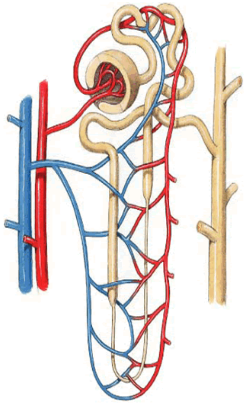
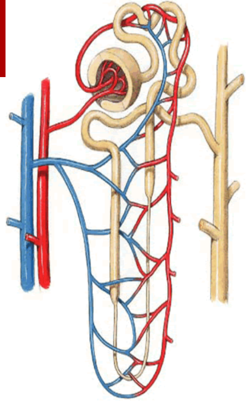


ACID-BASE BALANCE

Dr. Maha Saja

MBBS, MSc Physiology, PhD



Contents

- What are acids and bases?
- What is meant by a weak and a strong acid or base?
-
- What is the normal pH of body fluids?
- Why is it important to keep body fluid pH within certain limits?
- What are the body's defense mechanisms against changes in blood pH: body buffers, the lungs and the kidney.
- Understand the role of the kidney in regulating pH of body fluids.
- Acid-base disturbances.

Acid-Base Balance

- Acid-base balance is concerned with the precise regulation of free (unbound) hydrogen ion (H^+) concentration in body fluids.

- Normally, $[H^+]$ = 0.00004 mEq/L (40 nEq/L).

- ***Why is it important to control $[H^+]$?***

(Sherwood L. Human physiology: from cells to systems. 4th ed. 2001; Guyton & Hall. Textbook of medical physiology. 13th ed.)

Why Should $[H^+]$ be Tightly Controlled?

- Slight deviations in $[H^+]$ have profound effects on enzyme and protein activity and thus the body's metabolic activity in general.

- Changes in $[H^+]$ affects K^+ levels in the body.

(Sherwood L. Human physiology: from cells to systems. 4th ed. 2001; Guyton & Hall. Textbook of medical physiology. 13th ed.)

Why is the Body's [H^+] Constantly Changing?

A number of processes can alter [H^+] concentration in the body, such as;

1. Metabolism of ingested food.
2. GI secretions.
3. Generation of acids & bases from metabolism of stored fat & glycogen.
4. Changes in CO_2 production.

(Vander's Renal Physiology. 8th ed)

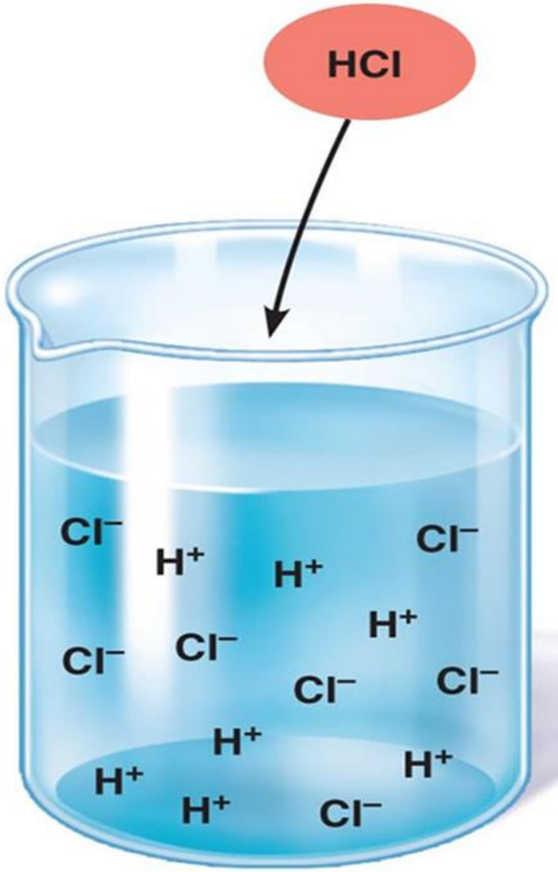
Acid-Base Fundamentals

- ***An Acid*** = a molecule that can release H^+ in a solution.
  - H_2CO_3 (carbonic acid)
  - HCl (hydrochloric acid)

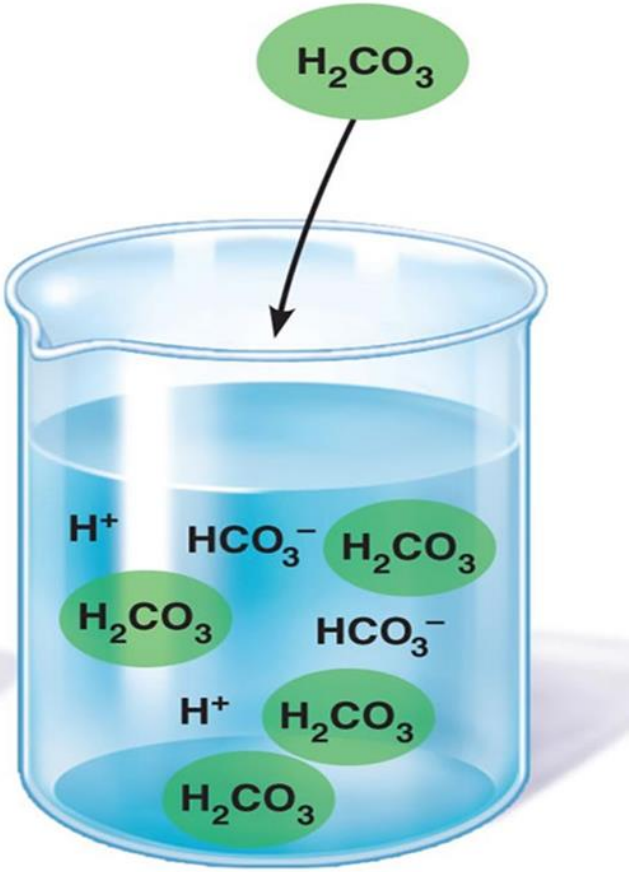
- ***A base*** = a molecule that accepts H^+ in a solution.
  - Bicarbonate ions (HCO_3^-).
  - Hydrogen phosphate (HPO_4^{-2})

- ***What is the difference between carbonic & hydrochloric acid?***

Strong vs Weak Acids & Bases



Strong acids dissociate rapidly and release large amounts of H^+ in solution



Weak acids dissociate incompletely and less strongly releasing small amounts of H^+ in solution

Weak Acids

$$\mathbf{AH} \leftrightarrow \mathbf{A^{-}} + \mathbf{H^{+}}$$

$$\boldsymbol{Acid} \leftrightarrow \boldsymbol{Conjugate\ base} + \boldsymbol{H^{+}}$$

The extent to which a given acid dissociates in solution is constant. And is known as the ***dissociation constant (K).***

$$\boldsymbol{K} = \frac{[\boldsymbol{H^{+}}][\boldsymbol{A^{-}}]}{[\boldsymbol{AH}]}$$

$$\boldsymbol{H_2CO_3} \leftrightarrow \boldsymbol{HCO_3-} + \boldsymbol{H^{+}} \Longrightarrow \boldsymbol{K} = \frac{[\boldsymbol{H^{+}}][\boldsymbol{HCO_3}^{-}]}{[\boldsymbol{H_2\,CO_3}]}$$

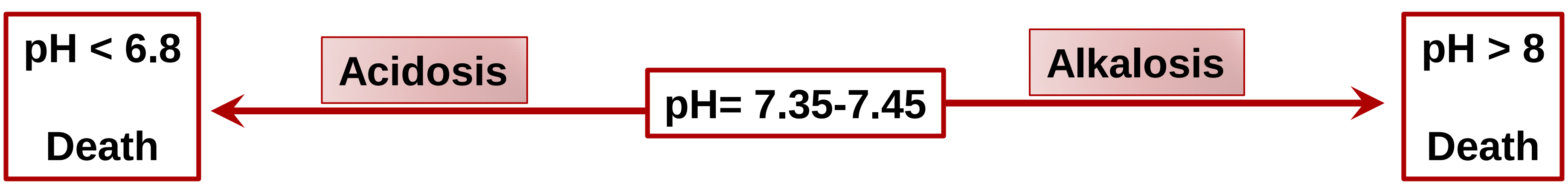
$[H^+]$ & the pH

- H^+ ion concentrations are expressed as pH.

- $pH = -\log [H^+]$
  - If the $[H^+]$ increase → pH will decrease (more acidic)
  - If the $[H^+]$ decrease → pH will increase (more alkaline)

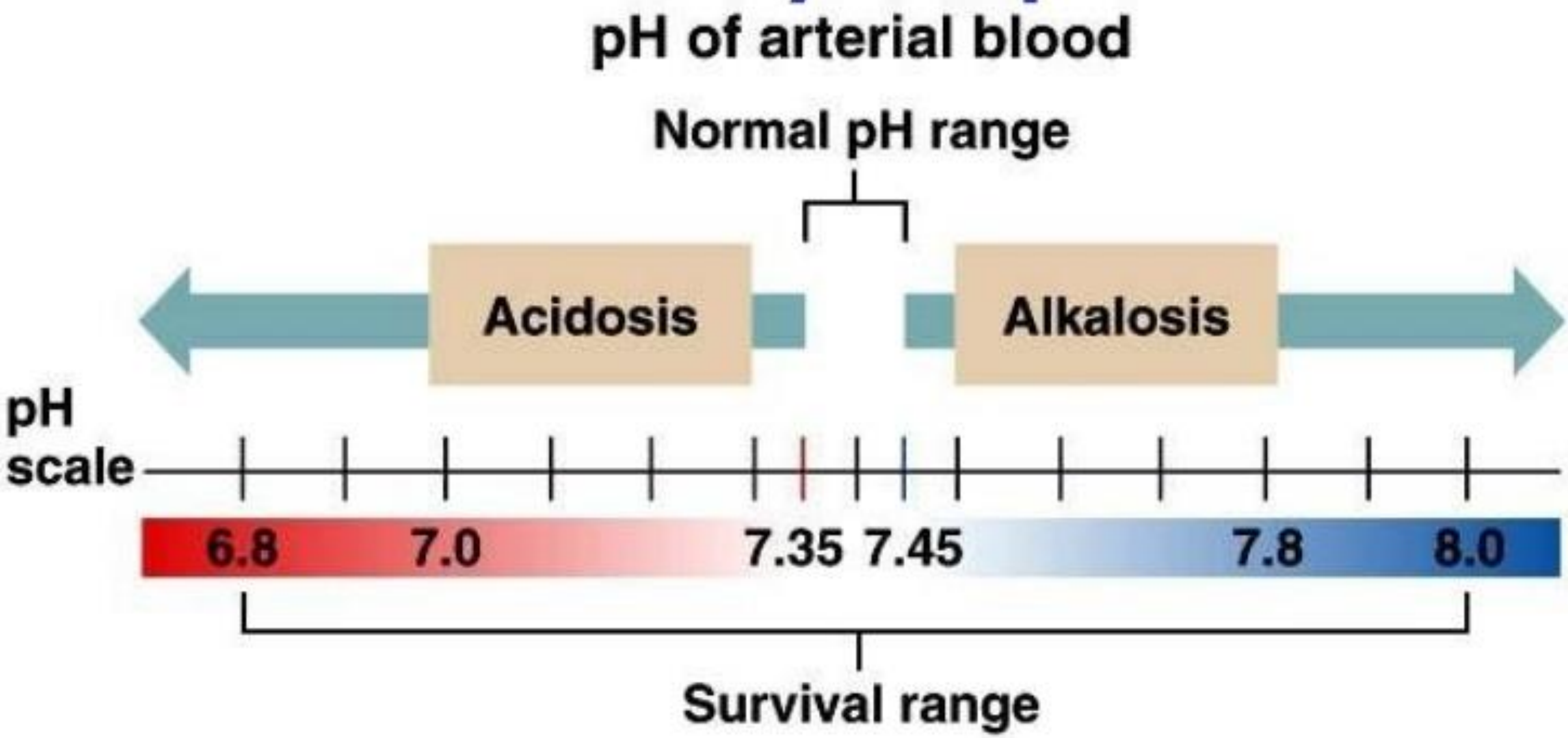
- ***What is the normal pH of the ECF?***

Normally pH= 7.35-7.45



(Guyton & Hall. Textbook of medical physiology. 13th ed.)

The Body and pH



pH and H^+ Concentration of Body Fluids

	$[H^+]$ (mEq/L)	pH
Extracellular fluid		
Arterial blood	4.0×10^{-5}	7.4
Venous blood	4.5×10^{-5}	7.35
IF	4.5×10^{-5}	7.35
Intracellular fluid	1×10^{-3} to 4×10^{-5}	6-7.4
Urine	3×10^{-2} to 1×10^{-5}	4.5-8
Gastric HCl	160	0.8

(Guyton & Hall. Textbook of medical physiology. 13th ed.)

Acid Production by the Body

- The body produces large amounts of acids on daily basis as by products of metabolism.
  - Metabolism of dietary proteins.
  - Anaerobic metabolism of carbs and fat.

- Acids in the body are of two kinds:
  1. Volatile (CO_2)
  2. Non-volatile “fixed” (sulfuric acid, lactic acid) (daily acid load ≈ 50-100 mEq/day) (0.8 mEq/kg/d).

(Vander’s Renal Physiology. 8th ed ; Guyton & Hall. Textbook of medical physiology. 13th ed.)

The Body's Defense Against Changes in $[H^+]$

Three main systems:

1. ***Body fluid buffers.***

   Works within seconds.

2. ***Lungs***

   Works within minutes.

3. ***Kidneys***

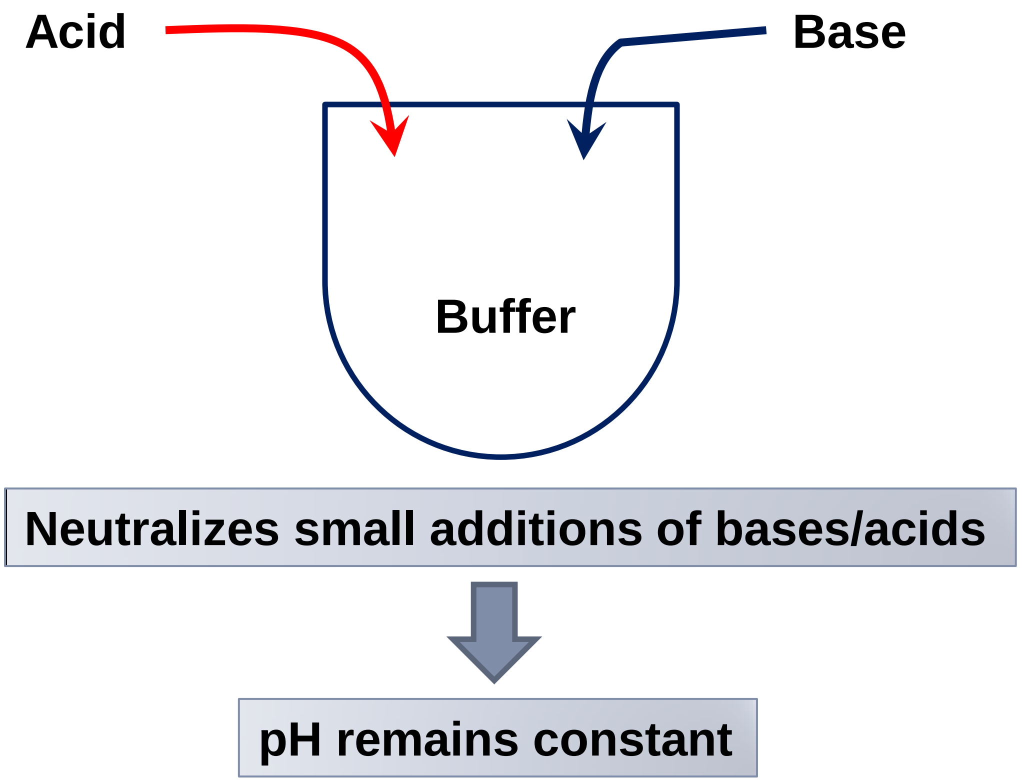
   Works within hours-days.

   The most powerful of the three.

BODY FLUID BUFFERS

What is a Buffer?

A buffer = a solution that resists changes in pH upon addition of small amount of acids and bases.



How do Buffers work?

- A buffer is a mixture of a weak acid and a weak base that are in equilibrium.

- To be more accurate, its either made of:
  - A weak acid and its conjugated base (H_2CO_3 & $NaHCO_3^-$).
  - A weak base and its conjugated acid (NH_3 & NH_4^+).

- ***How does a buffer do its job?***

Chemical Buffer Systems in the Body

- ***There are 3 chemical buffers in the body;***

1. The Bicarbonate buffer system.
2. The phosphate buffer system.
3. Proteins.

- They are the 1st line of defence against changes in pH i.e. $[H^+]$, act within seconds.

- Some are more powerful extracellularly and others are more powerful intracellularly.

The Bicarbonate Buffer System

- Composed of:
  - A weak acid (H_2CO_3).
  - Its conjugated base ($NaHCO_3$).

$$CO_2 + H_2O \underset{}{\overset{CA}{\rightleftharpoons}} H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

$$NaHCO_3 \rightleftharpoons Na^+ + HCO_3^-$$

The Bicarbonate Buffer System

1. ***H_2CO_3 forms in the body by the reaction of CO_2 & H_2O***

$$CO_2 + H_2O \underset{}{\overset{\text{Carbonic anhydrase}}{\rightleftharpoons}} H_2CO_3$$

2. ***H_2CO_3 ionizes weakly to form small amounts of H^+ & HCO_3^-***

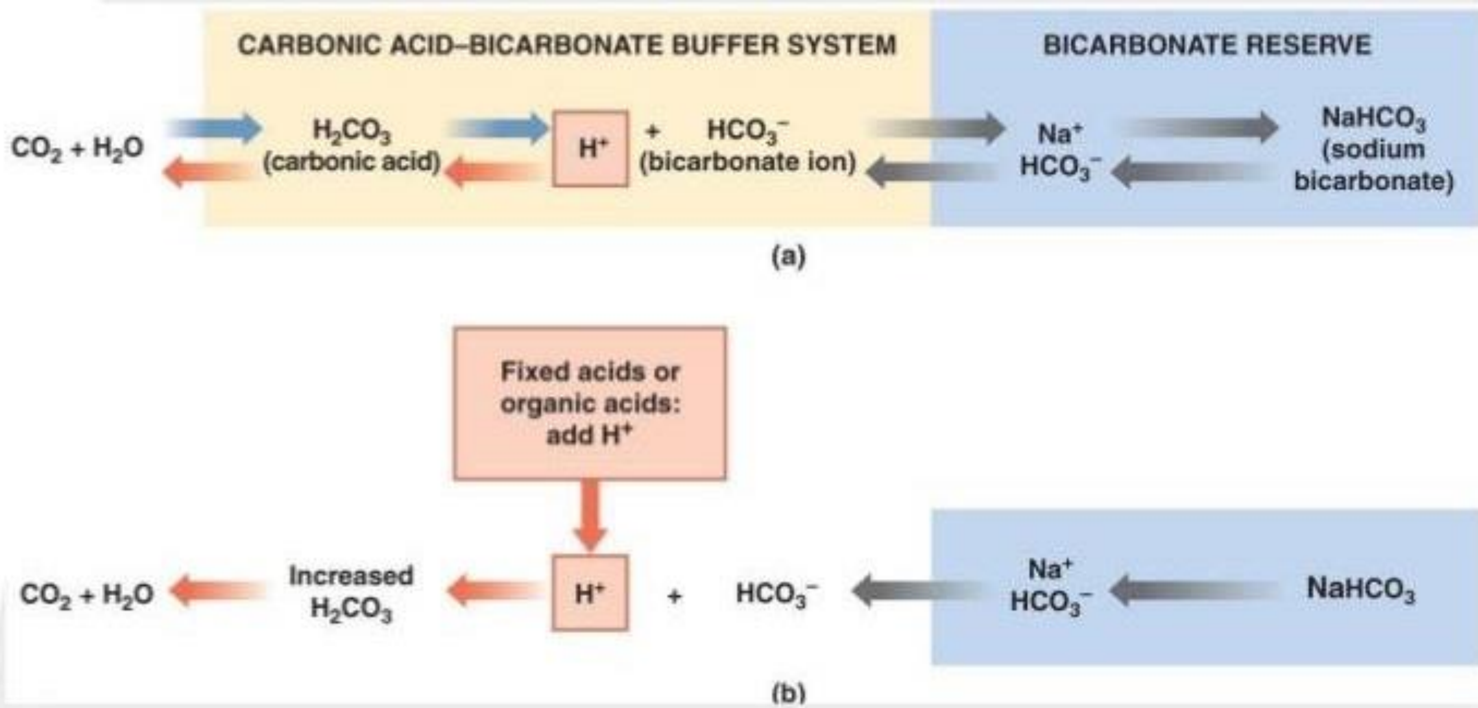
$$H_2CO_3 \rightleftharpoons H^+ \ \& \ HCO_3^-$$

3. ***The second component is $NaHCO_3$ which dissociates to form Na^+ & HCO_3^-***

$$NaHCO_3 \rightleftharpoons Na^+ \ \& \ HCO_3^-$$

The Bicarbonate Buffer System

Putting it all together;



The Carbonic Acid–Bicarbonate Buffer System

This is the main ECF buffer system

What happens if you add a base or an acid to the system?

The Henderson-Hasselbalch Equation

What is the HHE?

- It is an equation that enables the calculation of pH of a solution.

What is it?

$$pH = pK + log\frac{HCO3^{-}}{0.03\ X\ PCo_{2}}$$

K = dissociation constant, pK = 6.1

0.03 = solubility of CO_2

The Henderson-Hasselbalch Equation

How was it derived?

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

1. H_2CO_3 and its dissociated ions are always in equilibrium → the products of the reaction on one side of the equation are proportional to the product on the other side.

$$[H_2CO_3] \ \alpha \ [H^+] \ X \ [HCO_3^-]$$

2. Since H_2CO_3 is a weak acid, it will not dissociate completely and the concentration of its products will depend on its dissociation constant (K)

$$K \ X \ [H_2CO_3] = [H^+] \ X \ [HCO_3^-]$$

The Henderson-Hasselbalch Equation

3. Based on the previous equation, $[H^+]$ can be expressed as follows;

$$[H^+] = K \; X \; \frac{[H_2CO_3]}{[HCO_3^-]}$$

4. Because H_2CO_3 can rapidly dissociate into CO_2 and H_2O. And since CO_2 is much easier to measure it can replace H_2CO_3 in the equation;

$$[H^+] = K \; X \; \frac{[Co_2]}{[HCO_3^-]}$$

This is Henderson's equation (1908)

It means that;

↑ [CO2] →↑ $[H^+]$

↑ $[HCO_3^-]$ → ↓ $[H^+]$

The Henderson-Hasselbalch Equation

5. In 1909, Sorensen created the pH scale to express [H^+]

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

6. In 1916, Hasselbalch decided to merge Henderson's equation with Sorensen's pH scale creating what we now know as the ***"Henderson-Hasselbalch equation".***

$$[H^+] = K\ X\ \frac{[Co_2]}{[HCO_3^-]} \Longrightarrow -\log[H^+] = -\log\left(K\ X\ \frac{[CO2]}{[HCO3^-]}\right)$$

The Henderson-Hasselbalch Equation

$$-\log[H^{+}] = -\log\left(K\ X\ \frac{[CO2]}{[HCO3]}\right)$$

$$pH = pK + \log\frac{[HCO3]}{[Co2]}$$

This is Henderson-Hasselbach equation (1908)

7. Since it is much easier to measure PCO_2 rather than dissolved $[CO_2]$ and because dissolved CO_2 is proportional to PCO_2 multiplied by the solubility of CO_2 (0.03 mmol/mmHg) → $[CO_2]$ was replaced by PCO_2 X 0.03

$$pH = pK + \log\frac{[HCO3]}{0.03\ X\ PCO2}$$

Ta-Da

The Bicarbonate Buffer System

$$CO_2 + H_2O \overset{CA}{\rightleftharpoons} H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

$$pH = pK + \log \frac{[HCO3^-]}{0.03\ X\ PCO2}$$

- ***What do we understand from this equation?***

1. pH α $\frac{HCO3-}{PCO2}$

Regulated by kidneys

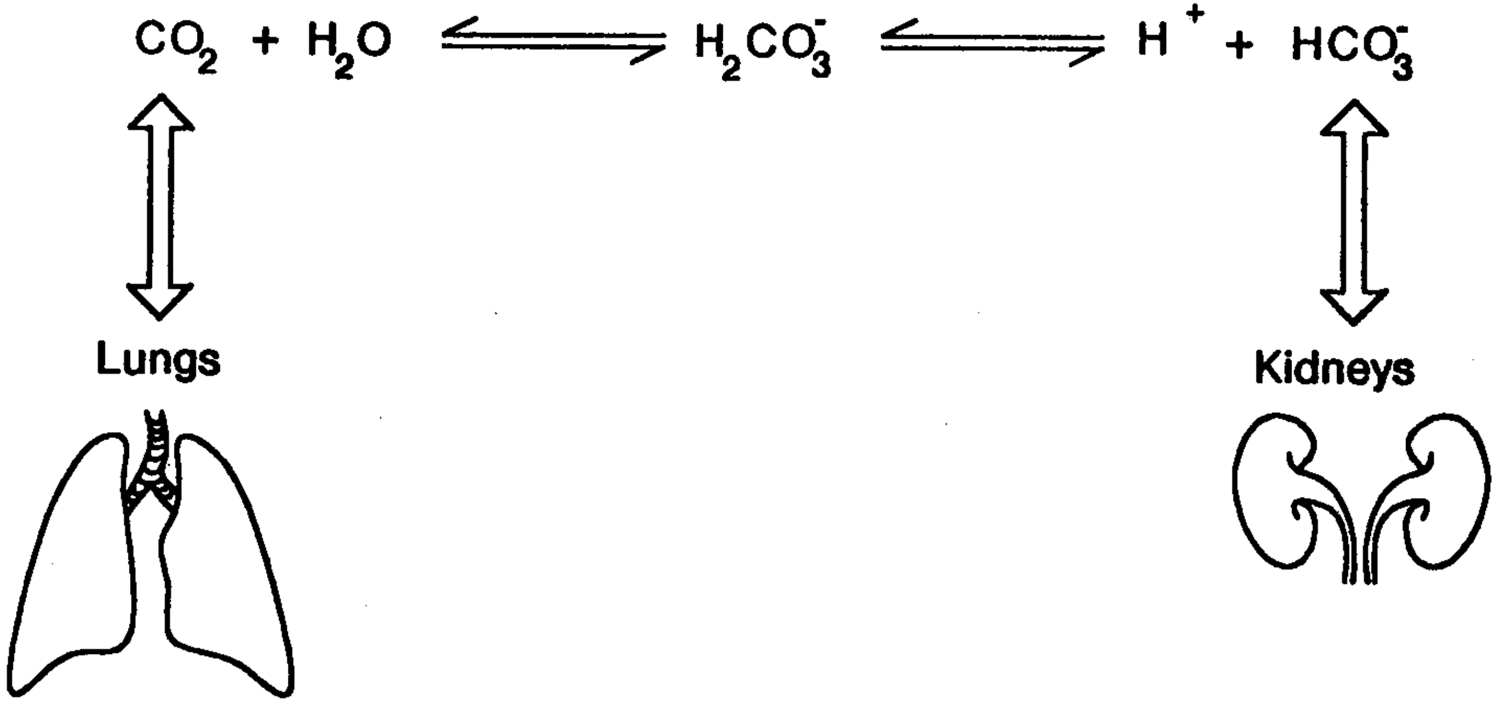
Regulated by lungs

Each element of the buffer system is regulated

- ↑↑ HCO_3^- will ↑↑ pH
- ↑↑ PCO2 will ↓↓ pH

Summary of the Bicarbonate Buffer System

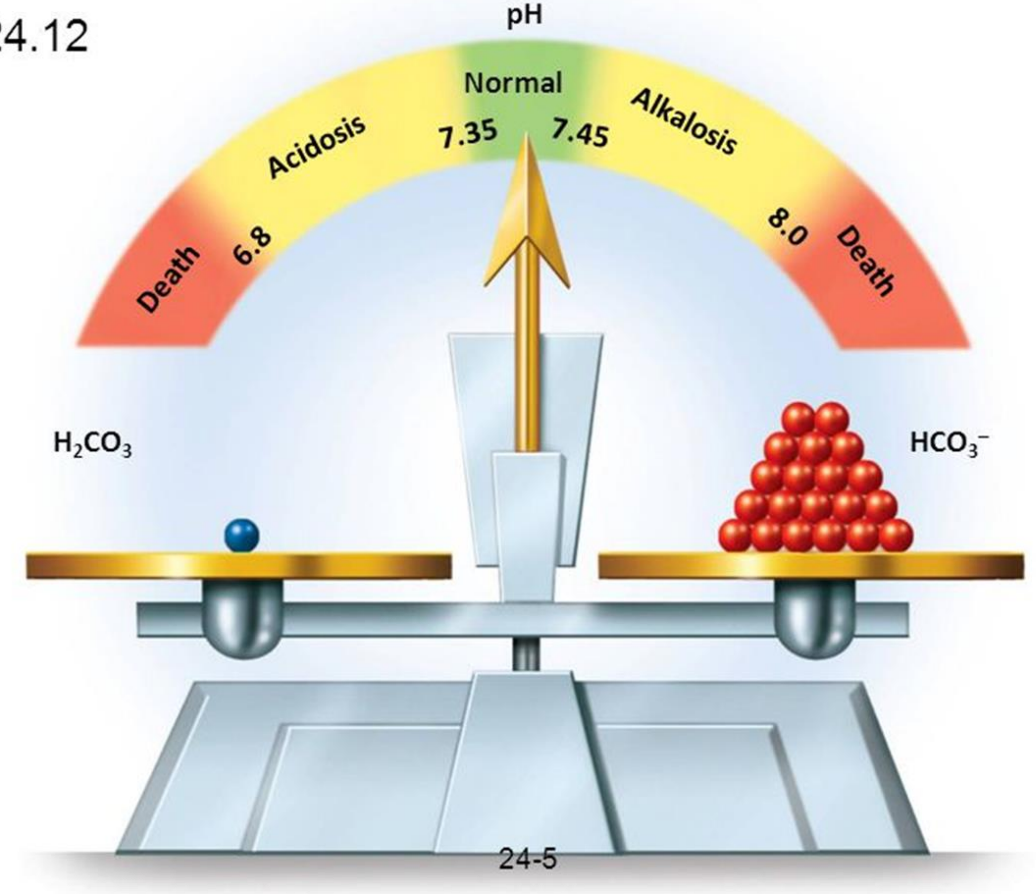
Why is it the most important buffer system in the ECF?



Ratio of $\frac{HCO3-}{PCO2}$ is ≈ 20:1

Acid-Base Balance

Figure 24.12



Other Buffering Systems

The phosphate buffer:

- Plays a major role in buffering intracellular & renal tubular fluid.

- Composed of;
  - $H_2PO_4^-$ (dihydrogen phosphate)
  - HPO_4^{-2} (Hydrogen phosphate)

Proteins:

- Contributes to buffering inside cells.
- E.g. Hb.

Summary of Body's Buffering Systems

- Buffer systems do not work independently in body fluids but actually work together.
- A change in the balance in one buffer system, changes the balance of the other systems.
- Buffers do not reverse the pH change, they only limit it.
- Buffers do not correct changes in $[H^+]$ or $[HCO_3^-]$, they only limit the effect of change on body pH until their concentration is properly adjusted by either the lungs or the kidney.

RESPIRATORY REGULATION OF ACID-BASE BALANCE

Respiratory Regulation of A/B

- 2nd line of defence against acid-base disturbances in the body.

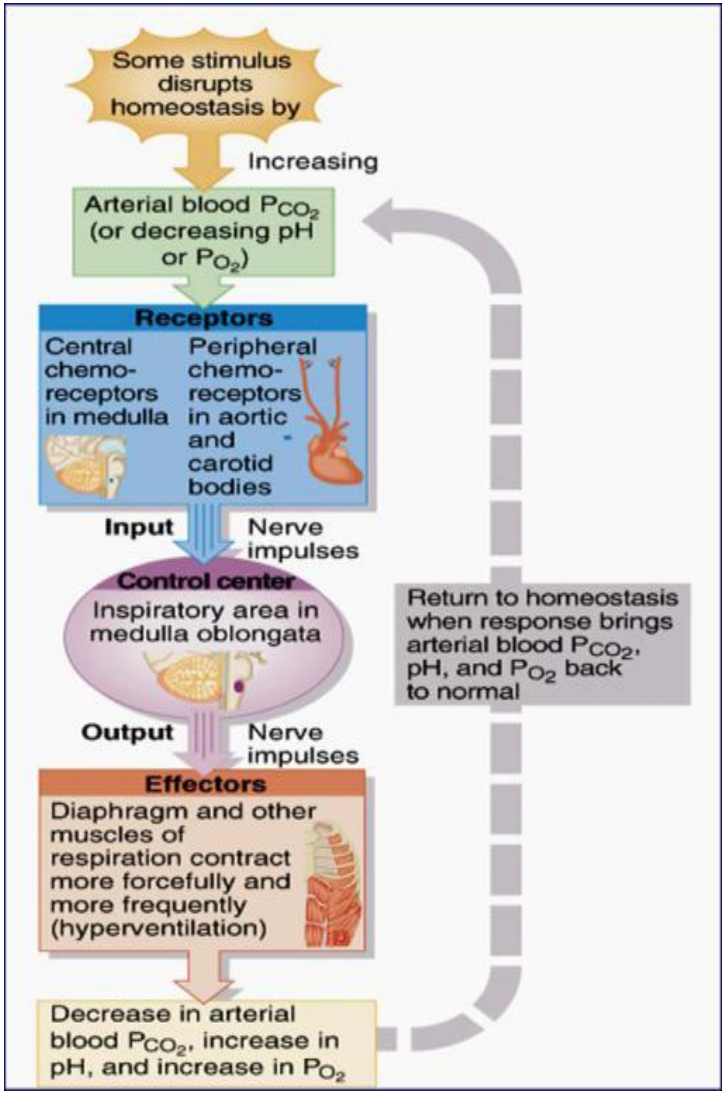
- ***HOW?***
  - By modulating CO_2 excretion.

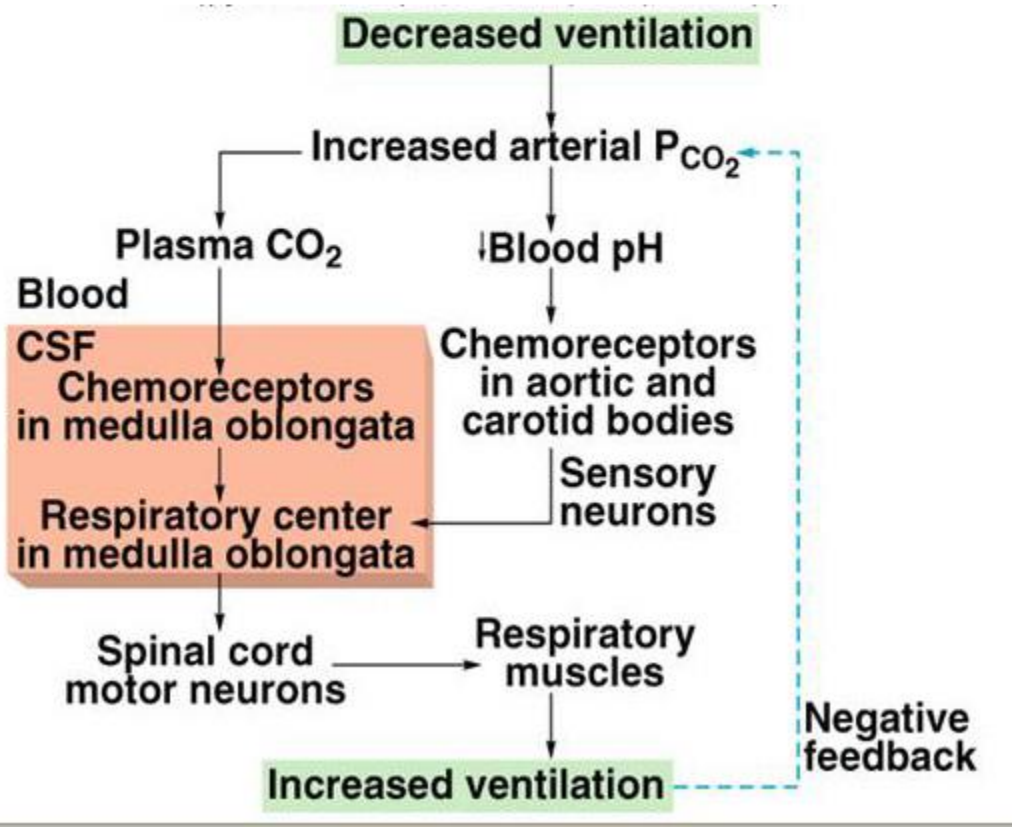
- ↑↑ [H^+] → ↑↑ ventilation (RR) → ↓↓ PCO_2

- ↓↓ [H^+] → ↓↓ ventilation (RR) → accumulation of CO_2→↑↑ PCO_2.

- Normally, PCO_2 = 40 mmHg (35-45 mmHg)

Respiratory Regulation of CO_2





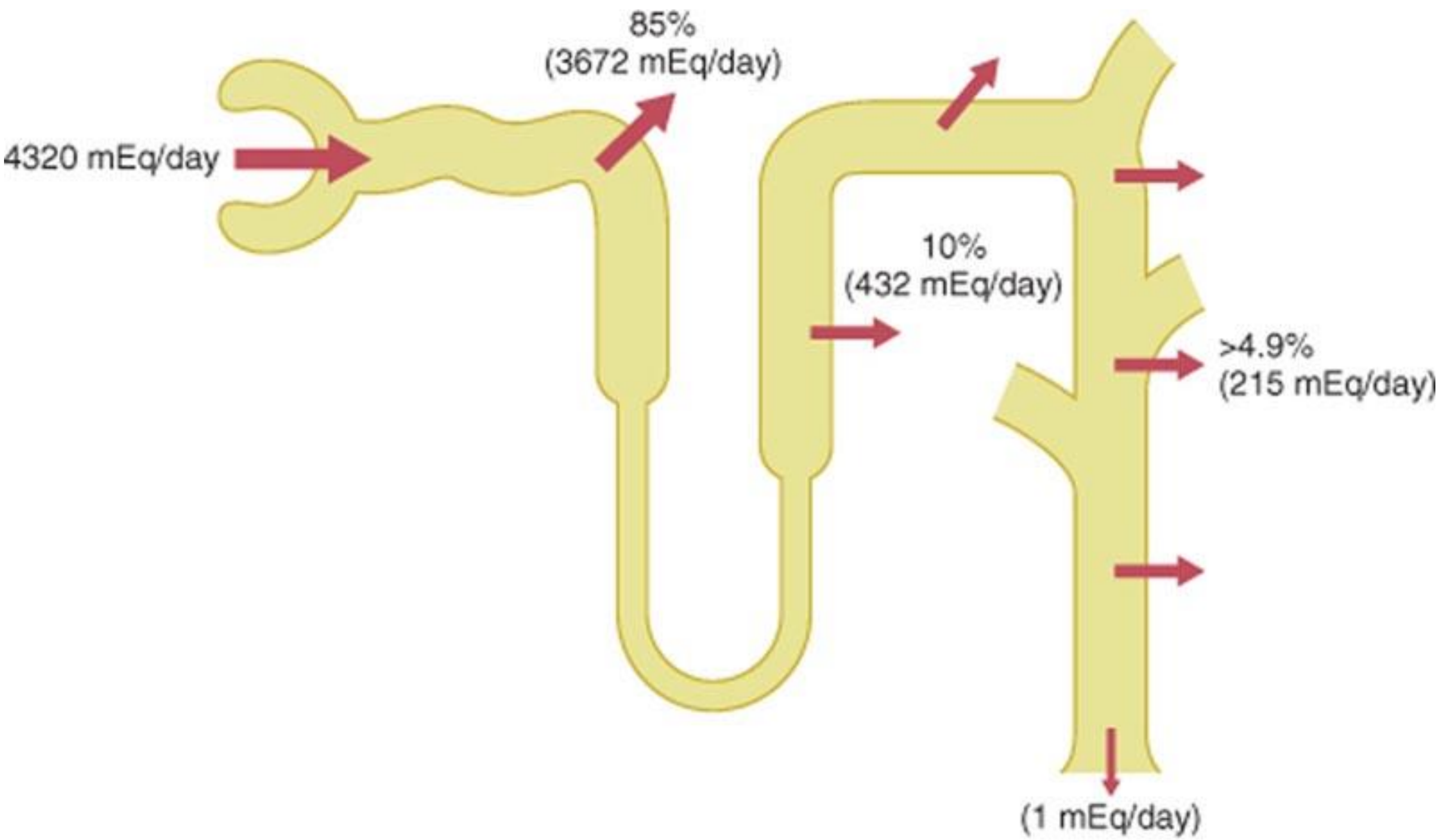
RENAL REGULATION OF ACID-BASE BALANCE

Renal Regulation of A/B Balance

- 3rd line of defence against acid-base disturbances and the most powerful.
- It regulates by excreting either an acidic or basic urine.
- ***HOW?***

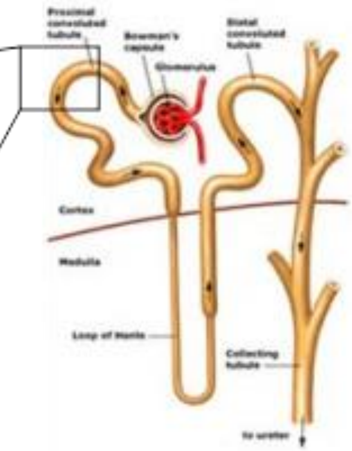
1. Secreting H^+
2. Reabsorbing HCO_3^-
3. Generating “new” bicarbonate ions.

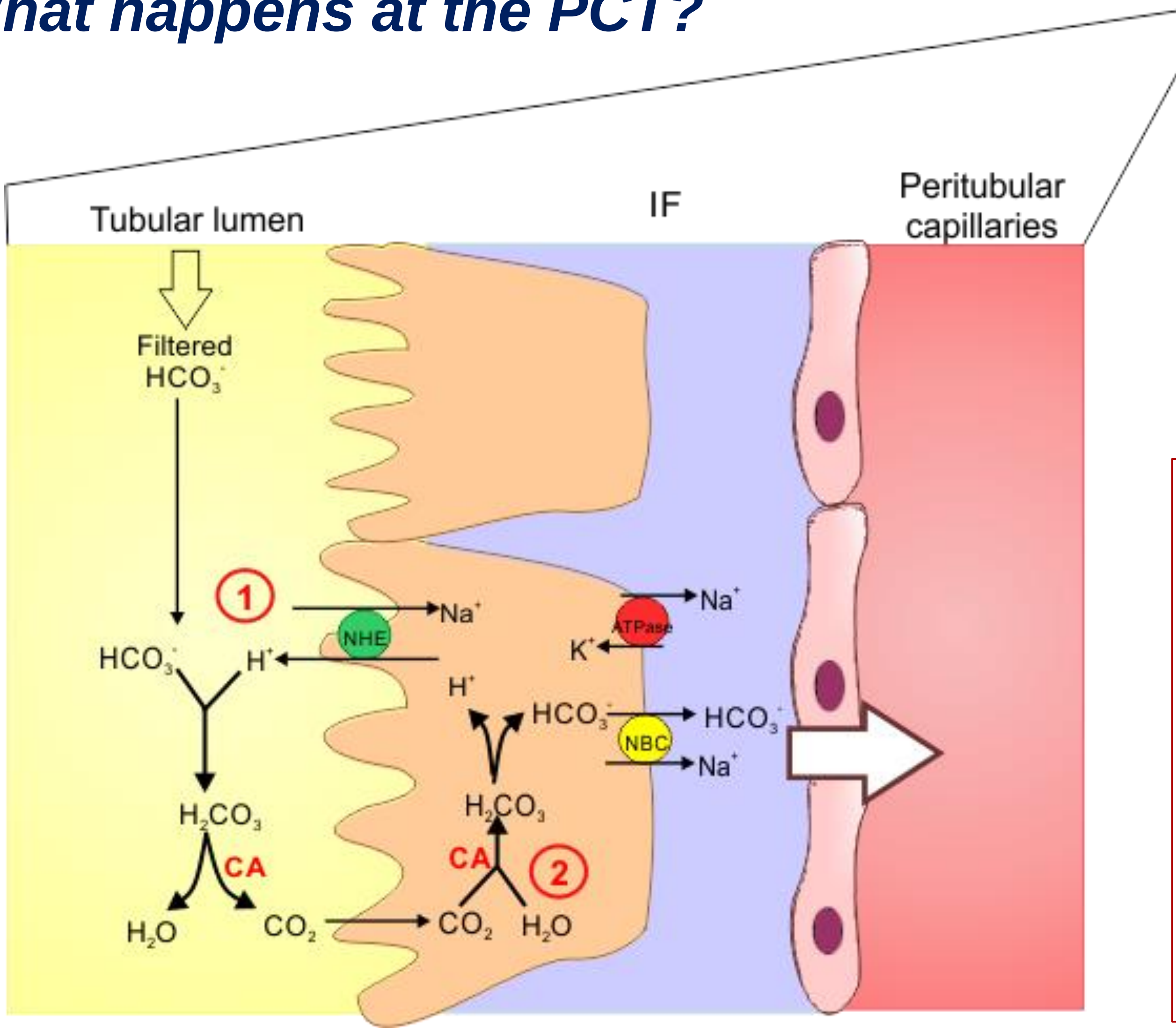
Overview HCO_3^- Reabsorption by the Renal Tubules



How is HCO_3^- Reabsorbed by the tubules?

What happens at the PCT?

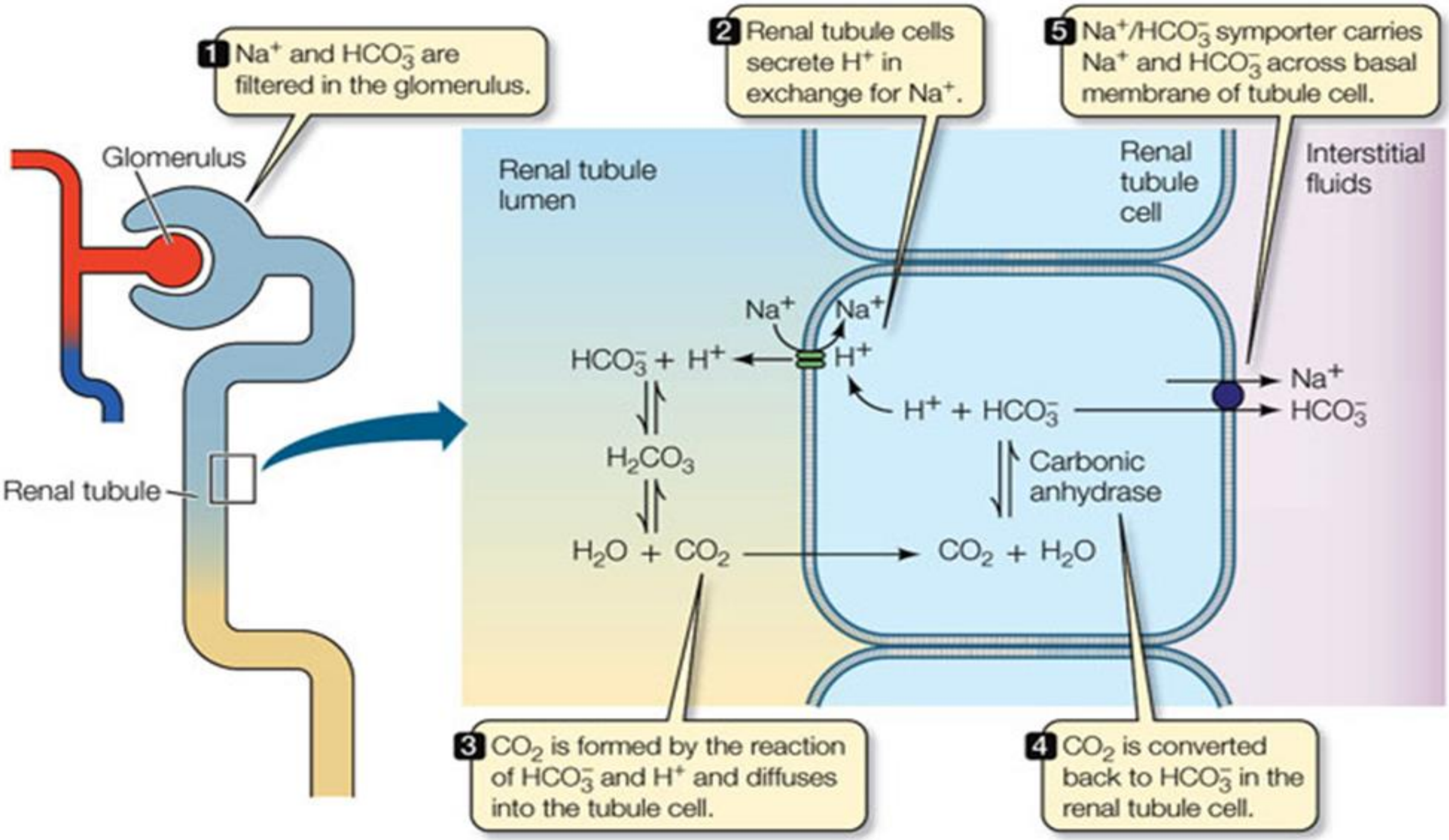




The PCT reabsorbs, "reclaims", 80-90% of the filtered HCO_3^-.

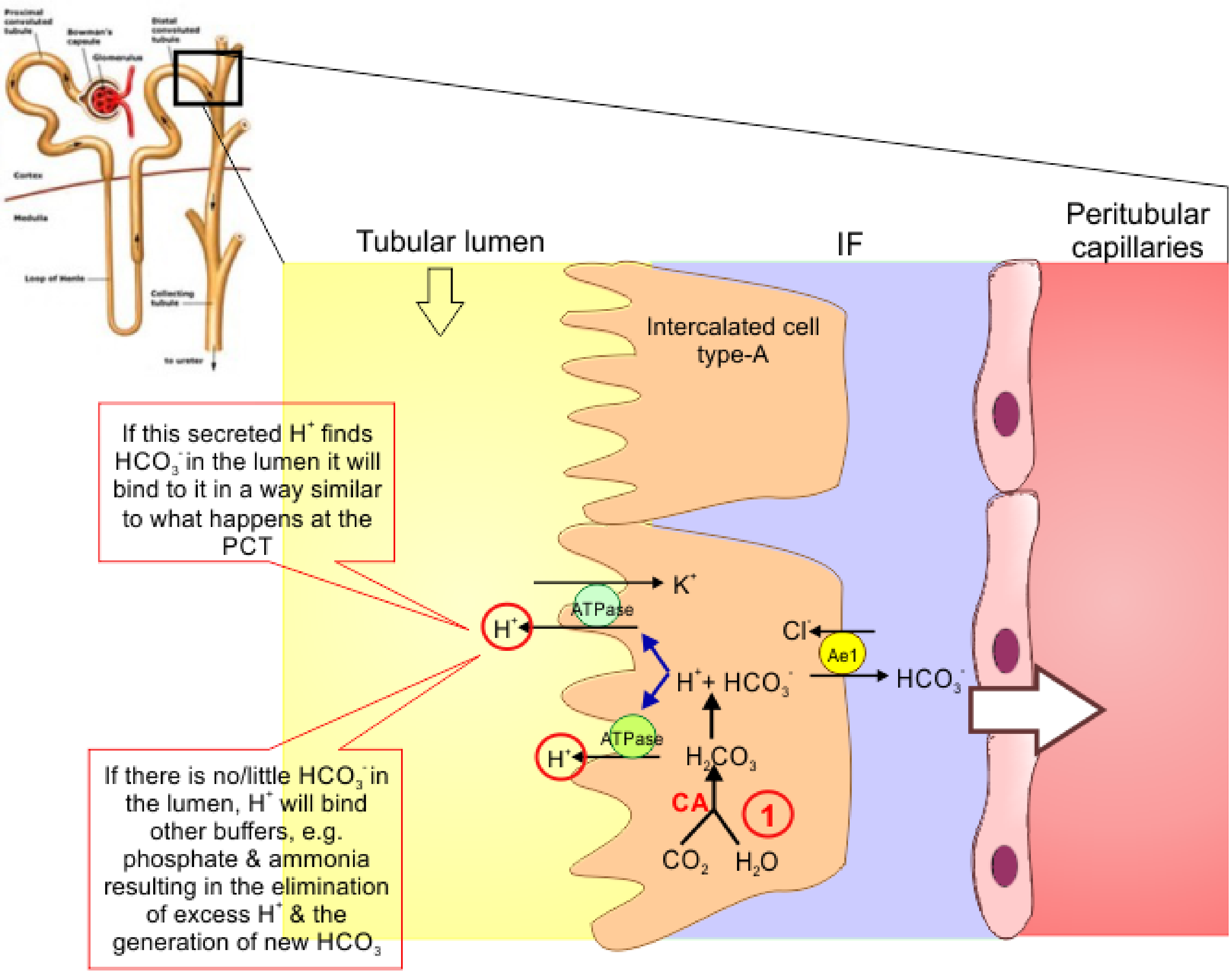
HCO_3^- reabsorption is linked to H^+ secretion.

HCO_3^- Reabsorption by the PCT



LIFE 8e, Figure 51.12

What happens at the DCT & CT?



What happens at the late DCT & CT?

- The filtrate arriving at the DCT & CT is low in HCO_3^-.
- The distal segments of the nephron are characterised by the presence of "intercalated cells" capable of ***actively secreting H^+*** through H^+-ATPase and H^+-K^+ ATPase present on their apical membrane (***Type-A intercalated cells***).
- Only a limited number of H^+ can be excreted in its free form in urine.
- Lowest possible urine pH=4.5 → ≈ 0.04 mmol/L of free H^+.
- ***How does the kidney excrete the extra H^+?***

(Vander's Renal Physiology. 8th ed)

Non-Bicarbonate Buffers in the Tubular Lumen?

The extra H^+ secreted will need to be buffered in the tubular lumen

2 main non-bicarbonate buffers in the tubule

Filtered

Phosphate buffer system

$$H_2PO_4^- \leftrightarrow HPO_4^{-2} + H^+$$

(acid) *(base)*

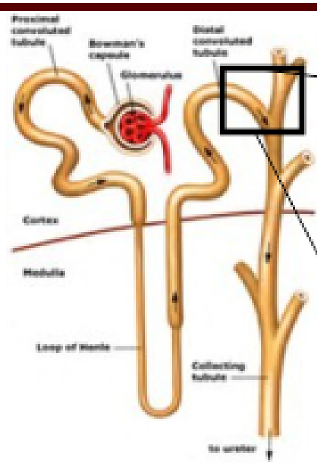
Synthesized

Ammonia buffer system

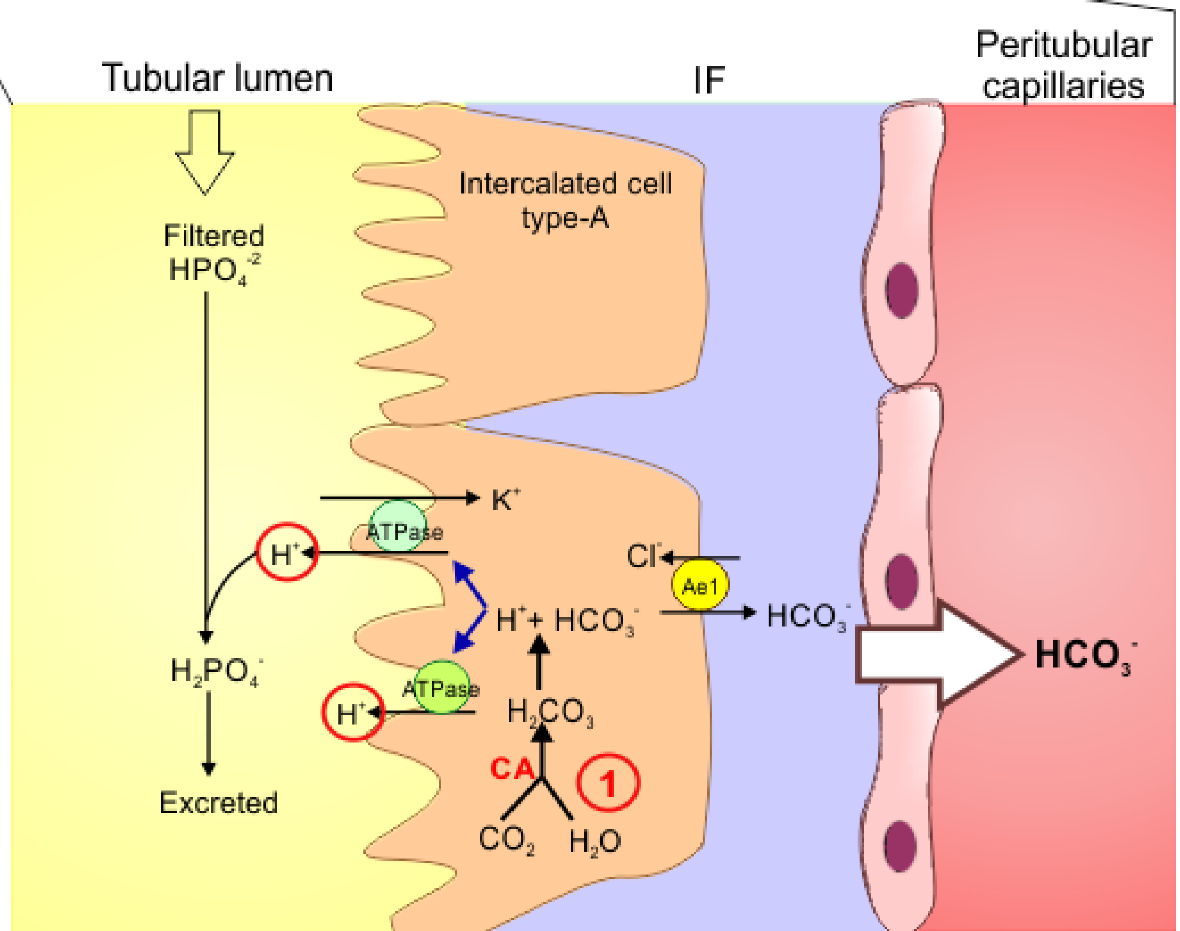
$$NH_4^+ \leftrightarrow NH_3 + H^+$$

(acid) *(base)*

Excretion of H^+ and Generation of New HCO_3^-



The phosphate buffer system



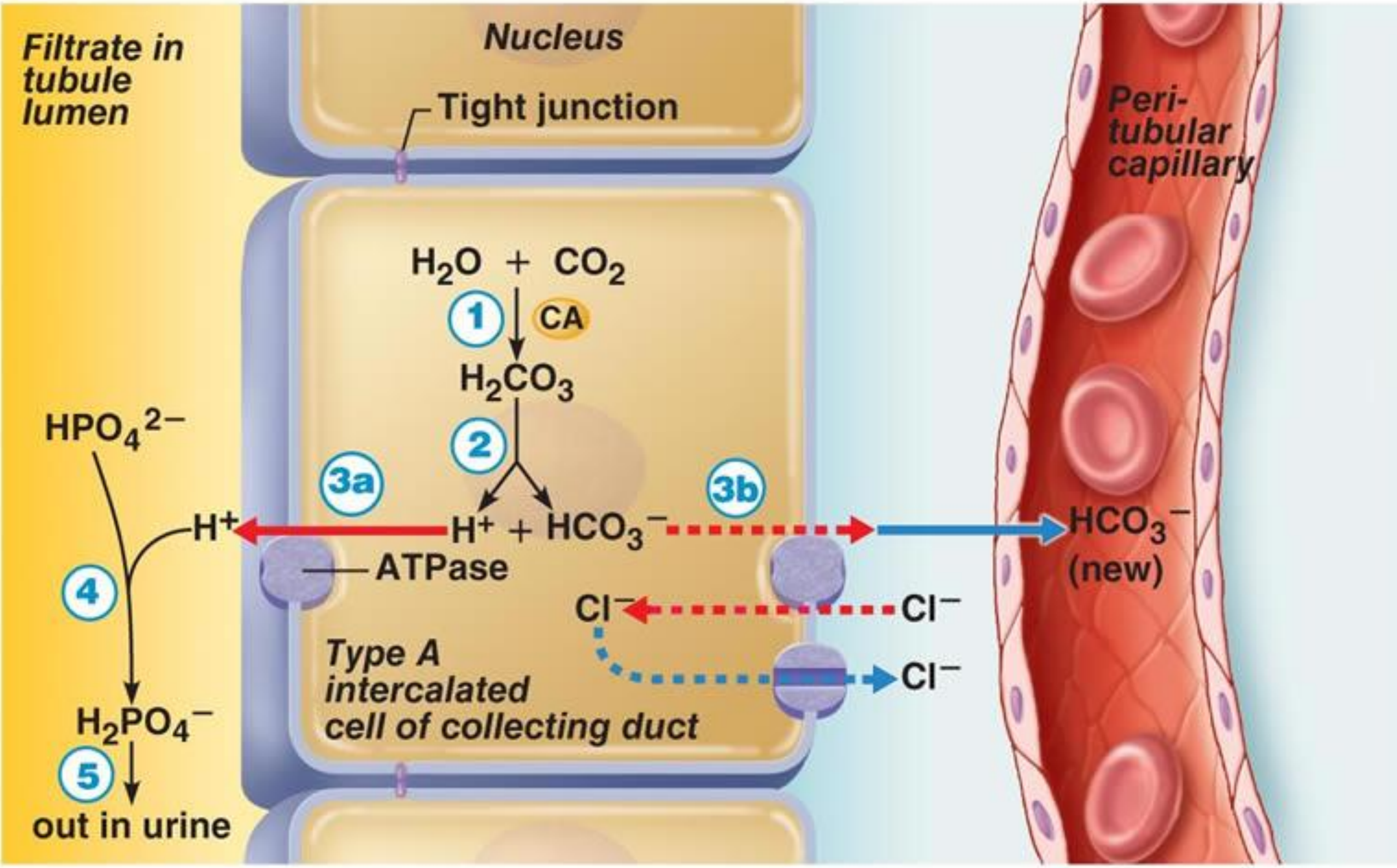
Excretion of H^+ as phosphate is capable of handling a limited amount of H^+ and will not be enough to rid the body of its daily acid load nor if there is unusually high acid production.

(Vander's Renal Physiology. 8th ed ; Guyton & Hall. Textbook of medical physiology. 13th ed.)

(1) CO_2 combines with water within the type A intercalated cell, forming H_2CO_3.

(2) H_2CO_3 is quickly split, forming H^+ and bicarbonate ion (HCO_3^-).

(3a) H^+ is secreted into the filtrate by a H^+ ATPase pump.



(3b) For each H^+ secreted, a HCO_3^- enters the peritubular capillary blood via an antiport carrier in a HCO_3^--Cl^- exchange process.

(4) Secreted H^+ combines with HPO_4^{2-} in the tubular filtrate, forming $H_2PO_4^-$.

(5) The $H_2PO_4^-$ is excreted in the urine.

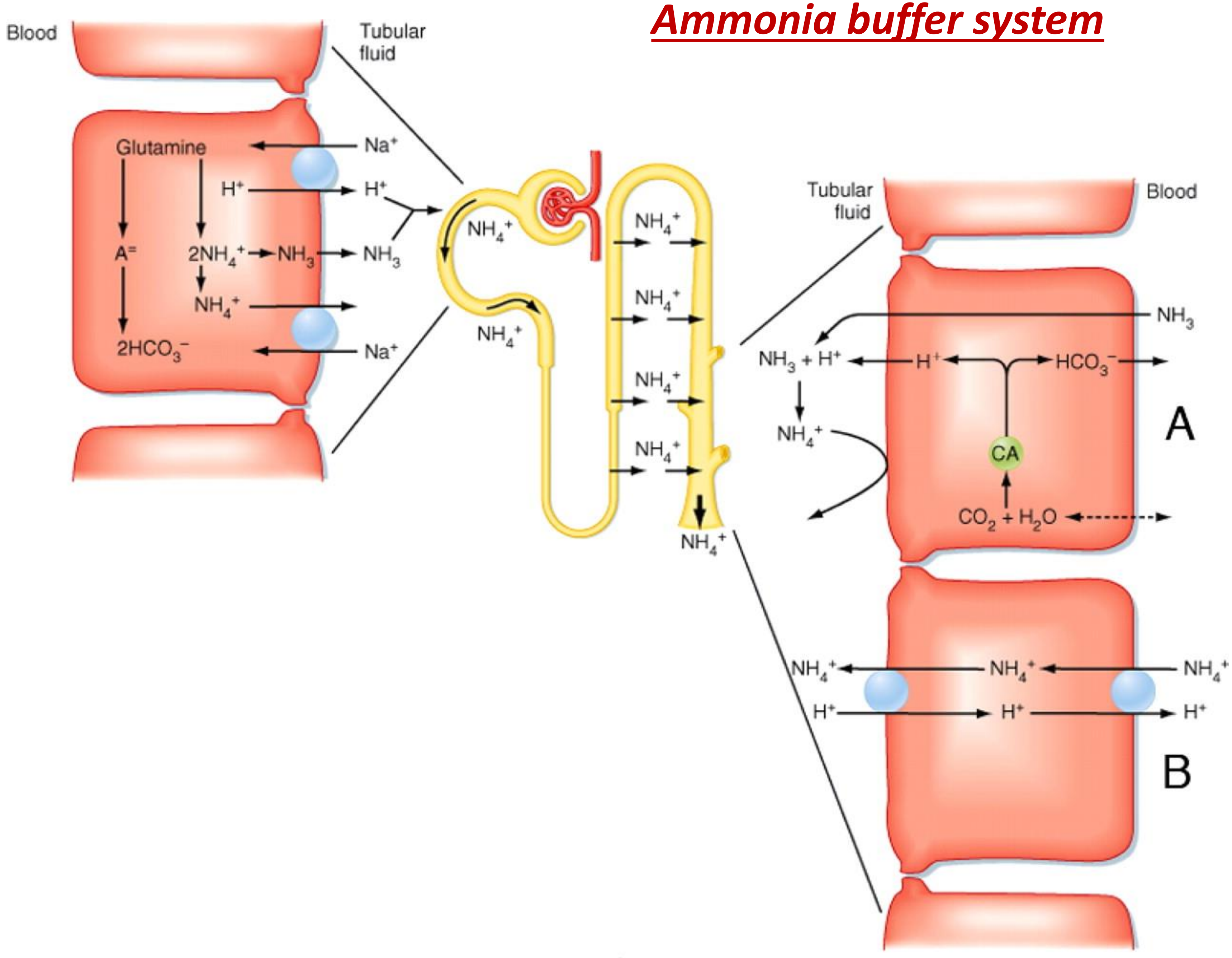
- Primary active transport
- Secondary active transport
- Simple diffusion
- Facilitated diffusion
- Transport protein
- Ion channel
- CA Carbonic anhydrase

Excretion of H^+ and Generation of New HCO_3^-

The Ammonia Buffer System

- Renal tubular cells, especially PCT, are capable of generating ammonium (NH_4^+) "***ammoniagenesis***" which is then excreted in urine carrying with it H^+.
- The rate of ammoniagenesis can be modified according to the needs of the body.
- Quantitatively, the ammonia buffer system is more important than the phosphate buffer system for H^+ excretion in urine.
- It is the most important system in case of acidosis.

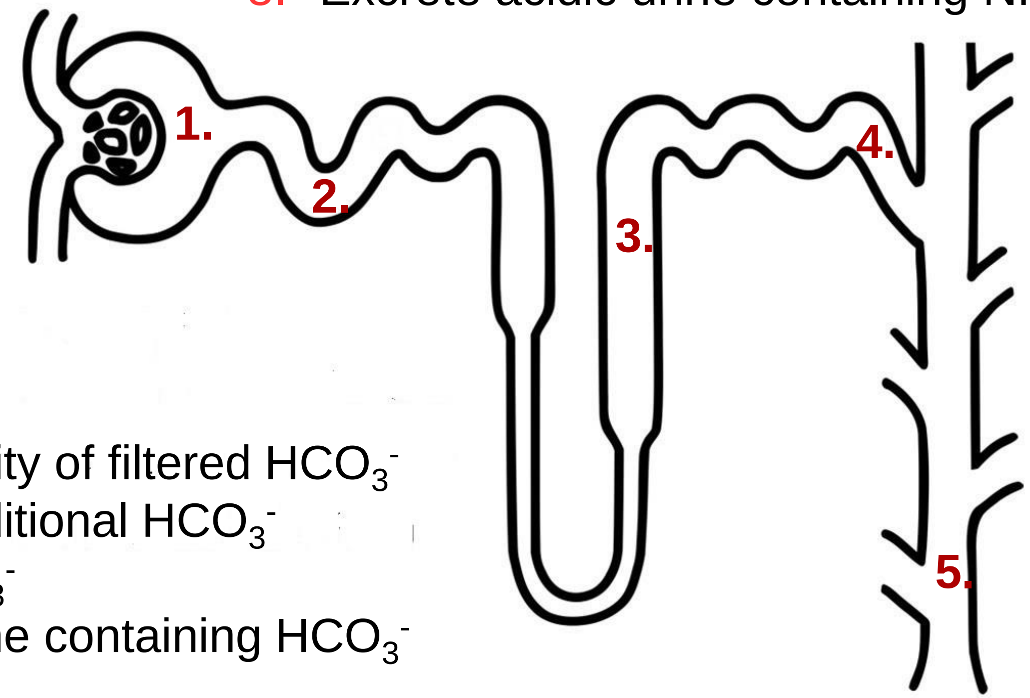
Ammonia buffer system



The Overall Scheme of Renal Excretion of Acids & Bases

To excrete acid:

1. Freely filter HCO_3^-
2. Reabsorb the majority of filtered HCO_3^-
3. Reabsorb some additional HCO_3^-
4. Secrete H^+ (titrate filtered bases, i.e. HPO_4^{-2}) and secrete NH_4^+
5. Excrete acidic urine containing NH_4^+



To excrete base:

1. Freely filter HCO_3^-
2. Reabsorb the majority of filtered HCO_3^-
3. Reabsorb some additional HCO_3^-
4. Secrete some HCO_3^-
5. Excrete alkaline urine containing HCO_3^-

(Adapted with modification from Vander's Renal Physiology. 8th ed)

THANK YOU