Major extra and intracellular electrolytes

Major extra and intracellular electrolytes:

Extracellular fluids (ECF)

- Interstitial fluid - fills the spaces between most cells of the body
- Intravascular fluid - plasma (WBC, RBC and platelets in this fluid)

Intracellular fluids (ICF)

- Liquids within cell membranes
- 40% of body weight

Extracellular Fluid (ECF) = interstitial fluid, plasma, lymph, CSF, synovial fluid, serous fluid, etc.

Intracellular Fluid (ICF) = cytosol

Fluid and Electrolyte Balance (water and ions move together)

- Average male ~ 60% H_2O (more muscle which can be ~ 75% H_2O)
- Average female ~ 50% H_2O (more adipose which is only ~ 10% H_2O)
- Most of the water in the body is found in the ICF (~ 2/3)
- The electrolytes vary depending on the fluid division:

ECF Principal cation = Na^+, Principal anions = Cl^- , HCO_3^-

ICF Principal cation = K^+, Mg^{2+}, Principal anions = HPO_4^{2-} and negatively charged proteins

Although different ions dominate, both fluid divisions have the same osmotic concentrations.

The ions cannot pass freely through cell membranes, but the water can by osmosis, and will move to equilibrium. Thus, solute/electrolyte concentrations of the fluid divisions will directly impact water distribution.

Electrolytes

Substances whose molecules dissociate into ions when they are placed in water.

CATIONS (+),　　ANIONS (-)

Medically significant / routinely ordered electrolytes include**:**

Cation: Positively Charged particles.

Examples : Sodium (Na^+), Potassium (K^+), Calcium (Ca^{++}), Magnesium (Mg^{++})

Anion: Negatively charged particles.

Examples : Chloride (Cl^-), Bicarbonate (HCO_3^-), Phosphate (HPO_4^-)

Electrochemical Equivalence

• **Equivalent (Eq/L) = moles x valence**

• **Monovalent Ions** (Na^+, K^+, Cl^-): – 1 milliequivalent (mEq/L) = 1 millimole

• **Divalent Ions** (Ca^{++}, Mg^{++}, and HPO_4^{2-}) – 1 milliequivalent = 0.5 millimole

Electrolyte Functions

- Volume and osmotic regulation
- Myocardial rhythm and contractility
- Cofactors in enzyme activation
- Regulation of ATPase ion pumps
- Acid-base balance
- Blood coagulation
- Neuromuscular excitability
- Production of ATP from glucose

Sodium

- Most abundant extracellular cation.
- Regulates body water distribution.
- Aids nerve impulse transmission.
- Aids transfer of calcium into cells.
- Transmission and conduction of nerve impulses
- Responsible for osmolarity of vascular fluids
- Regulation of body fluid levels
- Sodium shifts into cells and potassium shifts out of the cells (sodium pump)
- Assists with regulation of acid-base balance by combining with Cl or HCO3 to regulate the balance

Regulation of Sodium

Concentration depends on:

- intake of water in response to thirst
- excretion of water due to blood volume or osmolality changes
- Renal regulation of sodium - Kidneys can conserve or excrete Na+ depending on ECF and blood volume
- by aldosterone and the renin-angiotensin system- this system will stimulate the adrenal cortex to secrete aldosterone.

Aldosterone (adrenal cortex) - promote excretion of K in exchange for reabsorption of Na

Sodium normal values in Serum – 135-148 mEq/L

<u>Clinical Features: Sodium</u>

Hyponatremia: < 135 mmol/L

Increased Na+ loss

- Aldosterone deficiency - **Addison's disease (hypo-adrenalism,result in ↘ aldosterone)**
- Diabetes mellitus - **In acidosis of diabetes, Na is excreted with ketones**
- Potassium depletion **K normally excreted , if none, then Na**

- Loss of gastric contents
- Increased water retention
- Dilution of serum/plasma Na+ excretion of > 20 mmol /mEq urine sodium)
- Renal failure
- Nephrotic syndrome
- Water imbalance
- Excess water intake
- Chronic condition

Hypernatremia- Excess water loss resulting in dehydration **(relative increase)**

- Sweating
- Diarrhea
- Burns
- Dehydration from inadequate water intake,
- including thirst mechanism problems
- Diabetes insipidus (ADH deficiency … H_2O loss)
- Excessive IV therapy
- comatose diabetics following treatment with insulin. Some Na in the cells is kicked out as it is replaced with potassium**.**
- Cushing's syndrome **- opposite of Addison's**

Potassium

- Most abundant intracellular cation.
- Necessary for transmission and conduction of nerve impulses.
- Maintenance of normal cardiac rhythm.
- Necessary for smooth and skeletal muscle contraction.
- the major cation of intracellular fluid

Only 2 % of potassium is in the plasma Potassium concentration inside cells is 20 X greater
than it is outside. This is maintained by the Na pump, (exchanges 3 Na for 1 K)

$$\frac{\text{INSIDE}}{\text{OUTSIDE}} = \frac{20}{1}$$

- Potassium is the most abundant cation in the body cells
- 97% is found in the intracellular fluid
- Also plentiful in the GI tract
- Normal extracellular K+ is 3.5-5.3
- A serum K+ level below 2.5 or above 7.0 can cause cardiac arrest
- 80-90% is excreted through the kidneys
- Functions
  - Promotes conduction and transmission of nerve impulses
  - Contraction of muscle

– Promotes enzyme action
– Assist in the maintenance of acid-base
• Food sources – veggies, fruits, nuts, meat
• Daily intake of K is necessary because it is poorly conserved by the body

Regulation

- Diet - easily consumed (bananasetc.)
- Kidneys - responsible for regulation. Potassium isreadily excreted, but gets reabsorbed in the proximal tubule - under the control of ALDOSTERONE
- Potassium normal values Serum (adults) – **3.5 - 5.3 mEq/L**
- Newborns slightly higher – **3.7 - 5.9 mEq/L**

Hypokalemia

- Decrease in K concentration
- **neuromuscular weakness & cardiac arrhythmia**

Causes of hypokalemia

- Excessive fluid loss (diarrhea,vomiting, diuretics)
- ↑ Aldosterone promote Na reabsorption … K is excreted in its place (Cushing's syndrome = hyper aldosterone)
- Insulin IVs promote rapid cellular potassium uptake

- Increased plasma pH (decreased Hydrogen ion)
  K+ moves into RBCs to preserve electrical balance, causing plasma potassium to decrease.
  (Sodium also shows a slight decrease)

<u>Hyperkalemia</u>

- Increased K concentration
- IV'S or other increased intake
- Renal disease – impaired excretion
- Acidosis (Diabetes mellitus)
- H+ competes with K+ to get into cells & to be excreted kidneys
- Decreased insulin promotes cellular K loss
- Hyper osomolar plasma (from ↑ glucose)
- pulls H2O and potassium into the plasma

Calcium

- Extracellular cation
- Plays role in nerve impulse transmission.
- Increases force of muscle contractions.

- Functions as an enzyme co-factor in bloodclotting.
- Necessary for structure of bone and teeth.
- Hypercalcemia [Ca > 5.8 mEq/L; Normal = 4.5-5.8 mEq/L]

Causes
- Hyperparathyroidism
- Immobility
- Increased vitamin D intake
- Osteoporosis & osteomalacia [early stages]

Hypocalcemia [Ca < 4.5 mEq/L; Normal = 4.5- 5.8 mEq/L]
Causes
- Acute pancreatitis
- Diarrhea
- Hypoparathyroidism
- Lack of vitamin D In the diet
- Long-term steroid therapy

Magnesium
- Intracellular cation.
- Activates (ATP-ase) the primary energy source for the sodium potassium pump.
- Plays important role in the relaxation of smooth muscle.
- Stabilizes cardiac muscle cells – decreases fibrillation threshold.
- Normal = 1.5- 3.0 mEq/L

Hyermagnesemia [Mg > 3.0 mEq/L]
Causes
- Renal insufficiency, dehydration
- Excessive use of Mg-containing antacids or laxatives

Hypomagnesemia [Mg < 1.50 mEq/L]
Causes
- Low intake of Mg in the diet
- Prolonged diarrhea
- Massive diuresis
- Hypoparathyroidism

Chloride
- the major anion of extracellular fluid
- Chloride moves passively with Na+ or against HCO3 - to maintain neutral electrical charge
- Chloride usually follows Na (if one is abnormal, so is the other)

Function –

- not completely known
- body hydration
- osmotic pressure
- electrical neutrality & other functions
- **Found in ECF**
- **Changes the serum osmolarity**
- **Goes with Na in retention of water**
- **Assists with regulation of acid-base balance**
- **Cl combines with hydrogen to form hydrochloric acid in the stomach**

Regulation via diet and kidneys

- In the kidney, Cl is reabsorbed in the renal proximal tubules, along with sodium.
- Deficiencies of either one limits the reabsorption of the other.
- Normal values Serum – 100 -110 mEq/L

Hypochloremia

- Decreased serum Cl
- loss of gastric HCl
- salt loosing renal diseases
- metabolic alkalosis;
- increased HCO_3^- & decreased Cl

Hyperchloremia

- Increased serum Cl
- dehydration (relative increase)
- excessive intake (IV)
- congestive heart failure
- renal tubular disease
- metabolic acidosis
- decreased HCO_3^- & increased Cl

Bicarbonate

- Principle buffer of body pH. (extracellular) Neutralizes acids.
- Plays important role in acid / base balance.
- Acts as chemical sponge to soak up Hydrogen ions.(Acidic metabolic waste) For every one Hydrogen ion twenty bicarbonate ions are released to maintain balance.
- Carbon dioxide/bicarbonate – ***** the major anion of intracellular fluid 2nd most important anion (2nd to Cl)

Note: most abundant intra-cellular anion 2nd most abundant extra-cellular

Total plasma CO_2 = HCO_3^- + $H_2CO_3^-$ + CO_2

HCO_3^- (carbonate ion) accounts for 90% of total plasma

CO_2

H_2CO_3- carbonic acid (bicarbonate)
Regulation:
Bicarbonate is regulated by secretion / reabsorption of the renal tubules
Acidosis : ↓ renal excretion
Alkalosis : ↑ renal excretion
Kidney regulation requires the enzyme carbonic anhydrase **-** which is present in renal tubular cells & RBCs
carbonic anhydrase Reaction: $CO_2 + H_2O \leftrightharpoons H_2CO_3 \rightarrow H^+ + HCO_3^-$
Normal values **Total** Carbon dioxide (venous) – @ 22-30 mmol/L
includes bicarb, dissolved & undissociated H_2CO_3 - carbonic acid (bicarbonate)
Bicarbonate ion (HCO_3^-) – 22-26 mEq/L

Phosphate
Phosphate ($H_2PO_4^-$, $HPO4_2^-$, PO_43^-)
- Important ICF anions; plasma 1.7-2.6 mEq/liter
- most (85%) is stored in bone as calcium salts also combined with lipids, proteins, carbohydrates, nucleic acids (DNA and RNA), and high energy phosphate transport compound
- important acid-base buffer in body fluids

Regulation - regulated in an inverse relationship with Ca^{2+} by PTH and Calcitonin
Homeostatic imbalances
- Phosphate concentrations shift oppositely from calcium concentrations and symptoms are usually due to the related calcium excess or deficit.

Electrolytes used in the replacement therapy:
Under normal physiological conditions the body mechanisms are able to adjust the electrolyte balance. But in abnormal conditions of the body like prolonged fever, severe vomiting or diarrhoea, there are heavy loss of water and electrolytes. In order to compensate, administration of lost electrolyte in the concentration of tonicity becomes essential.
There are two types of solutions of electrolytes are used in replacement therapy.

1. **A solution for rapid initial replacement**
This solution having sodium in the concentration range of 130-150 mEq/l, 98-110 mEq/l of chlorine, 28-55 mEq/l of bicarbonate, 4-12 mEq/l of potassium, 3-5 mEq/l of calcium and 3 mEq/l of magnesium. These concentrations are closely related to the electrolytes in found in extracellular fluid.
2. **A solution for subsequent replacement**
This solution having the concentration range of 40-120 mEq/l of sodium, 10-105 mEq/l of chlorine, 16-53 mEq/l of bicarbonate, 16-35 mEq/l of potassium, 10-15 mEq/l of calcium, 3-6 mEq/l of magnesium and 0-13 mEq/l of phosporous.

Sodium chloride*

Formula – NaCl, Mol. Wt. 58.4. Sodium Chloride contains not less than 99% and not more than 100.5 % of NaCl, calculated on the dried basis.

Preparation –

1. It is prepared in the lab from common salt in water by passing HCl gas and the crystals are precipitated out.
2. Sodium chloride will be synthesized by reacting sodium bicarbonate with hydrochloric acid. The reaction equation is shown below:

$$NaHCO_3 + HCl \rightarrow NaCl + H_2O + CO_2$$

3. Industrially, it is prepared by evaporating sea water and purified.

Properties

- It is a white or colourless crystals or a white crystalline powder.
- It is odourless and saline(salty) taste.
- It is soluble in water and insoluble in alcohol.
- On oxidation, it liberates chlorine gas.

$$2Cl^- + MnO_2 + 2H_2SO_4 \longrightarrow Mn^{2+} + 2SO_4^{2-} + 2H_2O + Cl_2$$

- With silver nitrate solution, it gives water insoluble white precipitate.

$$NaCl + AgNO_3 \longrightarrow AgCl + NaNO_3$$

Identification

- It gives the reactions of sodium and chlorides.
- A 20 %w/v solution (Solution A) in *carbon dioxide-free water* prepared from *distilled water* gives the reactions of sodium salts.

Tests for purity:

Conduct the tests for acidity or alkalinity, arsenic, barium, bromide, calcium, magnesium, ferrocyanide, heavy metals, iodide, iron, sulphate as per IP.

Assay.

Modified Volhard method

Weigh accurately about 0.1 g and dissolve in 50 ml of *water* in a glass-stoppered flask. Add 50 ml of *0.1 M silver nitrate*, 5 ml of *2M nitric acid* and 2 ml of *dibutyl phthalate* or 5ml of *nitrobenzene*, shake well and titrate with *0.1M ammonium thiocyanate* using 2ml of *ferric ammonium sulphate solution* as indicator, until the colour becomes reddish yellow. 1ml of *0.1M silver nitrate* is equivalent to 0.005844 g of NaCl.

Sodium *Chloride* intended for use in the manufacture of parenteral preparations or in the manufacture of dialysis solutions complies with the tests for potassium and aluminium.
Storage. Store protected from light.

Official Preparations of sodium chloride in IP
1.Sodium Chloride and Dextrose Injection IP

Sodium Chloride and Dextrose Injection is a sterile solution of Sodium Chloride and Dextrose in Water for Injections. Sodium Chloride and Dextrose Injection contains not less than 95% and not more than 105% of the stated amounts of sodium chloride and dextrose.

2. **Compound Sodium Chloride and Dextrose Injection**
Compound Sodium Chloride and Dextrose Injection is a sterile solution containing 0.86 %w/v of Sodium Chloride, 0.03 %w/v of Potassium Chloride, 0.033 % w/v of Calcium Chloride and 5 % w/v of Dextrose in Water for Injections.

3. **Sodium Chloride Hypertonic Injection**
Sodium Chloride Hypertonic Injection is a sterile 1.6 %w/v solution of Sodium Chloride in Water for Injection.

4. Sodium Chloride Injection
Sodium Chloride Injection is a sterile 0.9 %w/v solution of Sodium Chloride in Water for Injections.

5. Compound Sodium Chloride Injection (Ringer's Injection)
Compound Sodium Chloride Injection is a sterile solution containing 0.86 %w/v of Sodium Chloride, 0.03 %w/v of Potassium Chloride and 0.033 %w/v of Calcium Chloride in Water for Injections.

6. Compound Sodium Chloride Solution(Ringer's Solution)
Compound Sodium Chloride Solution is a solution containing 0.86 %w/v of Sodium Chloride, 0.03 %w/v of Potassium Chloride and 0.033 % w/v of Calcium Chloride in Purified Water. The solution may be clarified by filtration.

7. Sodium Chloride Irrigation Solution
Sodium Chloride Irrigation Solution is a sterile solution containing 0.9 per cent w/v of Sodium Chloride in Water for Injections.

Potassium chloride
Mol. Formula KCl, Mol. Wt. 74.6, Potassium Chloride contains not less than 99% and not more than 100.5 % of KCl, calculated on the dried basis.

Preparation

1. In the laboratory, It is prepared by the reaction of HCl with Potassium carbonate or bicarbonate

$K_2CO_3 + 2HCl \rightarrow 2KCl + H_2O + CO_2$

$KHCO_3 + HCl \rightarrow KCl + H_2O + CO_2$

2. It is also prepared from the naturally occurring mineral carnallite (KCl, MgCl2.6H2O). The raw salt is grinded and treated with hot water, the less soluble KCl crystallizes out on cooling.

Properties

- ❖ Colourless crystals or a white, crystalline powder.
- ❖ It is odourless and saline taste.
- ❖ It is soluble in water and insoluble in alcohol.
- ❖ 10% of aqueous solution is neutral to litmus paper.
- ❖ The chloride is precipitated by adding Ag^{+}, Hg^{2+} and Pb^{2+}

Tests for purity:

Conduct the tests for acidity or alkalinity, arsenic, barium, bromide, calsium, magnesium, heavy metals, iodide, iron, sulphate as per IP.

Storage. Store protected from moisture.

Official Preparations of potassium chloride in IP

1.Potassium Chloride and Dextrose Injection

Potassium Chloride and Dextrose Injection is a sterile solution of Potassium Chloride and Dextrose in Water for Injections. Potassium Chloride and Dextrose Injection contains not less than 95% and not more than 110% of the stated amount of potassium chloride and not less than 95% and not more than 105% of the stated amount of dextrose.

2. **Potassium Chloride, Sodium Chloride and Dextrose Injection**

Potassium Chloride, Sodium Chloride and Dextrose Injection is a sterile solution of Potassium Chloride, Sodium Chloride and Dextrose in Water for Injections. Potassium Chloride, Sodium Chloride and Dextrose Injection contains not less than 95% and not more than 110% of the stated amounts of sodium, potassium, and chloride and not less than 95% and not more than 105% of the stated amount of dextrose.

Calcium gluconate*

Mol. Formula $C_{12}H_{22}CaO_{14},H_2O$ Mol. Wt. 448.4

Calcium gluconate is calcium D-gluconate monohydrate. Calcium Gluconate contains not less than 98.5 % and not more than 102% of $C_{12}H_{22}CaO_{14},H_2O$.

Preparation

It is prepared by the reaction between D-Glucose and calcium carbonate in presence of sodium bromide.

Properties

- ❖ It is a white, crystalline powder or granules.
- ❖ It is odourless and tasteless.
- ❖ It is slowly soluble in boiling water; insoluble in alcohol or other organic solvents.
- ❖ Melting point is 120^{o}C.

Assay.

Weigh accurately about 0.5 g and dissolve in 50 ml of warm *water*; cool, add 5.0 ml of *0.05 M magnesium sulphate* and 10 ml of *strong ammonia solution* and titrate with *0.05 M disodium edetate* using *mordant black II mixture* as indicator. From the volume of *0.05 M disodium edetate* required subtract the volume of the magnesium sulphate solution added.

1 ml of the remainder of *0.05 M disodium edetate* is equivalent to 0.02242 g of $C_{12}H_{22}CaO_{14}$, H_2O.

Official preparations of Calcium Gluconate as per IP

1.Calcium Gluconate Injection

Calcium gluconate Injection is a sterile solution of Calcium gluconate in water for Injections. Not more than 5% of the Calcium gluconate may be replaced with a suitable calcium salt as a stabilising agent. Calcium gluconate injection contains a quantity of calcium equivalent to not less than 8.5 % and not more than 9.4 % of the stated amount of calcium gluconate.

2.Calcium Gluconate Tablets

Calcium gluconate tablets contain not less than 95% and not more than 105% of the stated amount of calcium gluconate, $C_{12}H_{22}CaO_{14}$, H_2O.

Oral Rehydration Salt (ORS)

ORS Powder

- ❖ Oral Rehydration Salts are dry, homogeneously mixed powders containing Dextrose, Sodium chloride, Potassium chloride and either Sodium bicarbonate or Sodium citrate for use in oral rehydration therapy after being dissolved in the requisite amount of water.
- ❖ They may contain suitable flavouring agents and suitable flow agents in the minimum quantity required to achieve a satisfactory product but may not contain artificial sweetening agents like mono- and/or polysaccharides.
- ❖ If saccharin/saccharin sodium or aspartame is used in preparations meant for paediatric use, the concentration of saccharin should be such that its daily intake is

not more than 5 mg/kg of body weight and that of aspartame should be such that its daily intake is not more than 40 mg/kg of body weight.

Strength.

- ❖ A formulation of reduced osmolarity recommended by the World Health Organization (WHO) for the Diarrhoeal Diseases Control Programme, and of the United Nations Children's Fund (UNICEF).
- ❖ Composition of the formulation in terms of the amount, in g, to be dissolved in sufficient water to produce 1000 ml.

Sodium Chloride -	2.6		
Dextrose (anhydrous) -	13.5 (or)	Dextrose Monohydrate -	14.85
Potassium Chloride -	1.5		
Sodium Citrate -	2.9		

- ❖ The molar concentrations of sodium, potassium, chloride and citrate ions in terms of millimoles per litre are given below:

	mmol/l
Sodium -	75
Potassium-	20
Chloride -	65
Citrate -	10
Dextrose -	75

- ❖ The total osmolar concentration of the solution in terms of mmol per litre is 245.
- ❖ Oral Rehydration Salts contain not less than 90% and not more than 110% of the stated amount of Dextrose (anhydrous) or Dextrose Monohydrate (as appropriate) and of the requisite amounts of sodium, potassium, chloride and citrate, calculated from the stated amounts of the relevant constituents.

Description. A white to creamy-white, amorphous or crystalline powder; odourless.

Storage. Store protected from moisture in sachets, preferably made of aluminum foil, containing sufficient powder for a single dose or for a day's treatment or for use in hospitals, in bulk containers containing sufficient quantity to produce a volume of solution appropriate to the daily requirements of the hospital concerned.

Uniformity of weight. Comply with the test for contents of packaged dosage forms (2.5.6).

Seal test (*only for sachets*).

PHYSIOLOGICAL ACID-BASE BALANCE

- ❖ Normally body fluid pH is 7.35 - 7.45. There are three major mechanisms that maintain this range.

1. Buffer systems -- Buffer systems react quickly to bind H^+ or OH^- (hydroxide) ions to prevent drastic changes in pH.

2. exhalation of CO_2 -- Because of the relationship between CO_2 and H^+, alterations in respiratory rate affect changes in pH by changing the CO_2 concentration of the body.

3. kidney excretion of H^+ -- H^+ secretion from distal tubules of the nephrons directly into filtrate acidifies urine and removes the H^+ form the body.

1. BUFFER SYSTEMS

The buffer system present in our body are used to prevent drastic changes in the pH of a body fluid. There are three major buffer systems in body fluids.

carbonic acid - bicarbonate buffer system, phosphate buffer system, protein buffer system

the chemical reactions that take place in the carbonic acid - bicarbonate buffer system.

$$HCl + NaHCO_3 \rightarrow NaCl + H_2CO_3$$

strong acid + weak base → salt + weak acid

$$NaOH + H_2CO_3 \rightarrow H_2O + NaHCO_3$$

strong base + weak acid → water + weak base

the chemical reactions that take place in the phosphate buffer system, an important regulator of intracellular pH.

$$HCl + Na_2HPO_4 \rightarrow NaCl + NaH_2PO_4$$

strong acid + weak base → salt + weak acid

$$NaOH + NaH_2PO_4 \rightarrow H_2O + Na_2HPO_4$$

strong base + weak acid → water + weak base

The protein buffer system is the most abundant buffer in cells and plasma. Proteins act as both acidic and basic buffers because they have a free carboxyl group and a free amine group. The chemical reactions that demonstrate how a protein can serve in both capacities.

```
          R                        R
          |                        |
NH2---C---COOH    →    NH2---C---COO- + H+
          |                        |
          H                        H
```

```
          R                          R
          |                          |
COOH---C---NH2 + H+    →    COOH---C---NH3+
          |                          |
          H                          H
```

Show how hemoglobin (a protein) is an especially good buffer system in red blood cells.

$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^- \rightarrow 4\ O_2$-hemoglobin $\rightarrow$ H – hemoglobin + O_2

2. EXHALATION OF CARBON DIOXIDE

The role of the respiratory system is to control of body fluid pH. Breathing plays a most important role in the control of acid-base balance. Remember the reaction?

$CO_2 + H_2O <\text{--}> H_2CO_3 <\text{--}> H^+ + HCO_3^-$

In the tissues where carbon dioxide is abundant, the reaction is shifted to the right:

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

In lungs where hydrogen ions are liberated from hemoglobin, the reaction is shifted to left:

$CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow H^+ + HCO_3^-$

From an acid- base balance standpoint, increased respirations tend to cause a decrease in hydrogen ion concentration and therefore an increase in body fluid pH. The opposite is true for decreased respiration. Use of respiratory system to correct body fluid pH is called <u>respiratory compensation</u>.

Consider the following negative feedback situation:

<u>controlled condition</u> -- Homeostasis is disrupted by a decrease in body fluid pH (increased H^+ concentration.

<u>receptors</u> -- Chemoreceptors in the medulla detect the increased H^+ concentration and generate nervous input into the respiratory center of the medulla.

<u>control center</u> -- The inspiratory area of the respiratory center integrates the input and increases the rate of nerve impulse output to the inspiratory muscles.

<u>effectors</u> -- In response to nerve impulses the diaphragm and external intercostal muscles contract more forcefully and more often (hyperventilation).

<u>return to homeostasis</u> -- With an increased respiratory rate there is a loss of carbon dioxide and therefore H+, leading to an increase in body fluid pH and a return to homeostasis.

3. KIDNEY EXCRETION OF H^+

The third major mechanism by which body fluid is maintained is through kidney excretion of hydrogen ions. Distal tubules of the kidneys secrete hydrogen ions directly into the filtrate so that urine is acidified and the hydrogen ions are lost from the body. This is a normal process that occurs at some normal rate.

If other mechanisms for acid - base balance fail and the rate of kidney excretion of hydrogen ions increases above normal, the process is called <u>renal</u>

compensation. This is a much more permanent solution to hydrogen ion problems because the hydrogen ions are eliminated from the body.