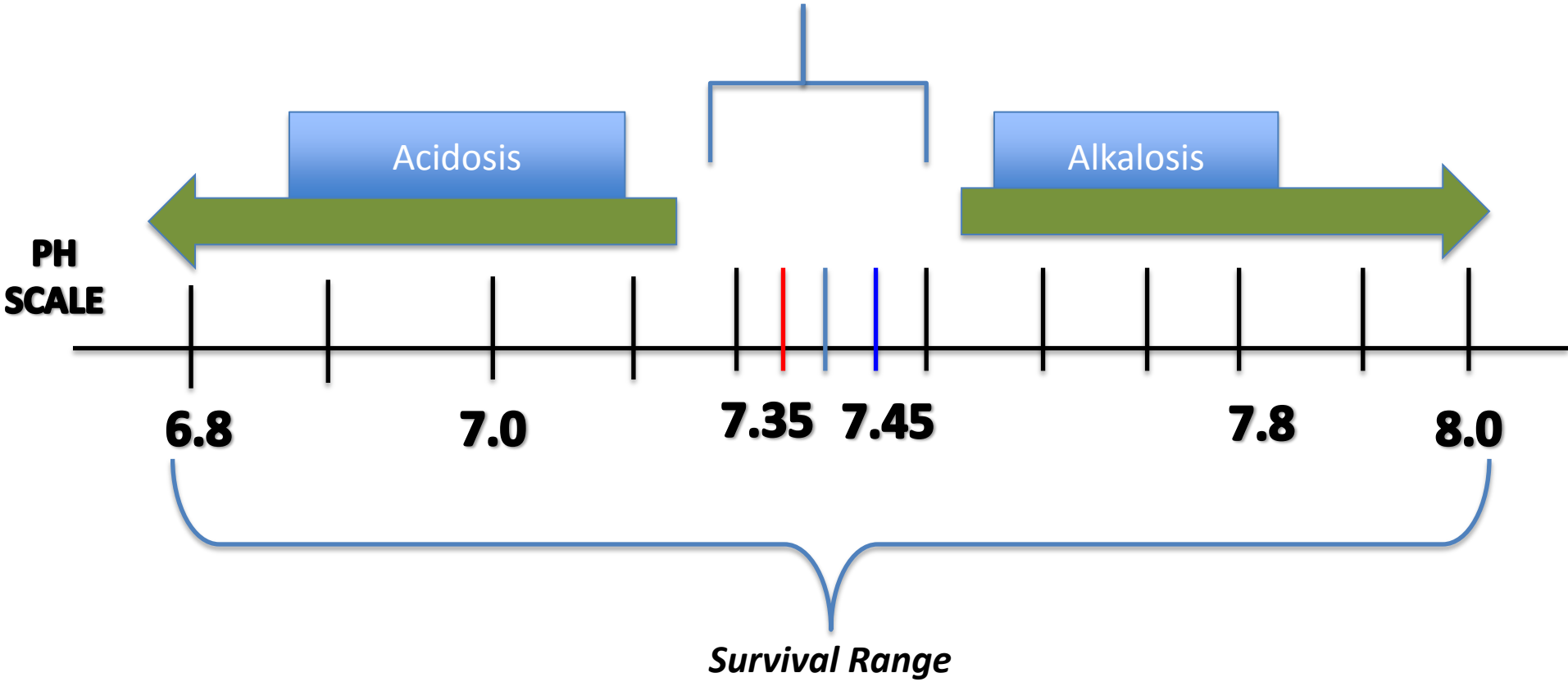
Alkalosis= an elevation in arterial PH (>7.4) due to excess base.

pH < 6.8 or > 8.0 not compatible with life.

If PH < 6.8 , person will pass out → coma !

PH of Arterial Blood

Normal PH range



- **Acid-Base Imbalances:**

In our body base is 20 times more than acid this is why our body has slightly alkaline

- pH< 7.35 acidosis

- pH > 7.45 alkalosis

When changes in the normal PH occur .. The body will try to restore the PH back to normal (compensate)

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

- Is complete if pH brought back within normal limits

<< bring back the PH exactly to normal

- Partial compensation if range is still outside norms.

- **System Compensation**

-If underlying problem is metabolic, We compensate either by hyperventilation or hypoventilation. This is a: respiratory compensation.

-If problem is respiratory, renal mechanisms can bring about metabolic compensation, done by the kidney.

NOTE:
Systems compensate only for PH to bring it back to normal ; so that enzymes activity won't be affected . But they don't compensate for treating the underlying cause or disease. (EX: a person with a respiratory disease, his kidneys will compensate only for PH to bring it back to normal, but he will still have his respiratory problem) !!

- **Normally our body produces more acids than bases**

- Most the things we eat are acidic
- One of the acids that is produced in our bodies is CO_2 (carbon dioxide).
- CO_2 immediately dissolves in water to form H_2CO_3 (CO_2 = volatile acid)

Acids take in with foods

Acids produced by metabolism of lipids and proteins

Cellular metabolism produces CO_2 (volatile acid)

$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO3^-$

- If you have excess amount of CO_2 you will have excess of acid
- Low CO_2 >>>> Less acid in the body

ACID LOAD

Amino Acid Metabolism yields about 50 meq/day for example H2SO4, HCl, and H3PO4

- **CO2 production yields 12,500 meq/day300 L of CO2**
- **Normal daily diet yields 80 meq/day**

- **ACID PRODUCTION**

- **H+ is continually produced by metabolic activity:**
- **Volatile acids: (e.g. carbonic acid, H_2CO_3; formation catalyzed by carbonic anhydrase)**
-
- **$H^+ + HCO_3 \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$**
-
- **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)**

- **Buffers**

Buffer system consists of a weak acid and its conjugate base (or a weak base and its conjugate acid).

Buffers are substances that neutralize acids or bases.

Chemical reactions which reduce the effect of adding acid or base to a solution PH.

- Why neutralize acid and base ?

To prevent drastic changes in the PH.

Example:

If you measured the PH of water it will be equal to 7 .. Add two drops of acid to the water and measure the PH after that it will be equal to 4 (the PH dropped). If the water contains Bicarbonate (which is a buffer) .. After adding the same drops of acid to it, (the PH will drop from 7.4 to 7.35) therefor, it will minimize the changes in PH by taking the excess H^+.

Definition:

Conjugate acids and conjugate bases are characterized as the acids and bases that lose or gain proton.

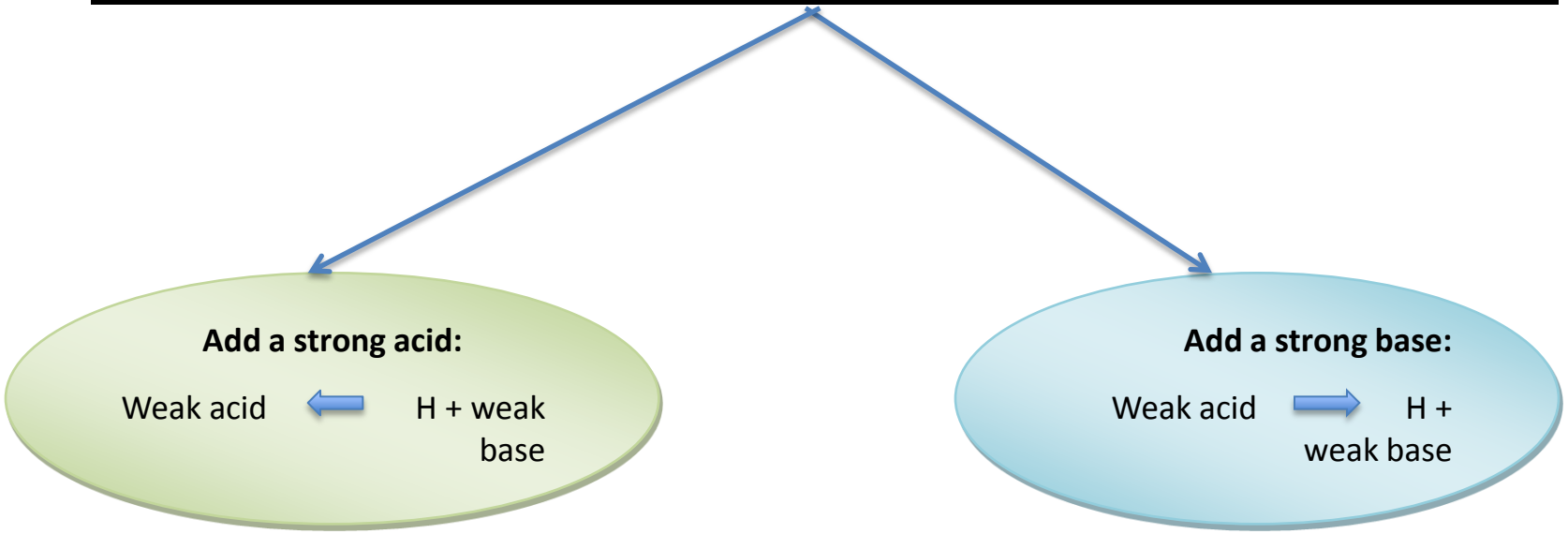
For example, H_2CO_3 is a weak acid, and HCO_3 is its conjugate base.

Note that the conjugate base in this example is “the weak acid” minus one proton “H”.

The main concept of buffers: When you add a strong acid to the body, the body will convert it “by buffers” into weak acid. And when you add a strong base to the body, the body will convert it into weak base. Because weak acids and weak bases are less harmful to the body than the strong ones.

WEAK ACID ⟷ H + WEAK BASE

- **-Direction of the reaction depends on the substance that is added to the body:**



- **How the Body defends against fluctuations in pH ??**

Three Systems in the body, that buffer any excess base or acid in our bodies to prevent changes in the PH.

1-Buffers in the blood. (First line of defense.. This will occur immediately)

2-Breathing through the lungs. (Respiratory system is the 2nd system will come to work /Gets rid of CO_2*getting rid of acids* it works faster than the kidneys , but it won't correct the PH completely)

3-Excretion by the kidneys. (This system will come late, it takes hours-days, BUT IT CORRECTS THE PH 100%)

1 - Blood Buffers

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

- Bicarbonate
- Protein
- Phosphate
- Hemoglobin

- **Bicarbonate Buffer (The best of all)**

Important extra cellular buffer.

BICARBONATE/CARBONIC ACID
HCO_3- "basic part" / H_2CO_3 "acidic part

HCO3=24-28 meq/ml in.

Present in larger quantities.

Can be regulated by respiratory and renal systems.

-How ??

Kidneys reabsorb HCO_3.

Respiratory regulation by CO_2.

- **Bicarbonate Buffer**

- All Buffers consist of weak acid + base.

1

Consist of: weak acid H_2CO_3 and Bicarbonate salt $NaHCO_3$.

HCO_3^- : H_2CO_3 is maintained at a ratio of 20:1

$$\text{pH of bicarbonate} = 6.1 + \log \frac{HCO_3}{0.03 \times PCO_2}$$

If Acid is added : $H^+ + HCO_3 \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$

If Base is added : $NaOH + H_2CO_3 \rightarrow NaHCO_3 + H_2O$

There is a continuous motion between HCO_3 and H_2CO_3 to keep a constant ratio.

2

Henderson-Hasselbach equation for Bicarbonate; 6.1 is the constant [each molecule has a different constant]:

- The upper part is the bicarbonate " you can measure it from the blood"
- The dominator should be the carbonic acid, but it's difficult to measure H_2CO_3 in the blood " so you find the carbon dioxide pressure then multiply it by 0.03" (solubility of CO_2 in water)

- If you add an acid (H) to the system, it will be picked up by the basic part of the buffer, which is the bicarbonate and it will give carbonic acid, which can give CO_2 and water. Therefor, the H^+ is transferred into water>> PH won't be affected by the H^+.

3

- If you add a base (OH) (a hydroxyl gp), it will react with the acid, which is the H_2CO_3. The end-product of the reaction will be sodium bicarbonate ($NahCO_3$) and again water so >> PH won't be affected.

HPO_4^- "basic part" / H_2PO_4 "acidic part"

- **Phosphates & Intracellular buffers:**

IMPORTANT NOTE: A pKa of 6.8 Makes Phosphate a Good Buffer in ECF. However, its plasma conc. is low (about 1 mmol/L) unlike HCO_3^- which is 24 mmol/L. Which make HCO_3 the major ECF buffer.

- Phosphate is an intra and extracellular buffer
- Minor role compare to HCO3 or HB.
- Intracellular buffers (proteins & phosphate) are needed because H does not cross PM. PM=Plasma membrane
- Intracellular pH is more acidic (7.2)

- Equationally, Phosphate is a better buffer than the bicarbonate .. Why??

Because the Pka of the phosphate is nearer to 7.4 (higher than the pka of bicarbonate)

- But phosphate isn't abundant as bicarbonate (It's mainly an intracellular buffer).
- Intra cellular PH is more acidic, because there is a lot of metabolism that is producing H ions inside the cell.

Proteins are known to be (**Zwitter ions**), which mean, they act as an acid in basic environment & as a base in acidic environment.

- **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. >> opposite to bicarbonate (here if you used all proteins you can't add more)

2- Respiratory regulation of pH

-Maintain normal ECF pH by changing the rate and depth of breathing to maintain constant PCO2 (volatile acid).

-Controlled by chemoreceptors.

-Respiratory sys doesn't affect fixed acids like lactic acid.

-increase in PCO2 → decrease pH

Hyperventilation reduces CO_2 in the blood. " washing out "

Respiratory system doesn't get rid of lactic acid accumulation.

↑PCO_2 = acid is high = PH is low.

3- 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 new bicarbonate ions.

Kidney is the most effective regulator of pH.

If kidneys fail, pH balance fails

- H is secreted in exchange for Na or by special H channels.
- Kidney is more efficient than any other system in bringing PH back to normal.
- If there is alkalosis the kidneys will not reabsorb HCO_3 , instead they get rid of it by excreting it in the urine.
- The kidney itself can use glutamine to make new bicarbonate.
- In Renal Failure >> acidosis occur.

-In acid-base balance, the kidney is responsible for 2 major activities:

- **1- Re-absorption of bicarbonate**

-Since our body is slightly alkaline, and the **Bicarbonate** is the predominant extracellular buffer against the acids in the body, kidneys will try to re-absorb it after it is filtrated to keep the buffer system working properly.

2- Excretion of Non-volatile acids

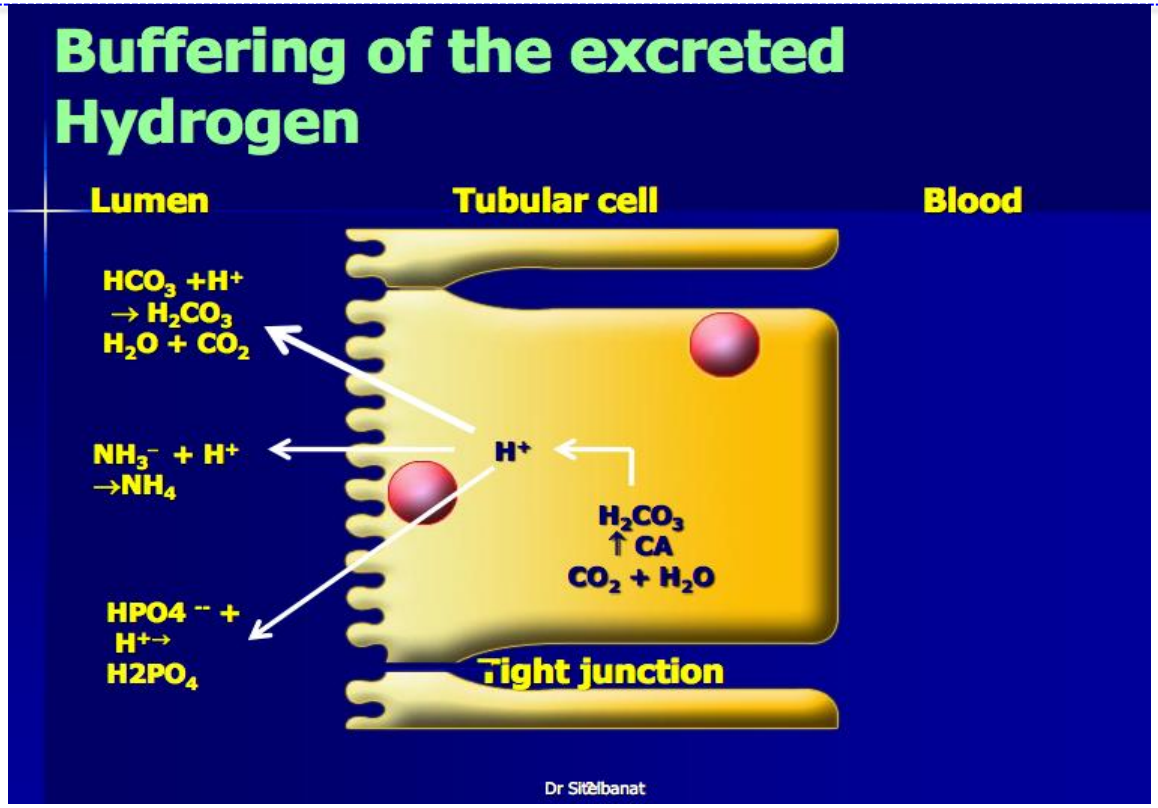
-**The lungs** are responsible for excretion of CO_2 (**the volatile acid**).

-The remaining acids (**NON-volatile acids**) is excreted by **the kidneys**.

H^+ inside the filtrate should be buffered, so that the urine won't be very acidic.

- H^+ secreted in the urine can combine with HCO_3 to give water and carbon dioxide.
- It can combine with ammonia to give ammonium.
- It can combine with phosphate to give dihydrogen phosphate.

Acidic urine will destroy the renal tubules !!



- **Diagnosis of Acid-Base Imbalances**

1. pH low (acidosis) or high (alkalosis).

2. If pCO_2, is abnormal the problem is respiratory. If $HCO3^-$ is abnormal the problem is metabolic.

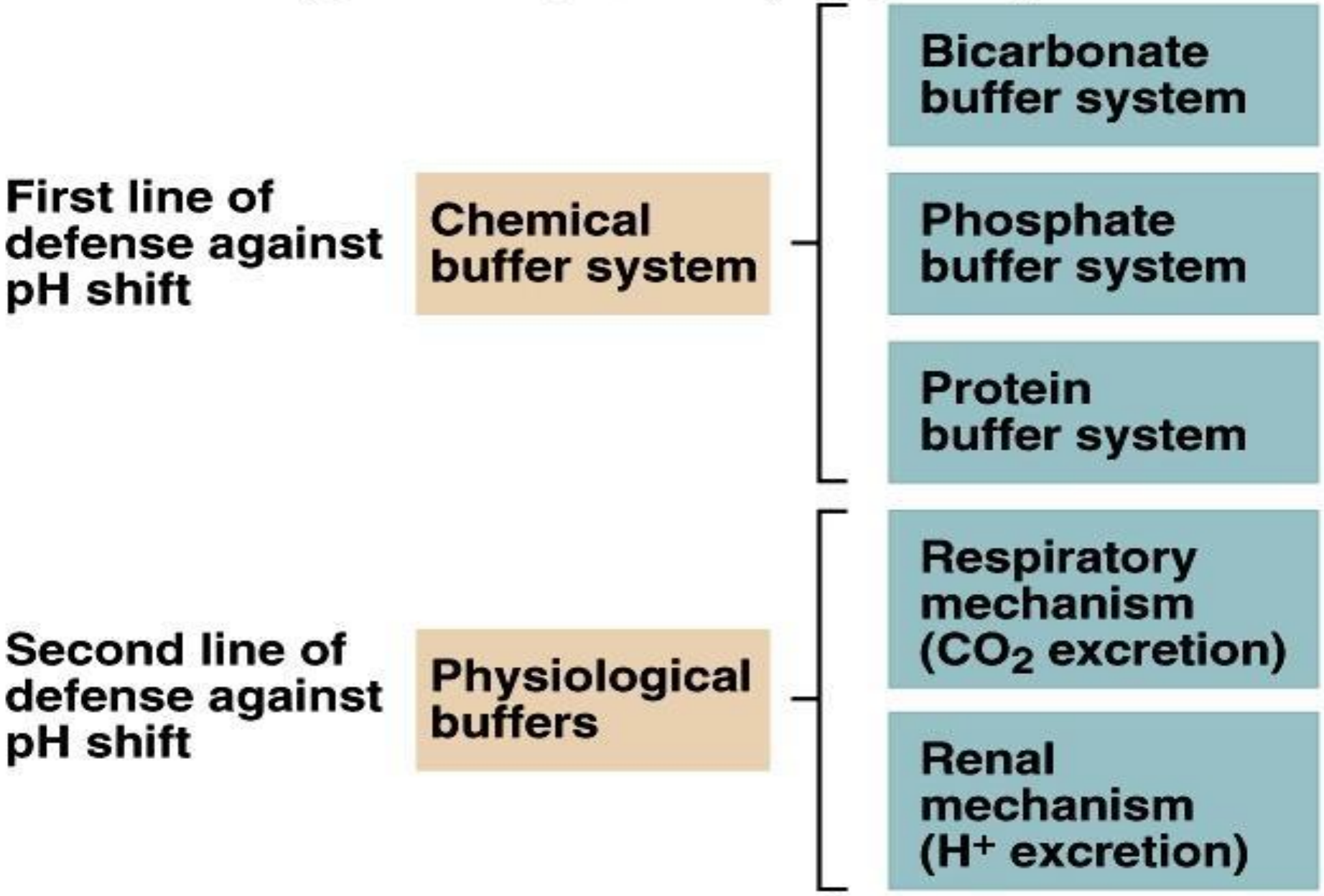
3. If pH is within the normal range, there is full compensation. If it is outside the normal range, the body is partially compensating for the problem.

- To diagnose Imbalances :
- Measure PH , PCO_2 and HCO_3.
- Explanation for #3: IF PH is 7.4 and PCO_2 is 60 >> he/she has a respiratory acidosis but the PH here is normal ?!! >> so this means there is a full compensation by the kidneys.

- **Compensation**

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

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

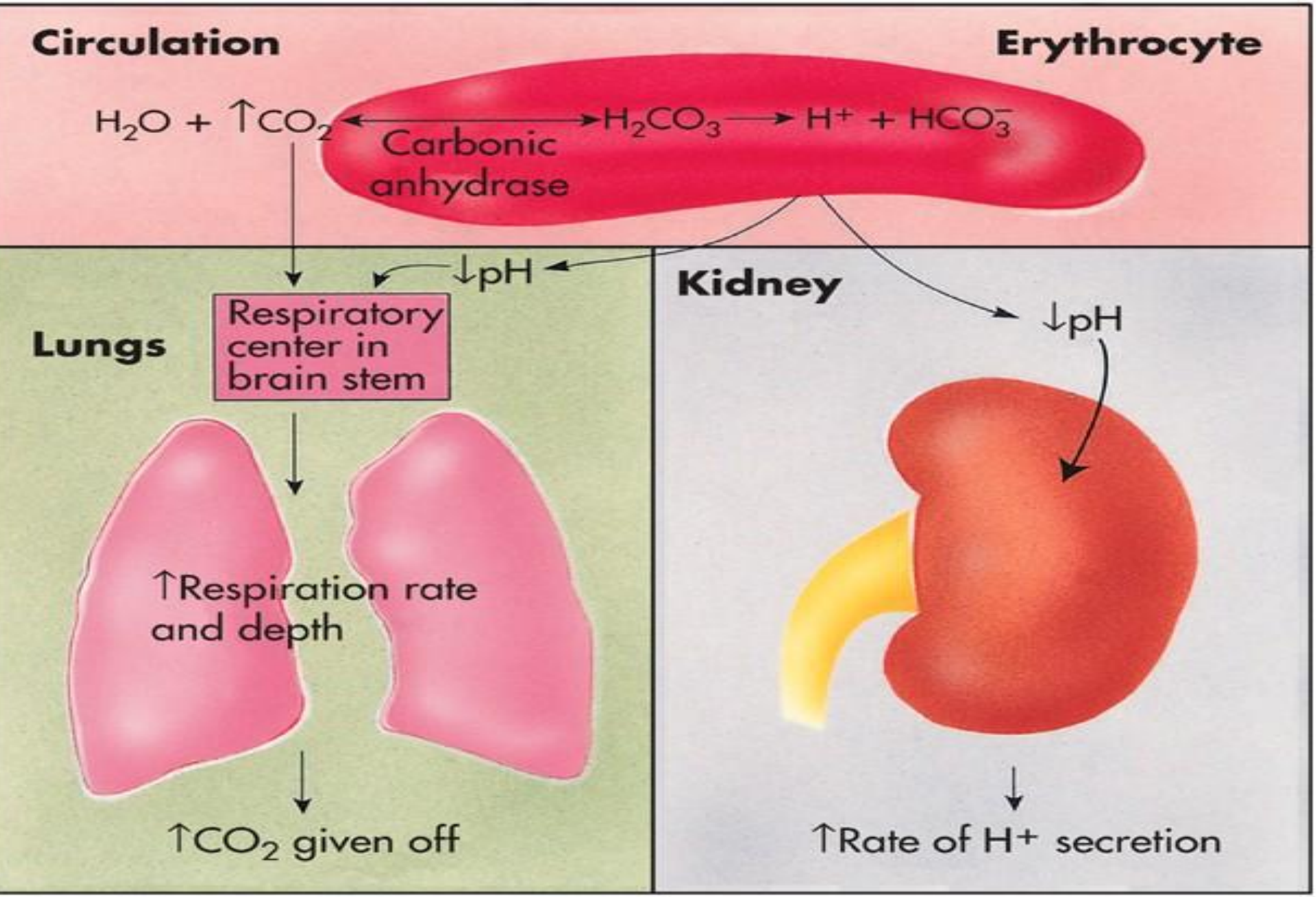


- **Rates of correction**

Buffers function almost instantaneously.

Respiratory mechanisms take several minutes to hours.

Renal mechanisms may take several hours to days.



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

- **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**

- Respiratory Alkalosis
- Respiratory Acidosis
- Metabolic Alkalosis
- Metabolic Acidosis

- **Acidosis**

Principal effect of acidosis is depression of the CNS through ↓ in synaptic transmission.

Generalized weakness.

- **Severe acidosis causes:**
- **– Disorientation**
- **– coma**
- **– death**
- **Best EX: is Diabetic Ketoacidosis !!**

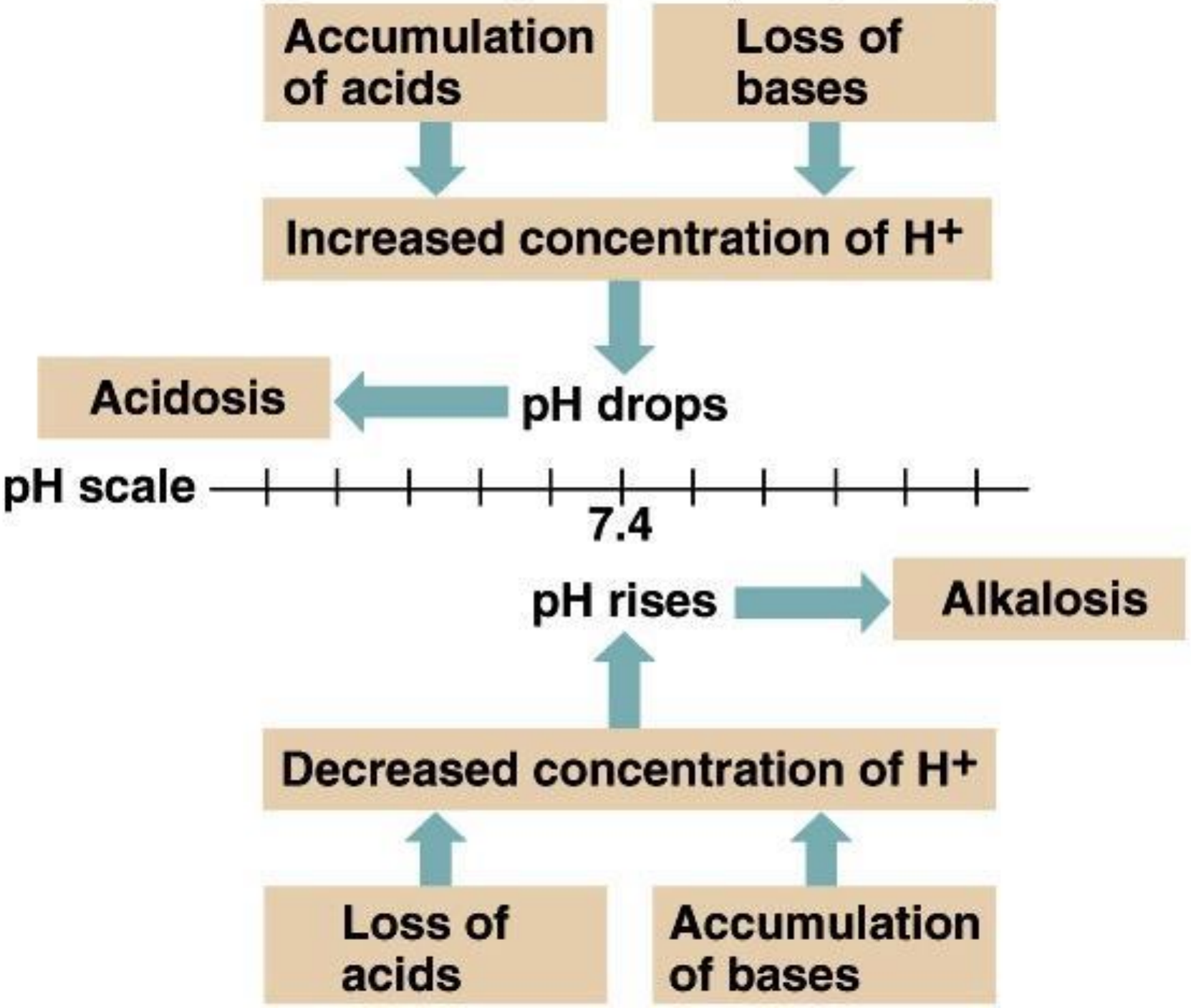
- **Alkalosis**

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

Numbness.

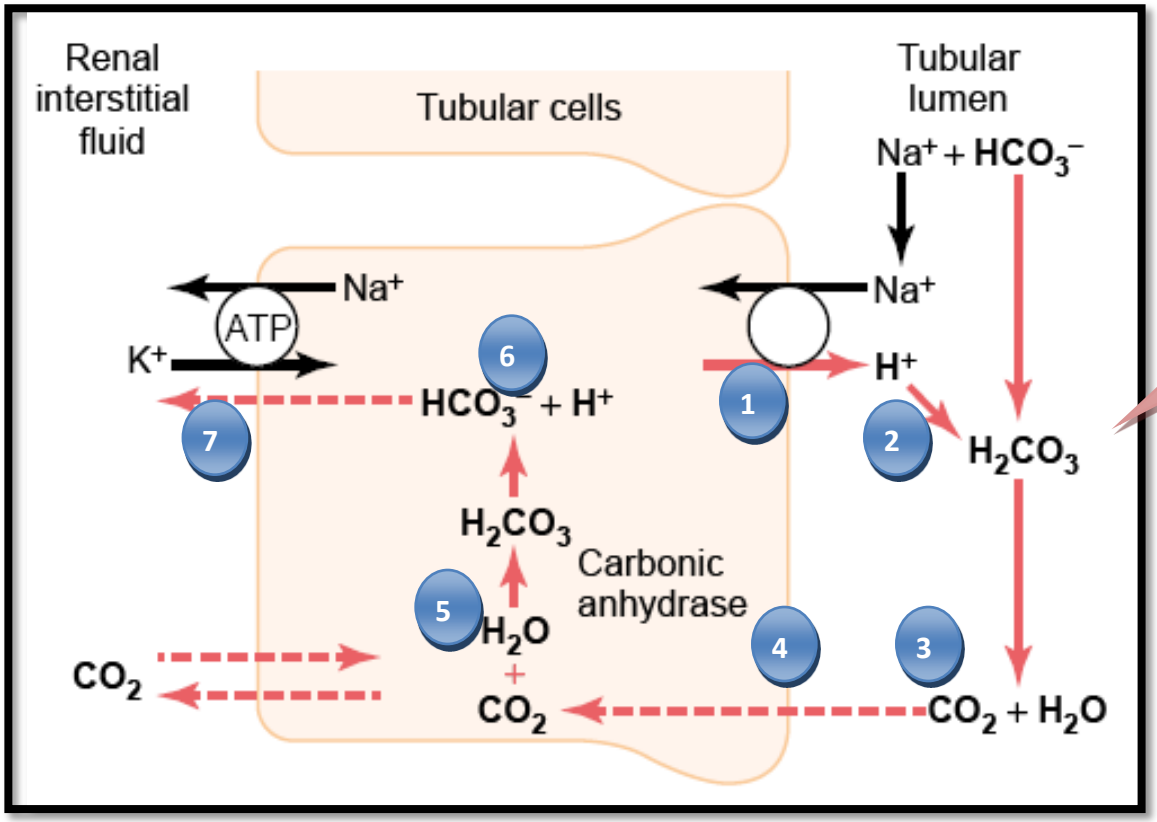
Lightheadedness.

- **It can cause :**
- **– Nervousness**
- **– muscle spasms or tetanic**
- **– Convulsions**
- **– Loss of consciousness**
- **– Death**



-Hydrogen Secretion:

•In (Proximal tubules + Ascending loop of Henle + Early Distal tubules)



This process is known as:

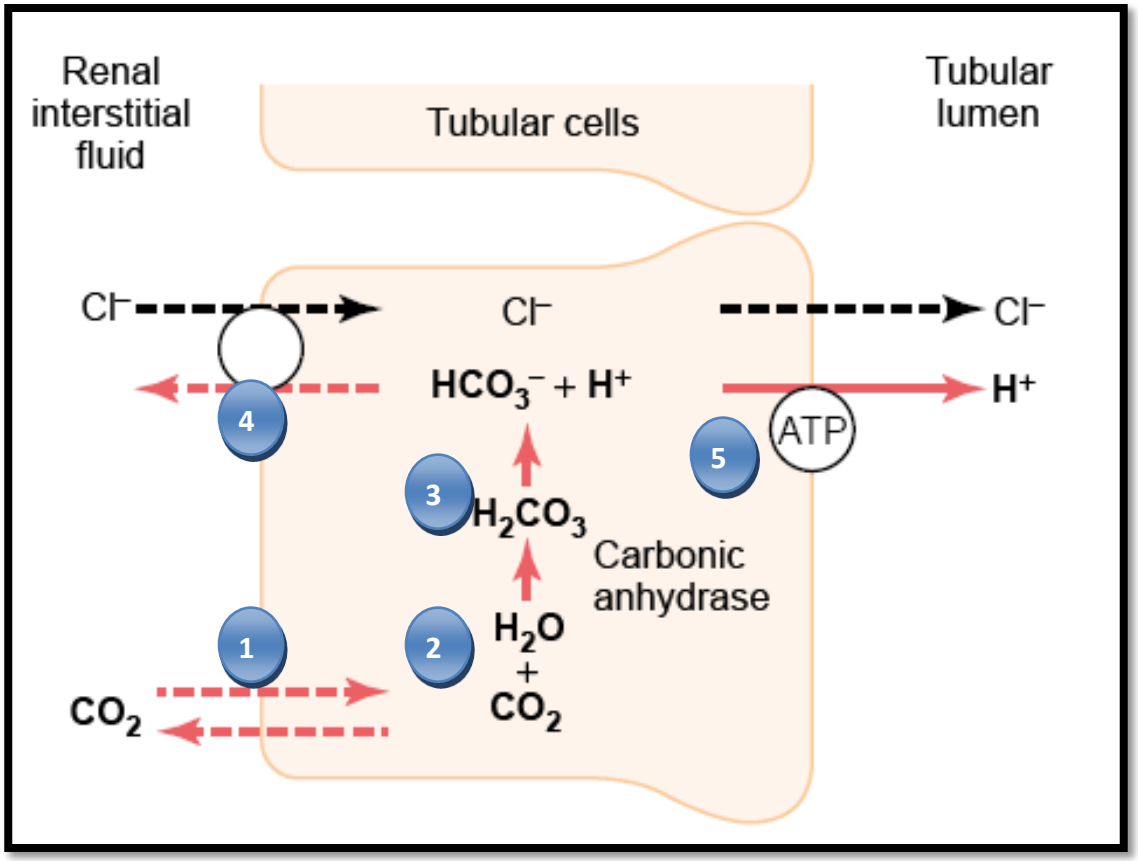
Titration of Bicarbonate with Hydrogen.

1: Hydrogen is secreted by the sodium-hydrogen counter transport.
2: The secreted Hydrogen binds with the bicarbonate in the filtration and form carbonic acid.
3: The carbonic acid breaks into (water & carbon dioxide).
4: The carbon dioxide diffuse into the cell.
5: CO_2 combines with water and form carbonic acid. (in presence of Carbonic anhydrase).
6: Carbonic acid will break into (Hydrogen & Bicarbonate).
7: Bicarbonate is re-absorbed.
8: same as 1. And repeat the cycle.

B- In (Late distal tubules + Collecting Tubules):

-They have two types of cells, principal cell & intercalated cell. This mechanism depends on the intercalated cell.

-Intercalated cell has H-ATPase & H/K-ATPase



-Normally, α intercalated cells are more oftenly used in the kidney, since our body is more alkaline. But in some cases, when the person is taking more alkaline food, the body will become more alkaline than normal, and in response, the kidney will start to secrete bicarbonate by the β intercalated cell . (e.g. Vegetarian people)

1: CO_2 diffuse into the cell from the interstitial tissue.

2: CO_2 combines with water and form carbonic acid. (in presence of Carbonic anhydrase).

3: Carbonic acid will break into (Hydrogen & Bicarbonate).

4: Bicarbonate is re-absorbed.

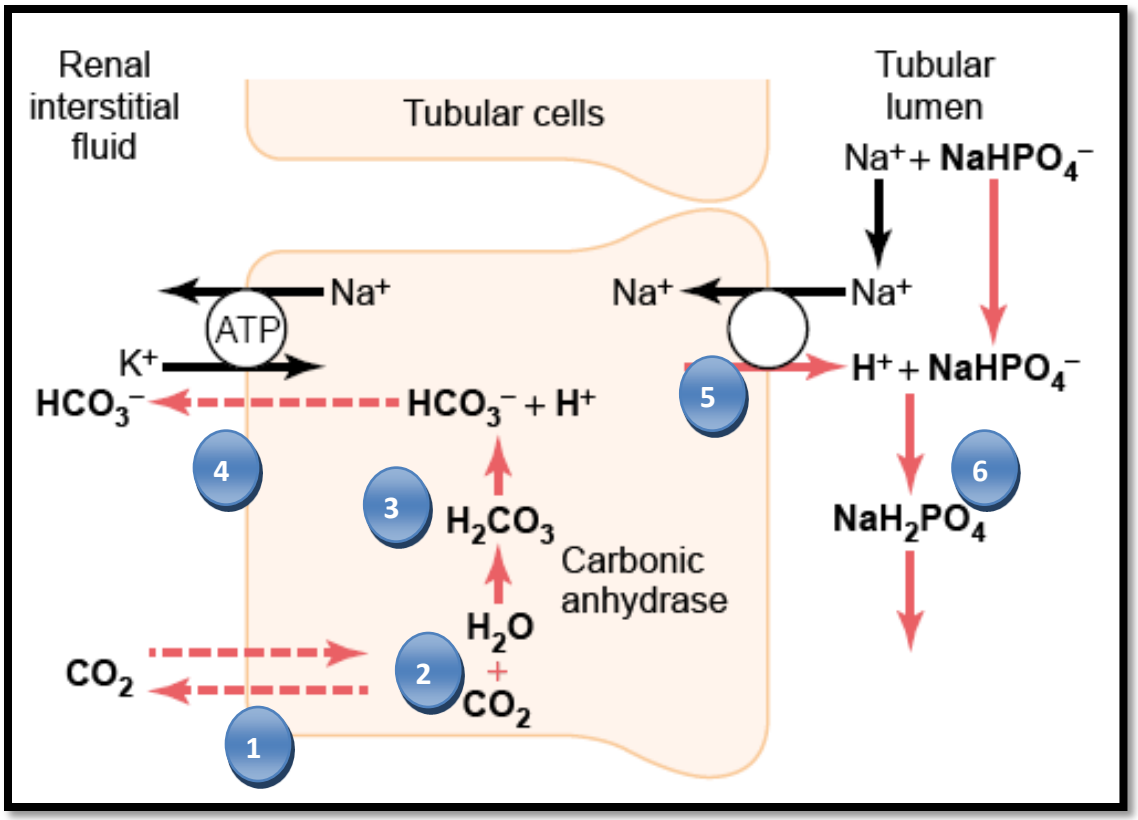
5: Hydrogen is secreted through the Hydrogen pump. "primary active transport"

-There are two types of intercalated cells:

- ***α* intercalated cell for acid-secretion.**
- ***β* intercalated cell for bicarbonate-secretion.**

-Phosphate Buffer System:

•In (Proximal tubules + Ascending loop of Henle + Early Distal tubules)



1: CO_2 diffuse into the cell.

2:CO_2 combines with water and form carbonic acid. (in presence of Carbonic anhydrase).

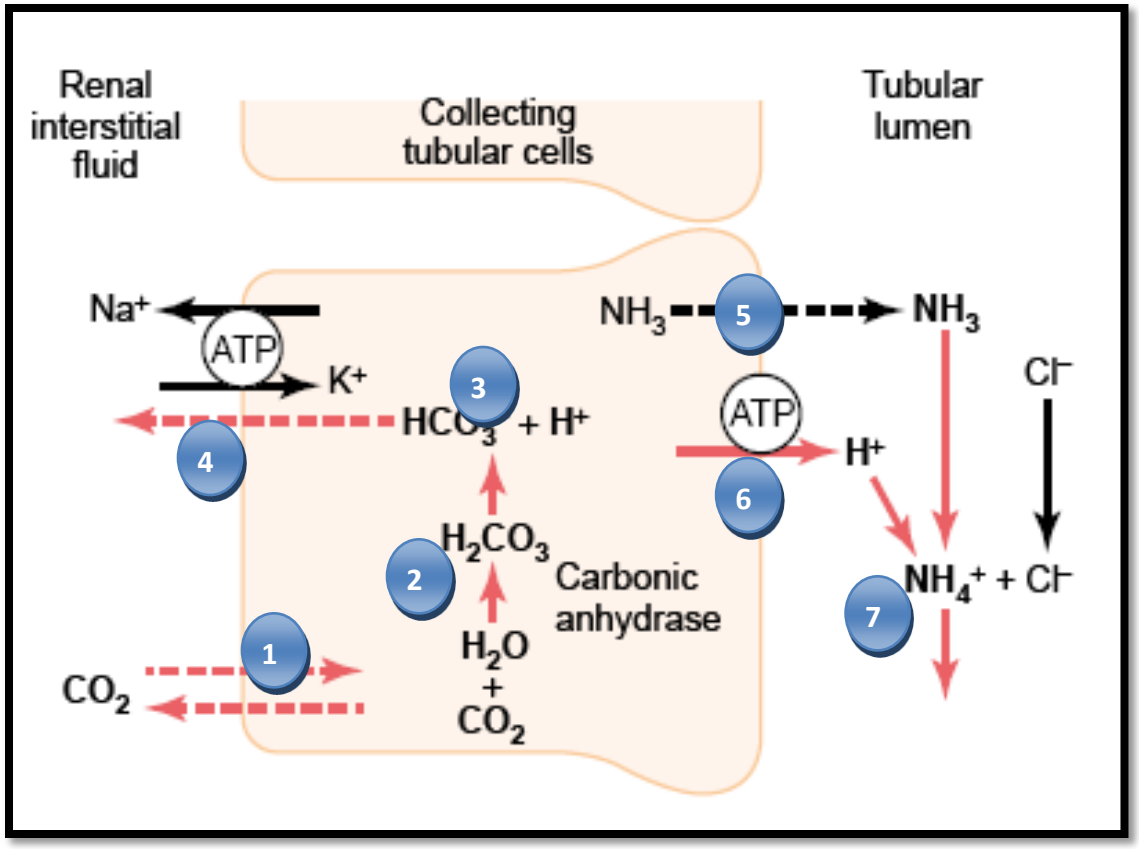
3: Carbonic acid will break into (Hydrogen & Bicarbonate).

4: Bicarbonate is re-absorbed.

5: Hydrogen is secreted by the sodium-hydrogen counter transport.

6: Hydrogen will bind to (sodium mono-hydrogen phosphate) and make (sodium Di-hydrogen phosphate), Which is excreted.

Collecting Tubules:•



1: CO_2 diffuse into the cell.
2:CO_2 combines with water and form carbonic acid. (in presence of Carbonic anhydrase).
3: Carbonic acid will break into (Hydrogen & Bicarbonate).
4: **Bicarbonate is re-absorbed.**
5: Ammonia is secreted by diffusion from the cell into the filtrate.
6: **Hydrogen is secreted through the Hydrogen pump. "primary active transport"**
7: **Hydrogen binds with ammonia to form ammonium which is eventually excreted.**

Summary:

- **The body pH must remain in normal range so the body enzymes can function normally.**
- **Any change in pH will affect the normal body function.**
- **There certain mechanisms that adjust any changes in body pH.**
- **Chemical buffers are the 1st line in correcting the changes in pH.**
- **Chemical buffers characterised by converting a strong acid when added into a weak acid, OR converting strong base when added into a weak base.**
- **Bicarbonate is the predominant extracellular buffer against the acids in the body.**
- **Respiratory response is the 2nd line in correcting changes in pH.**
- **Respiratory response is characterised by controlling the ventilation (hypo or hyper) based on the pH value.**
- **Renal Control is the 3rd line in correcting pH changes.**
- **Renal control is based on:**
- **1- excrete non-volatile acids & 2- re-absorption of bicarbonate.**

Questions:

- **Regarding a person who is taking a very deep and rapid breathes, which ONE of the following statements is correct?**

- His pH is decreasing, and CO2 is increasing.
- His pH is increasing, and CO2 is increasing.
- His pH is increasing, and CO2 is decreasing.
- His pH is decreasing, and CO2 is decreasing.
-
- **Which ONE of these systems is NOT included in the major buffer systems in the body?**
- lactic acid buffer system.
- carbonic acid/bicarbonate buffer system.
- phosphate buffer system.
- protein buffer system.
-
- **The reaction between CO2 and H2O is catalyzed by.....?**
- angiotensin-converting enzyme.
- carbonic anhydrase.
- sodium bicarbonate.
- phosphate.

Answers:
1:C 2:A 3:B