Renal Block

Physiology Team

9th Lecture

Basics of Acid-Base Balance

this lecture is done by:

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10th Lecture

Buffer System

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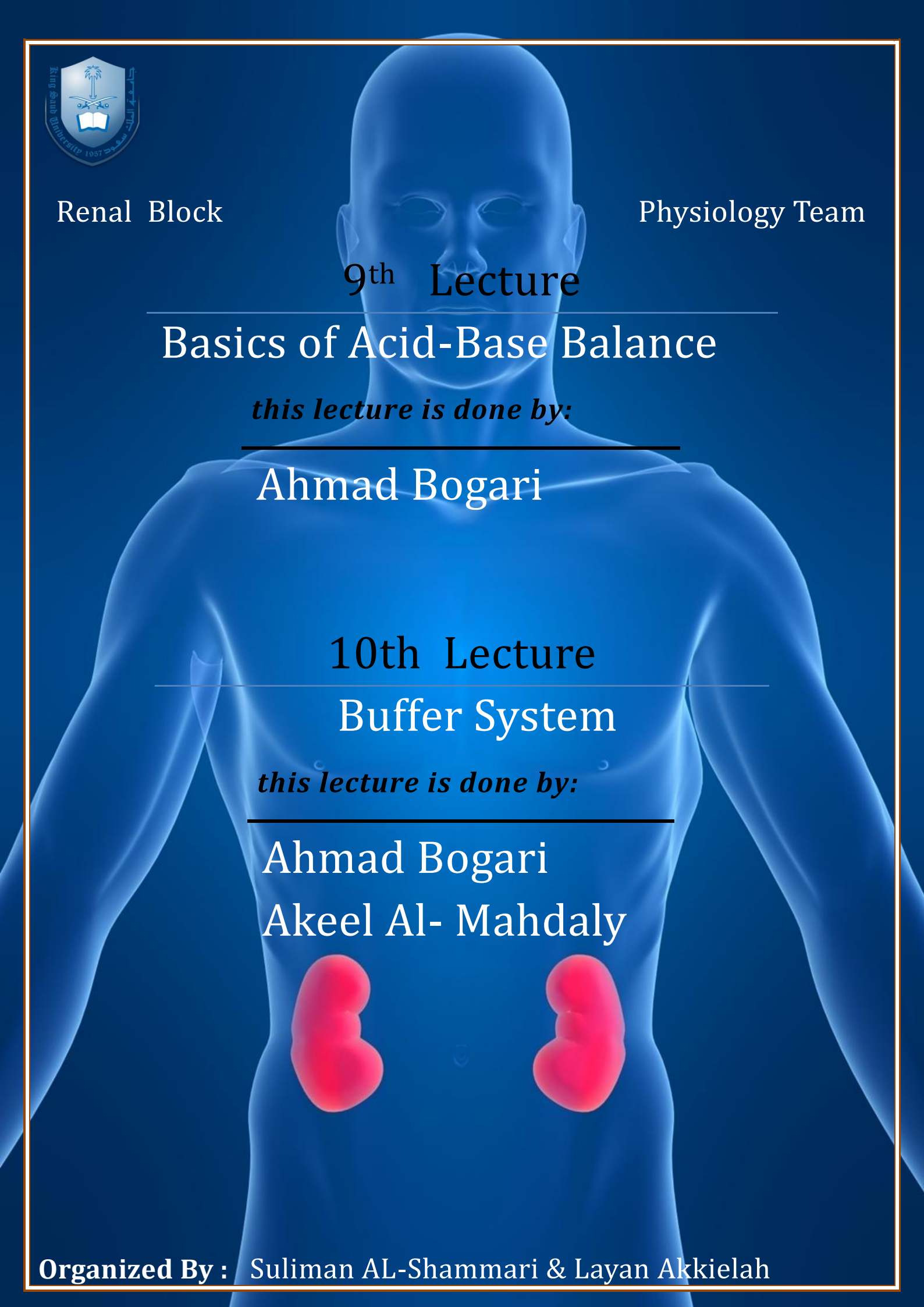


Organized By : Suliman AL-Shammari & Layan Akkielah

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 Review :

•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 which is equal to pH 7.4

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.

An Acid :

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

A Base :

- Bases are ions or molecules that bind free H+ and remove it from a solution (accept a hydrogen ion).
- 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)

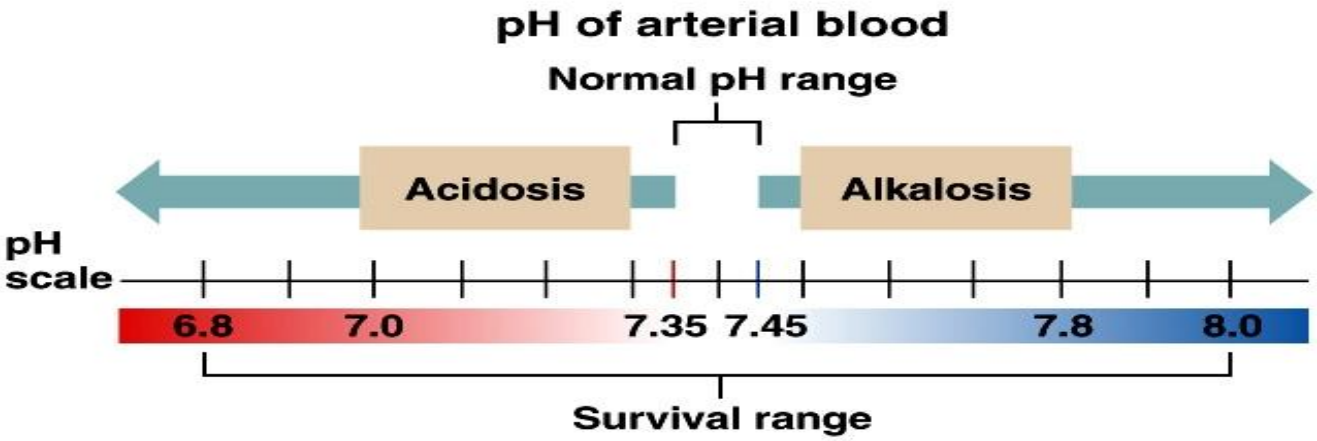
- Homeostasis of pH is important for the function of body enzymes, certain hormones and electrolytes concentration (Na+, K+, and Cl-)
- Blood pH = 7.35 –7.45 (normal pH: around 7.4)
- Blood pH can be calculated by Henderson-Hasselbach equation
- pH = pKa+ log10 [Base]/[Acid]

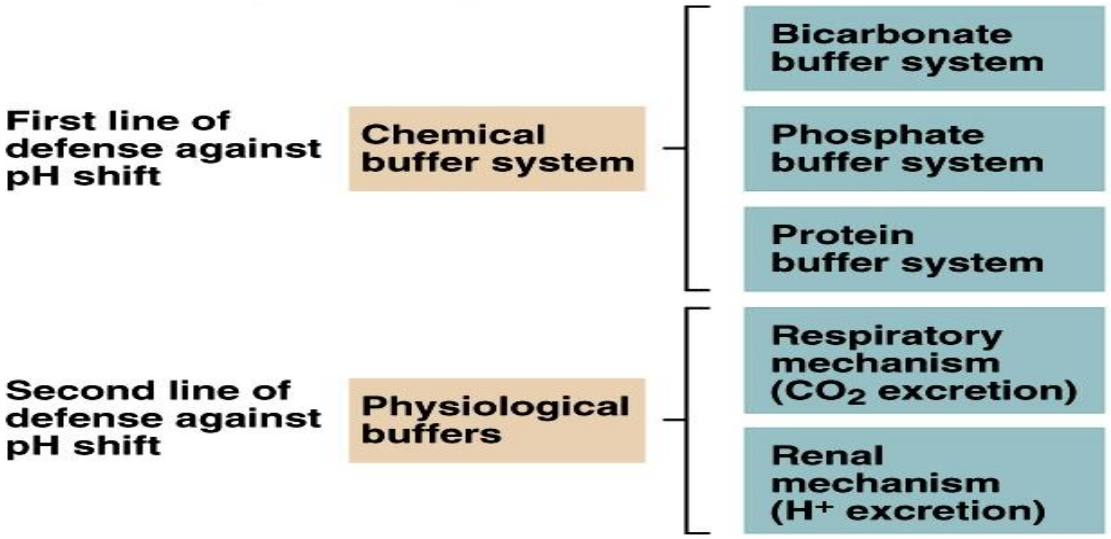
Note: Arterial blood pH = Blood pH = Extracellular fluid pH

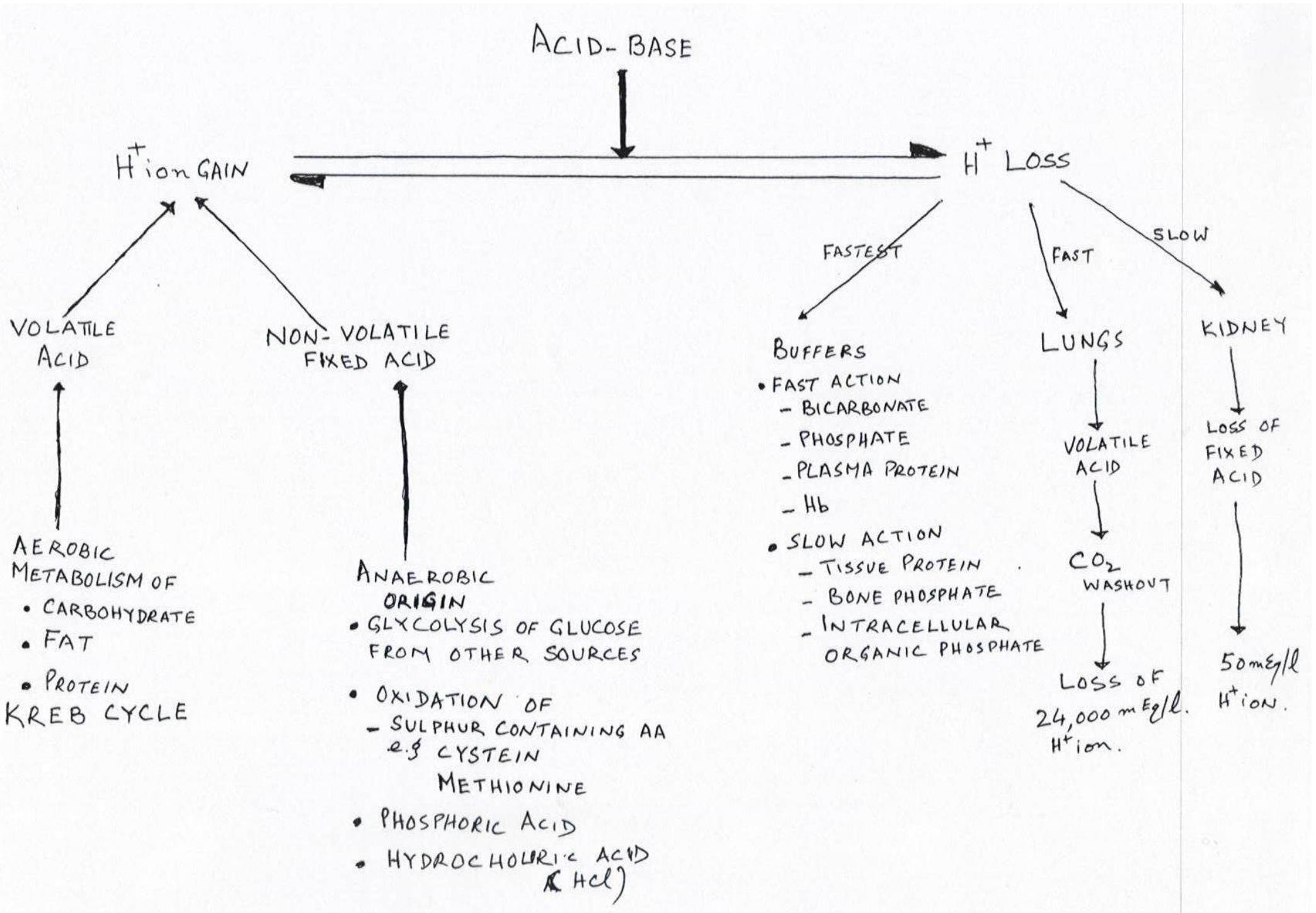
- Acidosis= decrease in arterial pH (< 7.4) due to excess H+ (pH< 7.35 = acidosis)
- Alkalosis= an elevation in arterial PH (>7.4) due to excess base (pH > 7.45 alkalosis)
- At pH < 6.8 or > 8.0 death occurs

- 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)
- $CO_2 + H_20 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
- All acids produced in the body are nonvolatile except carbonic acid.

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).






ACID-BASE
H+ ion GAIN
H+ LOSS
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
• HYDROCHLORIC ACID (HCl)
FASTEST
FAST
SLOW
BUFFERS
• FAST ACTION
- BICARBONATE
- PHOSPHATE
- PLASMA PROTEIN
- Hb
• SLOW ACTION
- TISSUE PROTEIN
- BONE PHOSPHATE
- INTRACELLULAR ORGANIC PHOSPHATE
LUNGS
VOLATILE ACID
CO_2 WASHOUT
LOSS OF 24,000 mEq/l. H^+ ion.
KIDNEY
LOSS OF FIXED ACID
50 mEq/l H^+ ion.

Buffers :

- Buffer is an agent that minimizes the change in pH when an acid or base is added (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)

Buffer power :

- Depends on relative amount of acid and base in a buffer solution
- It is maximum when both are in equal amounts

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

- If the pH of medium is near pK of buffer system it becomes more effective
  - Buffers take up H+ or release H+ as conditions change
  - Buffers do not eliminate H ion but they soak H ion as sponge soaks water.
  - 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

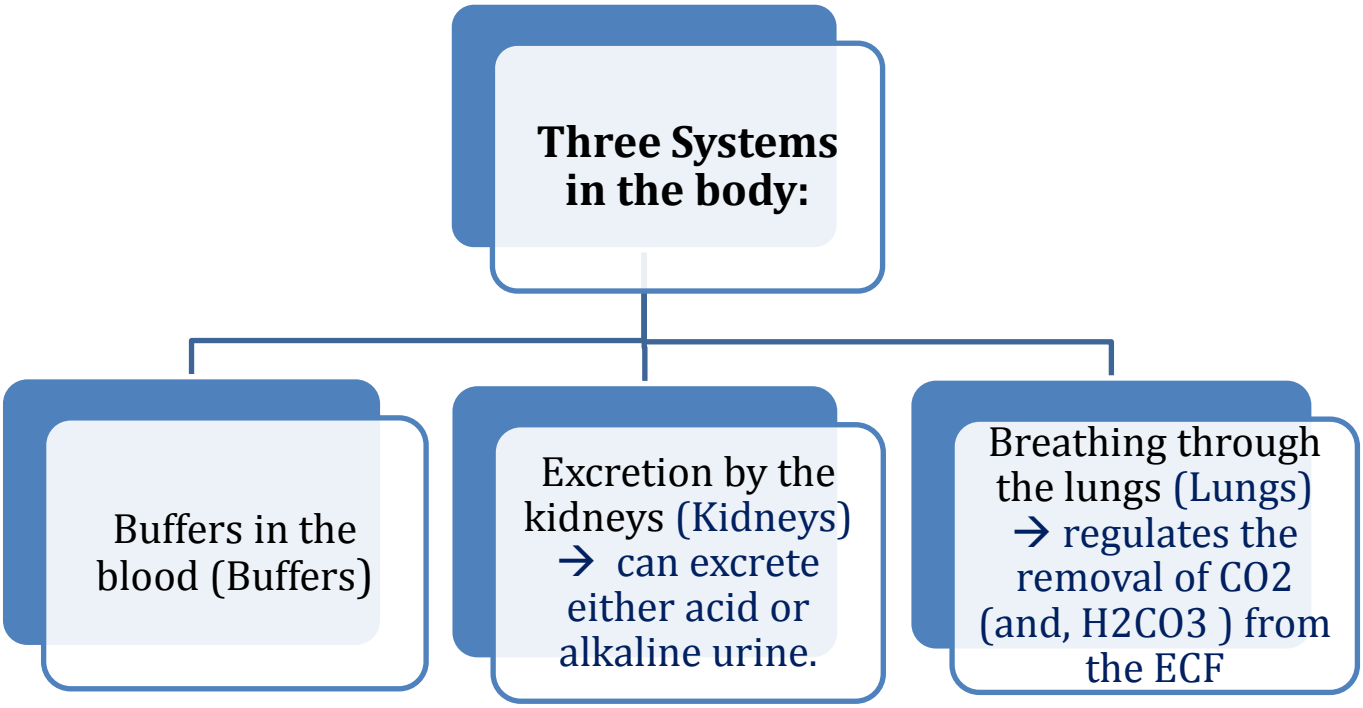
Buffer + ↑↑ H^+ ↔ H

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

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.



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 Buffers**
  - Bicarbonate buffer system (Blood)
  - Phosphate buffer (Kidney)
  - Ammonia

- **Intracellular Buffers**
  - Proteins (all the cellular elements which contains protein)
  - Phosphate
  - Hemoglobin
  - 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	• HCO3 = 24-28 mEq/ml
• Present in larger quantities	• Water solution consists of: weak acid H2CO3 and Bicarbonate salt NaHCO3
• Can be regulated by respiratory and renal	• HCO3-:H2CO3 Maintain at a ratio of 20:1
• $pH = 6.1 + log \frac{HCO3}{0.03 \times Pco2}$	
• If Acid is added – H+ + HCO3 ↔ H2CO3 ↔ CO2 + H2O (And excess CO2 greatly stimulate respiration, which eliminates the CO2 from the ECF)	• If Base is added – NaOH + H2CO3 ↔ NaHCO3 + H2O

- ↓ CO2 → the decreased CO2 in the blood inhibits respiration and decreases the rate of CO2 expiration.

- The rise in blood HCO3 that occurs is compensated for by increased renal excretion of HCO3.

Note: It is not only the amount of base and acid that is important but the ratio between them must remain constant

Phosphates & Intracellular Buffers

Note:

- 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.
- 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).
  - Desoxygenated Hb (deoxygenated) (H^+ + Hb ↔ HHb)

Respiratory regulation of pH :

- Maintain normal ECF pH by changing the rate and depth of breathing to maintain constant PCO2 (volatile acid) (متقلب , سريع الزوال)
- Controlled by chemoreceptors
- **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^+

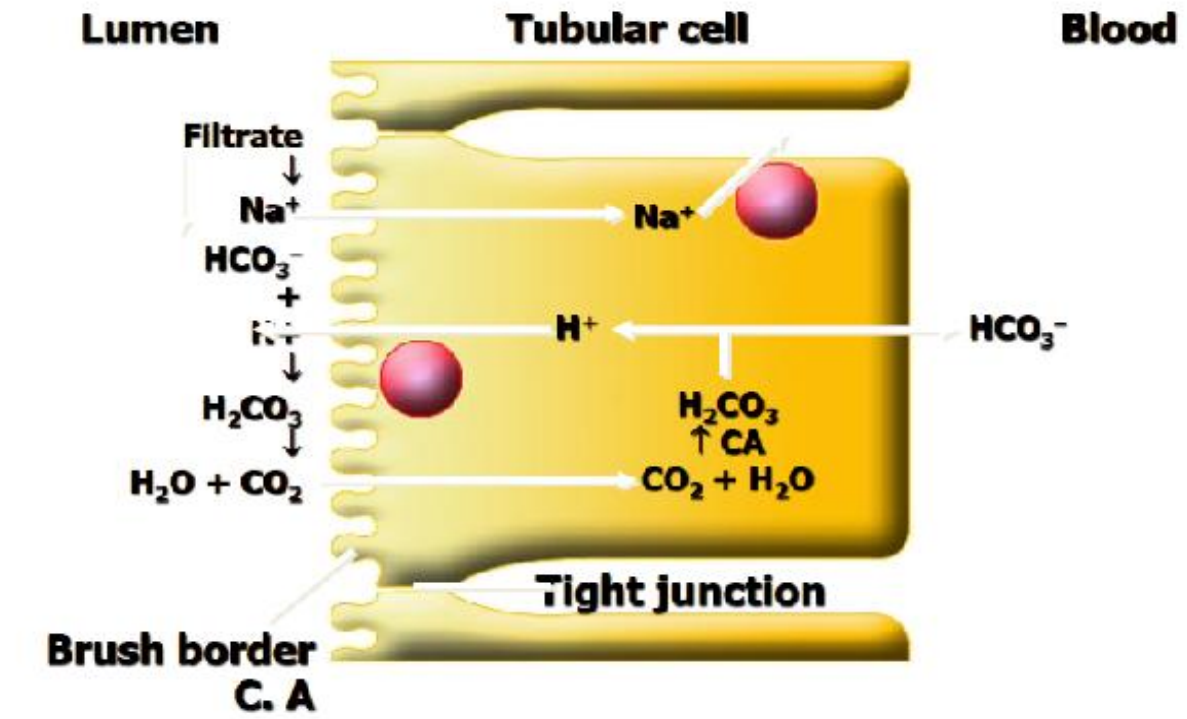
■ Kidney excretion :

- 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**



-- 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)

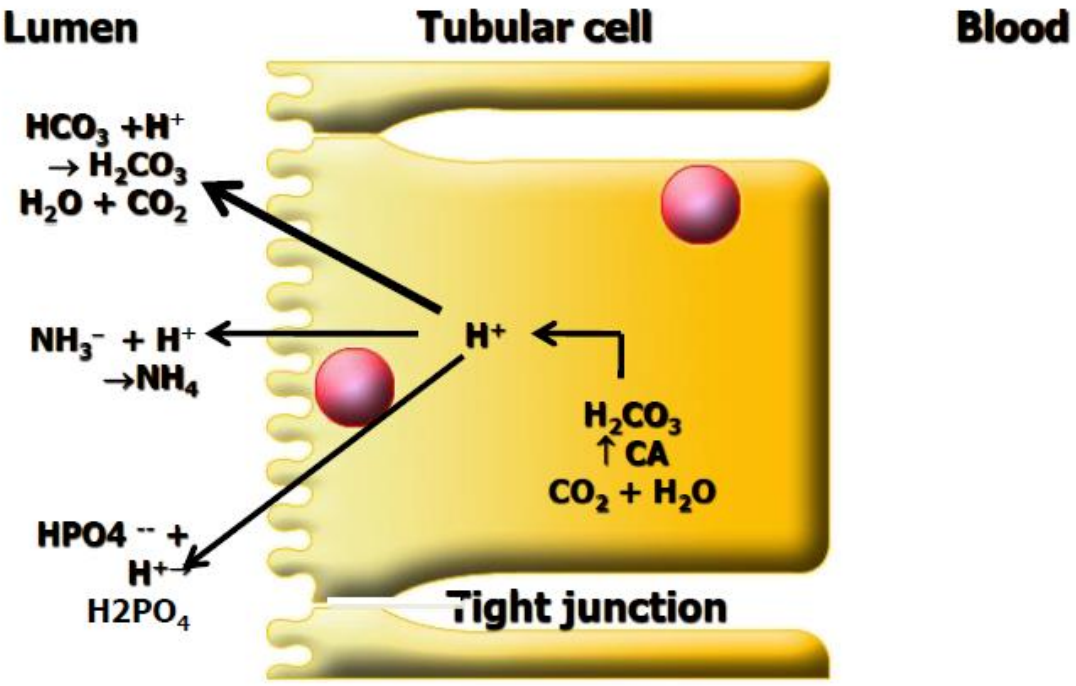
-- Buffering of Secreted H+ with ammonia buffer

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

Ammonia: NH3 / NH4+

- pK = 9.0
- used to buffer the urine

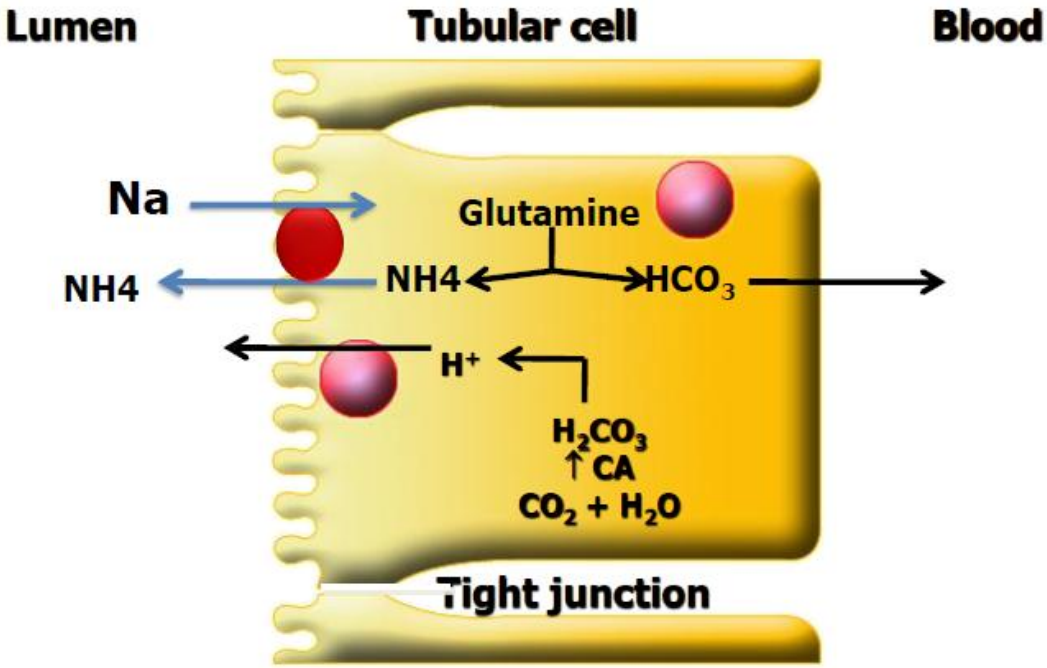
Buffering of secreted and the excreted Hydrogen in urine



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+

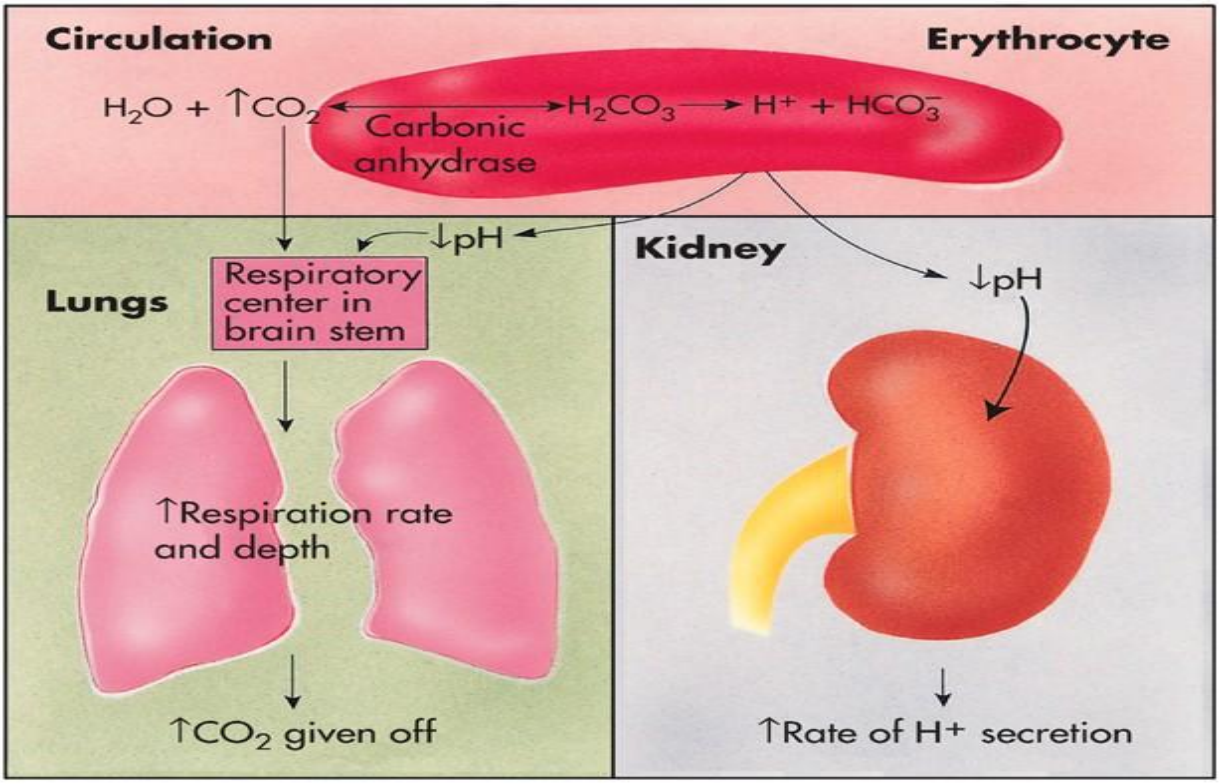
Formation of new Bicarbonate



Diagnosis of Acid-Base Imbalances :

- 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.
- 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.

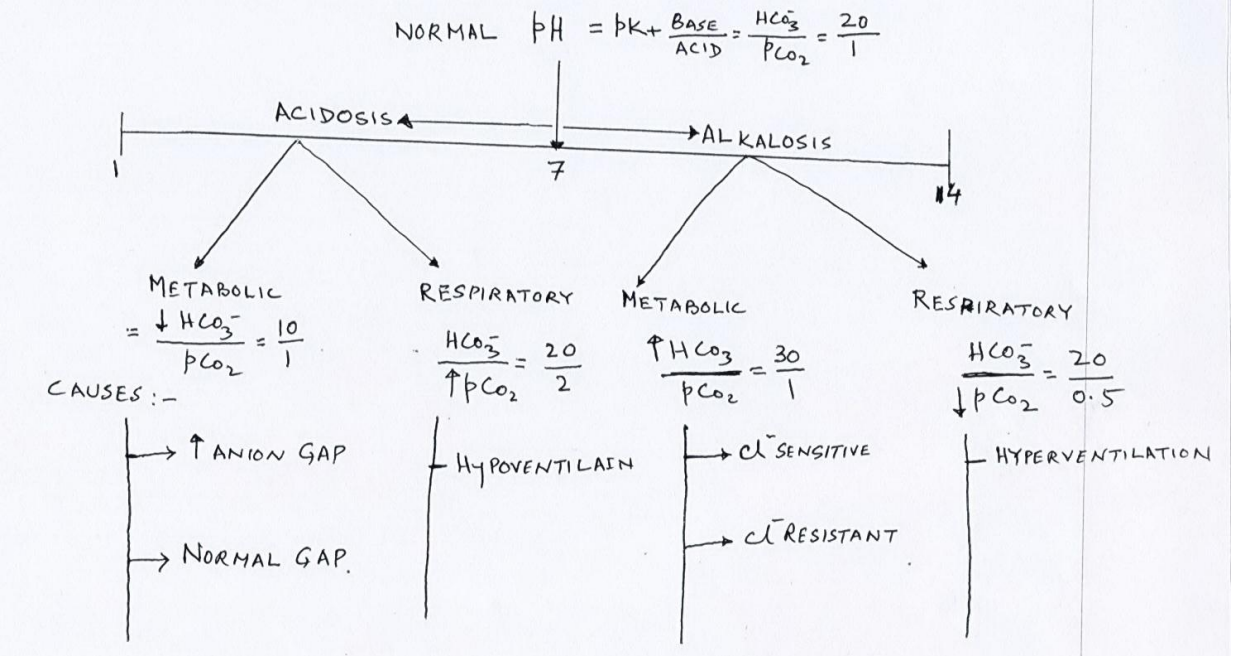
The body response to acid-base imbalance is called **compensation**



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

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

2. Alkalosis

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

- **It can cause :**
  - Numbness
  - Lightheadedness
  - Nervousness
  - muscle spasms or tetany
  - Convulsions
  - Loss of consciousness
  - Death

There are 4 Types of Acid-base Imbalances

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