Renal Clearence

Unit V

Chapter 28

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Clearance

- "Clearance" describes the rate at which substances are removed (cleared) from the plasma.

- Renal clearance of a substance is the volume of plasma completely cleared of a substance per min by the kidneys.

Clearance Technique

$$C_s \times P_s = U_s \times V$$

$$C_s = \frac{U_s \times V}{P_s} = \frac{\text{urine excretion rate}}{\text{Plasma conc}}$$

Where : C_s = clearance of substance S

P_s = plasma conc. of substance S

U_s = urine conc. of substance S

V = urine flow rate

Osmolar Clearance

osmolar clearance (C_{osm})= total clearance of solutes from the **blood**
= Volume of plasma cleared of solutes each minute

$$C_{osm} = \frac{U_{osm} \times V}{P_{osm}}$$

where:

Uosm = urine osmolarity
V = urine flow rate
P = plasma osmolarity

example

If plasma osmolarity is 300 mOsm/L, urine osmolarity is 600 mOsm/L, and urine flow rate is 1 ml/min. Calculate the volume of plasma cleared of solutes each minute?

plasma osmolarity = 300 mOsm / L

urine osmolarity = 600 mOsm /L

urine flow rate = 1 ml/min

→

$$C_{osm} = \frac{U_{osm} \times V}{P_{osm}}$$

$$C_{osm} = \frac{600 \times 1/1000}{300}$$

=0.002 L/min

=2 ml of plasma are being cleared of solute each minute

“Free” Water Clearance (C_{H_2O})

Free-water clearance (C_{H2O}) =rate of solute-free water excretion
is calculated as the difference between water excretion (urine flow rate) and osmolar clearance

$$C_{H_2O} = V - C_{osm} = V - \frac{(U_{osm} \times \dot{V})}{P_{osm}}$$

If: Uosm < Posm, C_{H2O} = + indicating water is being removed

If: Uosm > Posm, C_{H2O} = - indicating water conservation

Question

Given the following data, calculate "free water" clearance :

urine flow rate = 6.0 ml/min

urine osmolarity = 150 mOsm /L

plasma osmolarity = 300 mOsm / L → Is free water clearance in this example positive or negative ?

$$C_{H_2O} = V - \frac{U_{osm} \times V}{P_{osm}}$$

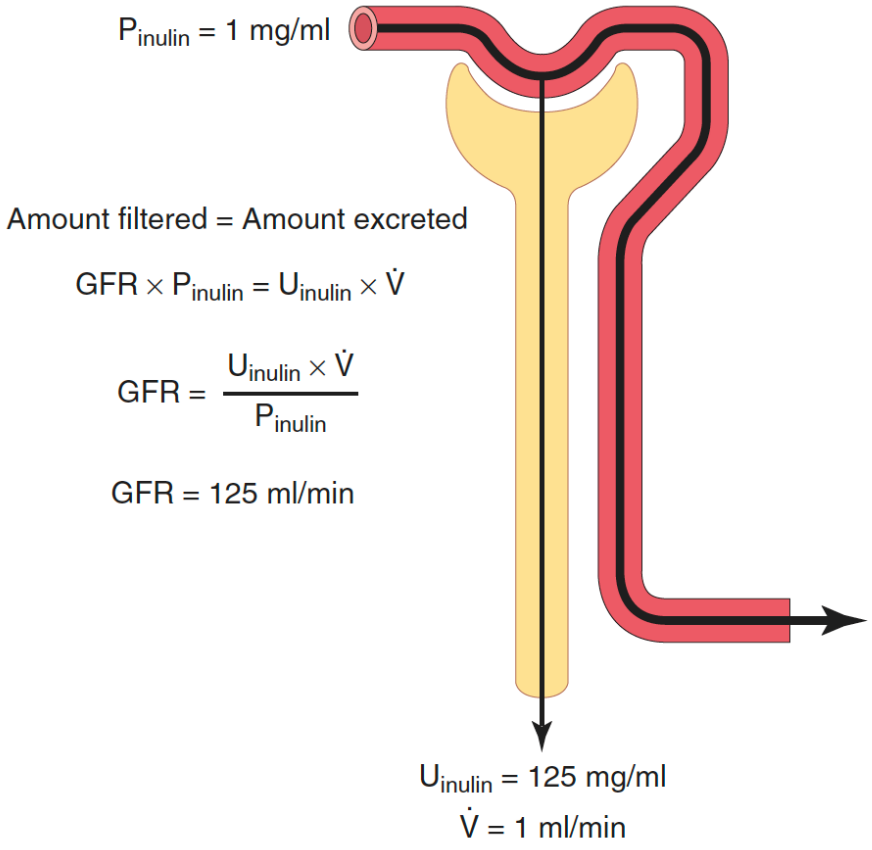
$$= 6.0 - \frac{(150 \times 6)}{300}$$

$$= 6.0 - 3.0$$

$$= +3.0 \text{ ml / min}$$ (positive)

Use of Clearance to Measure GFR

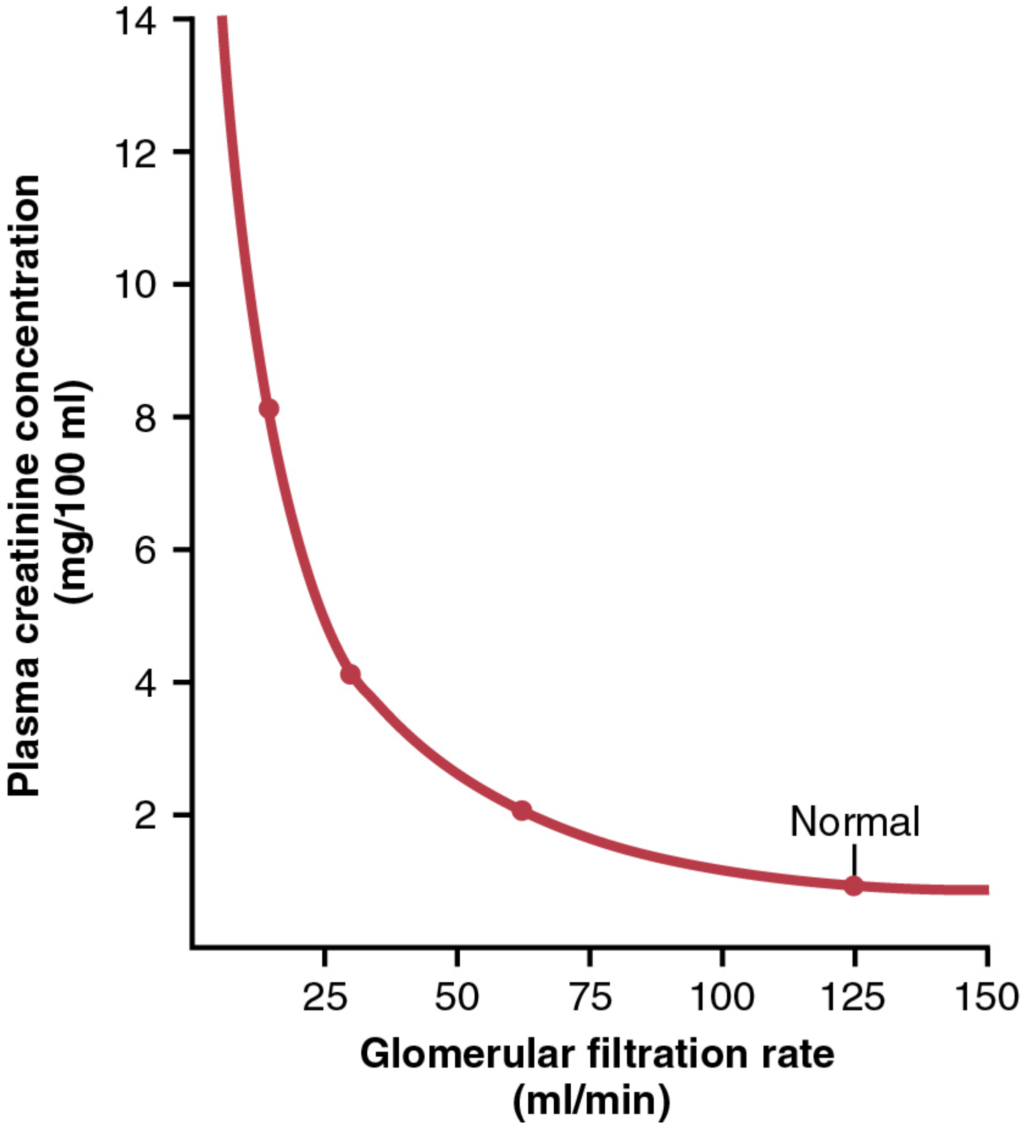
For a substance that is freely filtered, but <u>not</u> reabsorbed or secreted (inulin, ^{125}I-iothalamate, creatinine), renal clearance is <u>equal</u> to GFR



Creatinine clearance and plasma creatinine concentration can be used to estimate GFR

- cleared from the body fluids almost entirely by glomerular filtration
- not require intravenous infusion
- is not a perfect marker of GFR because a small amount of it is **secreted** by the tubules → amount of creatinine excreted > amount filtered
- a slight error in measuring plasma creatinine

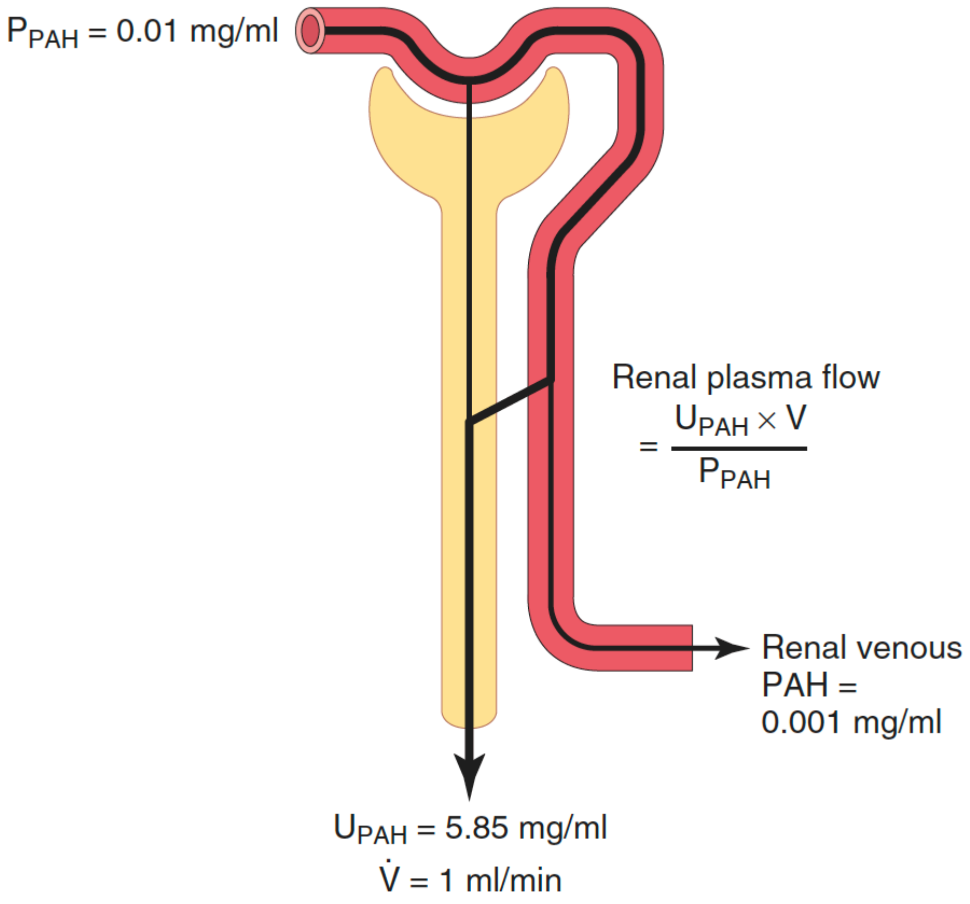
Plasma creatinine can be used to estimate changes in GFR



Use of Clearance to Estimate Renal Plasma Flow

Theoretically, if a substance is completely cleared from the plasma, its clearance rate would equal <u>renal plasma flow (RPF)</u>

Paraminohippuric acid (PAH) is 90% filtered and secreted and is almost completely cleared from the renal plasma



amount of substance delivered to kidneys in blood= amount excreted in urine

(RPF x Ps) = (Us xV)

RPF = Us xV/ Ps=Cs

Cx = renal plasma flow

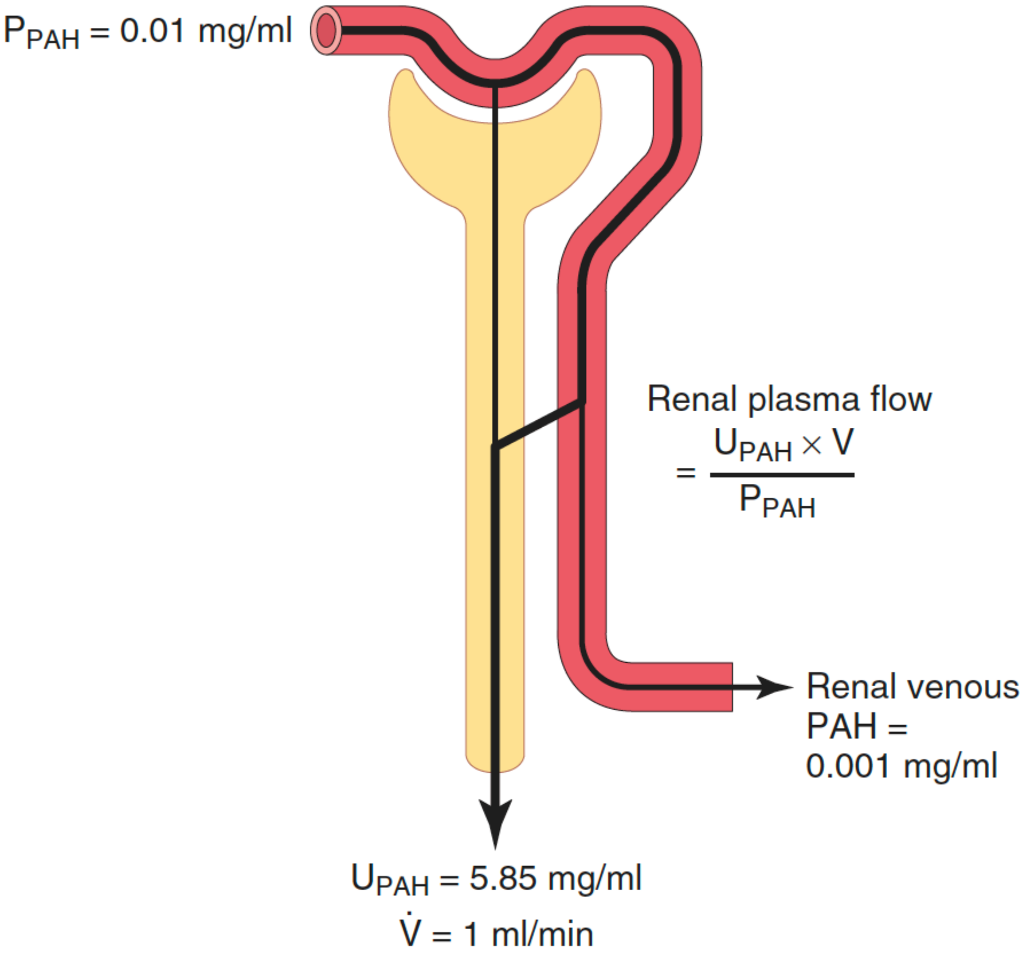
To calculate <u>actual</u> RPF , one must correct for incomplete extraction of PAH

$$E_{PAH} = \frac{A_{PAH} - V_{PAH}}{A_{PAH}}$$

$$= \frac{0.01 - 0.001}{0.01} = 0.9$$

normally, $E_{PAH} = 0.9$

i.e., PAH is 90% extracted



Filtration fraction is calculated from GFR divided by RPF

RPF =PAH clearance
GFR =inulin clearance

If the RPF is 650 ml/min and the GFR is 125 ml/min, the filtration fraction (FF) is calculated as

FF = GFR/RPF = 125/650 = 0.19

Calculation of Tubular Reabsorption

If the rates of **glomerular filtration** and **renal excretion** of a substance are known, one can calculate whether there is a net reabsorption or a net secretion of that substance by the renal tubules.

if the rate of **excretion** of the substance (Us x V) < the **filtered** load of
the substance (GFR x Ps), then some of the substance must have been **reabsorbed** from the renal tubules.

if the **excretion rate** of the substance > **filtered load**, then the rate of excretion= **sum of the rate of glomerular filtration plus tubular secretion.**

Calculation of Tubular Reabsorption

Reabsorption = Filtration - Excretion

Filt s = GFR x Ps

Excret s = Us x V

Urine flow rate = 1 ml/min
Urine concentration of sodium (U_{Na}) = 70 mEq/L
= 70 μ Eq/ml
Plasma sodium concentration = 140 mEq/L
= 140 μ Eq/ml
GFR (inulin clearance) = 100 ml/min
Calculate
1-Filtered sodium load
2- Urinary sodium excretion
3- Tubular reabsorption

Answer
1-filtered sodium load= GFR x P_{Na}
=100 ml/min x 140 μ Eq/ml = 14,000 μ Eq/min.

2-Urinary sodium excretion =U_{Na} x urine flow rate=70 x1 =70 μ Eq/min.

3- tubular reabsorption of Na= filtered load - urinary excretion
14,000 μ Eq/min – 70 μ Eq/min = 13,930 μ Eq/min.

Acid-Base Regulation

Chapter 31
Unit V

Dr Iman Aolymat

Introduction

Multiple acid-base buffering mechanisms are nvolved in maintaining normal H+ concentrations in both the extracellular and intracellular fluid:

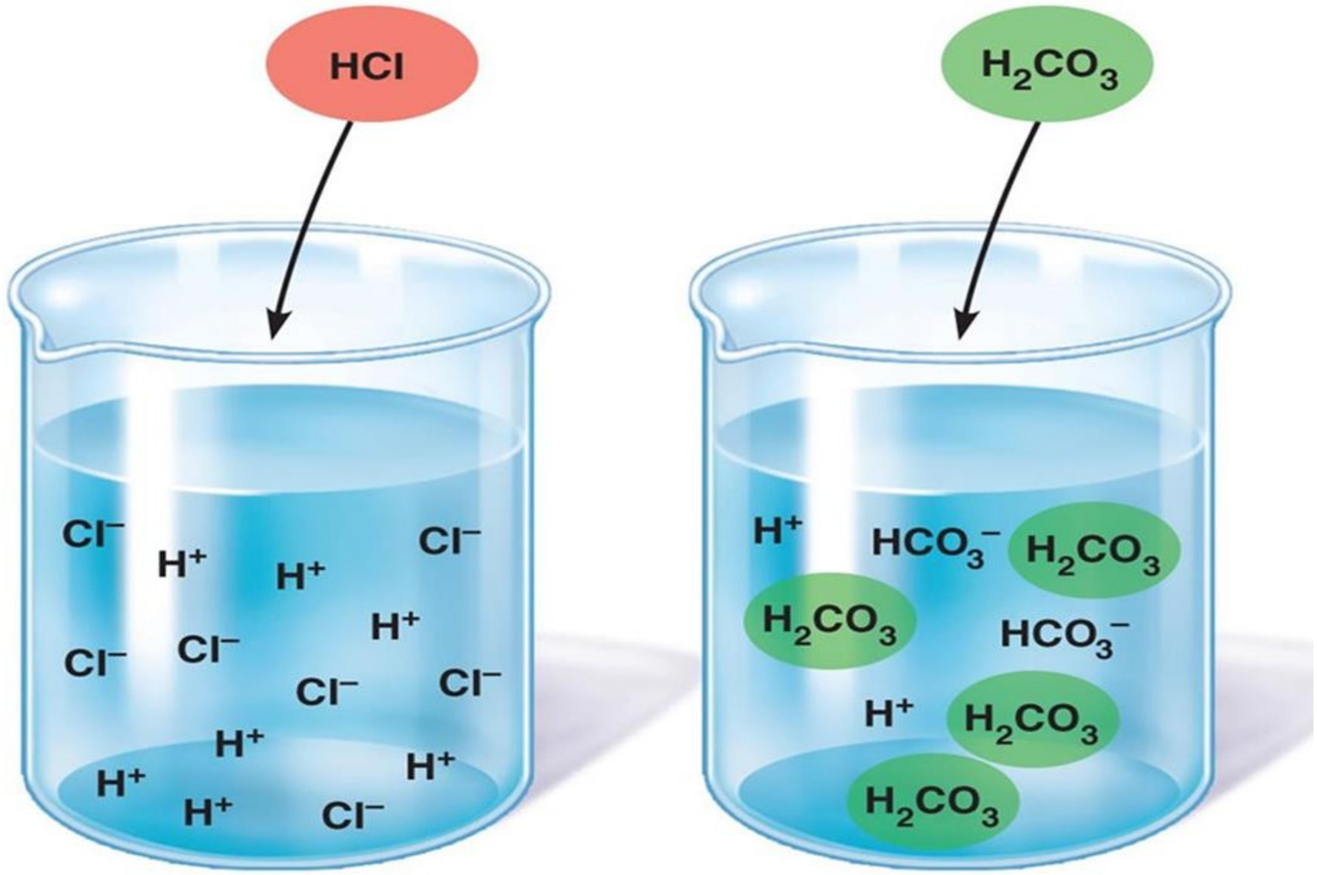
1-blood
2-cells
3-lungs
4-kidneys

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})
  - Proteins in body function as bases because some of amino acids that make up proteins have net negative charges that readily accept H+.

Strong vs weak Acid/Base



A strong base is one that reacts **rapidly** and strongly with H+ → quickly removing H+ from a solution.
Example is OH– + H+ → H2O

weak base e.g HCO3– because it binds with H+ much more weakly than does OH–.

Most acids and bases in ECF that are involved in normal acid-base regulation are **weak** acids and 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**

Alkalosis= excess removal of H^+ from the body fluids

Acidosis= excess addition of H^+

[H^+] & the pH

- H+] is precisely regulated at 0.00004 mEq/L (important for enzyme functions)
- 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)

Normally pH= 7.2-7.44

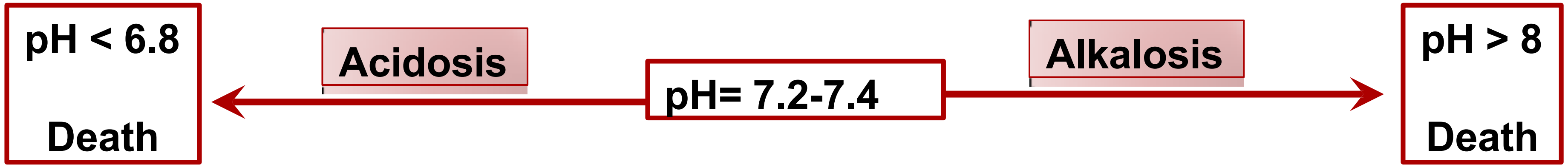


Table 31-1 pH and H^+ Concentration of Body Fluids

	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}	6.0-7.4
Urine	3×10^{-2} to 1×10^{-5}	4.5-8.0
Gastric HCl	160	0.8

Intracellular pH usually is< plasma because the metabolism of the cells produces acid especially (H_2CO_3).

Hypoxia of and poor blood flow to tissues → acid accumulation and ↓intracellular pH.

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)

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

Three main systems:

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

   Works within seconds (bind acid/base).

2. ***Lungs***

   Works within minutes (eliminate CO2).

3. ***Kidneys***

   Works within hours-days (EXCRETE ACID/BASE).

   The most powerful of the three.

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

- The main ECF buffer system
- Composed of:
  - A weak acid (H_2CO_3).
  - Its conjugated base ($NaHCO_3$).

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;

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + \underbrace{HCO_3^-}_{\substack{+ \\ Na^+}}$$

Adding ACID (HCl) $(HCl \rightarrow H^+ + Cl^-)$

$$+ HCO_3^- \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$$

lung

Weak acid

Adding base (NaOH)

$$CO_2 + H_2O \longrightarrow \underset{\substack{+ \\ NaOH}}{H_2CO_3} \longrightarrow \uparrow \underset{\substack{+ \\ Na}}{HCO_3^-} + H^+$$

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

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

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

pK = dissociation constant= 6.1

0.03 = solubility of CO_2

- ***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

Other Buffering Systems

The phosphate buffer:

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

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

Proteins: PLENTIFUL

- Contributes to buffering inside cells→ H+ /HCO3- diffusion to the cell.
- 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.