MAGNESIUM

The fourth most abundant element in the earth's crust

- Magnesium is the fourth most abundant and important cation in humans .
- It is extremely essential for life and is present as intracellular ion in all living cells and tissues .

MAGNESIUM

- The adult body contain about 20 g of magnesium
- About 70% of which is found in bones in combination with calcium and phosphorus.
- The remaining 30% occurs in the soft tissue and body fluids.

SOURCES

- Vegetables
- Cereals
- Beans
- Green vegetables
- Potatoes
- Almonds ,dairy products

MAGNESIUM

Biochemical functions:

- Magnesium is required for the formation of bone and teeth.
- Mg^{+2} serves as a cofactor for several enzymes requiring ATP e.g hexokinase, glucokinase, phosphofructokinase, adenylate cyclase.
- Mg^{+2} is necessary for proper neuro muscular function. Low Mg^{+2} levels lead to neuromuscular irritability.

Can it be synthesized by the human body or must it come from other sources

- Magnesium is a mineral, so therefore just like calcium, magnesium must be absorbed through dietary intake.

Daily Requirement (RDA)

- Adult man ---------- 350mg/day
- Adult woman ---------- 300mg/day

Absorption

- Magnesium is absorbed by the intestinal cells through a specific carrier system.
- About 50% dietary Mg is normally absorbed
- consumption of large amount of calcium phosphate and alcohol diminishes Mg absorption.
- PTH increases Mg absorption

Serum Mg

- Normal serum concentration of Mg is 2—3 mg/dl. It is present in ionized form (60%),
- In combination with other ions (10%).
- Bound to proteins (30%)

- FACTORS AFFECTING ABSORPTION
- Absorption is doubled when normal dietary Mg requirement is doubled .
- Absorption is increased when diet is deficient in calcium .
- Absorption is decreased when the motility of intestine is increased
- Vitamin D increases and favours absorption of Mg

- Parathyroid harmone increases absorption .
- Growth harmone increases absorption .
- High protein intake increases absorption .
- Fatty acid , phytates , and phosphate decreases absorption .

- EXCRETION
- Magnesium is lost from the body in faeces , sweat and urine
- 60 % to 80 % of orally taken magnesium is lost in faeces .

- NORMAL SERUM LEVEL OF MAGNESIUM
- Normal serum magnesium is 1.8 – 2.2 mg / dl.
- Inside the RBC the magnesium content is 5 mEq /dl .In muscle magnesium is 20 m Eq /l .
- About 70 % of magnesium exists in free state and remaining 30 % is protein bound .
- Serum must be separted from the clot as soon as possible , hemolyzed samples as well as blood collected with citrate , oxalate or EDTA are unacceptable for analysis .

Deficiency/Disease Treatment

- Hypomagnesemia, resulting in low blood calcium levels, muscle cramps,spasms or seizures, nausea, weakness, irritability and confusion
- Chronic diseases such as heart disease, high blood pressure, osteoporosis and type 2 diabetes
- Early signs of magnesium deficiency include loss of appetite, nausea,vomiting,fatigue,and weakness

- WHEN TO TEST FOR MAGNESIUM
- Cardiac arrhythmia
- Resistant hypokalemia
- Pregnancy with pre eclampsia
- Tetany not responding to tetany

- It is commonly seen in hospital patients .
- When serum levels falls below 1.7 mg /dl it is called hypomagnesemia .
- Deficiency of magnesium leads to neuromuscular hyperirritability and cardiac arrhythmias .
- The magnesium deficiency symptoms are similar to those of calcium deficiency , but symptoms will be relieved only when magnesium is given .

- Acute symptomatic deficiency can be treated by giving parental magnesium .
- Oral therapy may lead to diarrhea, hence intravenous magnesium sulphate is given .

CAUSES OF HYPOMAGNESEMIA

- Increased urinary loss
- Familial hypomagnesemia
- Increased intestinal loss
- Liver cirrhosis
- Malabsorption
- Protein calorie malnutrition

- Hypoparathyroidism
- Toxemia of pregnancy
- Drugs
- Thiazide diuretics
- Aminoglycosides
- Cisplatin
- Alcohol

- HYPERMAGNESEMIA
- It is uncommon and always due to excessive intake either orally (antacids)
- Rectally (enema)
- Parentally .
- Magnesium intoxication causes depression of neuromuscular system causing lethargy , hypotention ,respiratory depression ,bradycardia and weak tendon reflexes .

- In severe conditions acute rhabdomyolsis results .
- Hypermagnesemia induces decrease in serum calcium .
- CAUSES OF HYPERMAGNESEMIA
- Excess intake orally or parentally
- Renal failure
- Hyperparathyroidism
- Rickets
- Dehydration

- Drugs
- Antacids
- Tacrolimus

Fun Facts

- “HARD” water contains more magnesium than “Soft” water
- Craving chocolate? Take some magnesium to help take the cravings away

IODIDE

Iodide

- Thyroid hormone synthesis
- Regulates metabolic rate, growth, development
- Absorbed along the GI tract.
- Transported free or bound to proteins in the blood.

IODINE METABOLISM

- 1 Daily requirement of iodine is 150 – 200 micrograms / day . Its sources
- are drinking water , fish , cereals , vegetables , and iodinated salt .
- 2 Total body contains 25 – 30 mg 0f iodine . All cells do not contain iodine
- , but 80 % of the total is stored in the thyroid gland .Iodine level in blood
- Is 5 – 10 micro grams / dl

3 I n most parts of the world iodine is a scarce component of the soil . Upper regions of mountains generally contain less iodine . Such regions are called goiterous belts as Himalayan region

- Commercial source of iodine is seaweeds .The program of iodination of common salt has resulted in increased availability of iodine .
- 5 Ingredients in food stuffs which prevent utilization of iodine are called
- Goitrogens . Goitrogens are seen in cassava maize , bamboo shoots , sweet
- Potatoes and beans . Cabbage and tapioca contain thiocyanate , which
- Inhibits iodine uptake by thyroid . Mustard seed contain thiourea which inhibits
- Iodination of thyroglobulin .
- 6 The only biological role of iodine is in formation of throid harmones thyroxine and
- tri iodothyroxine

Food Sources of Iodide

- Iodize salt (1/2 tsp. meets RDA for iodide)
- Saltwater fish, seafood
- Plant source dependent on soil content
- RDA for adult is 150 ug/day (50ug to prevent goiter)
- Average intake exceeds RDA

Functions of Iodide

- Synthesis of T_4 in response to TSH secretion
- T_4 is converted to T_3 (active hormone)
- T_3 regulates basal metabolic rate, production of body heat ,energy, human growth.
- Development of the CNS

Stages of Iodination

Stages of Iodination of tyrosine and final formation of the two important thyroid hormones, thyroxine (T_4) & triiodothyronine (T_3). Tyrosine is first iodized to monoiodotyrosine and then to diiodotyrosine. Then during the next few minutes to hours, more and more of the iodotyrosine residues become coupled with one another.

Stages of Iodination

Thyroxine (T4), which is formed when two molecule of diiodotyrosine are joined together. Then One molecule of monoiodotyrosine couples with one molecule of diiodotyrosine to form triiodothyronine (T3). Small amount of reverse T3 are formed by coupling of diiodotyrosine with monoiodotyrosine, but RT3 does not appear to be functional significane in humans.

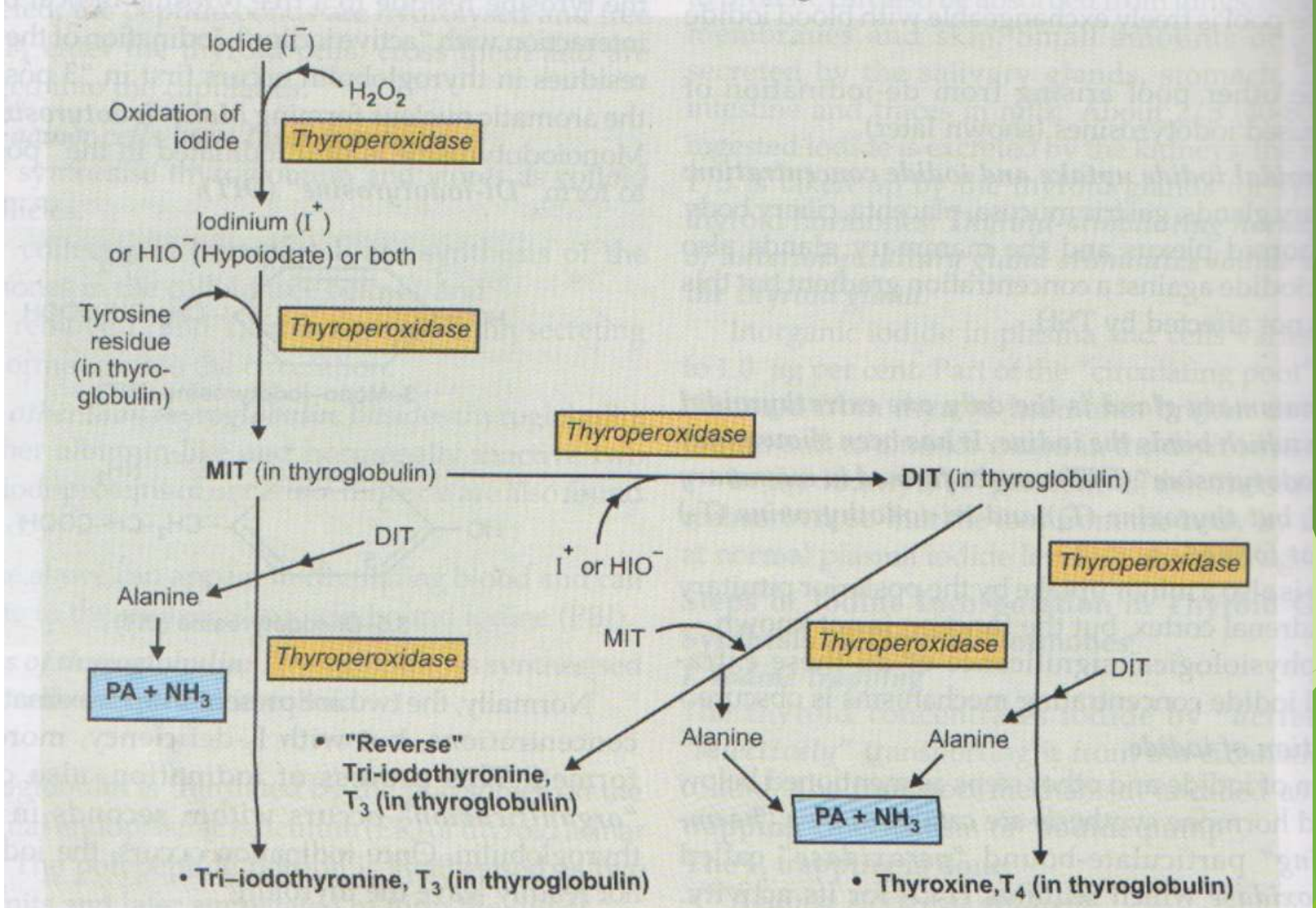

Fig. 33.4: Biosynthesis of thyroid hormones

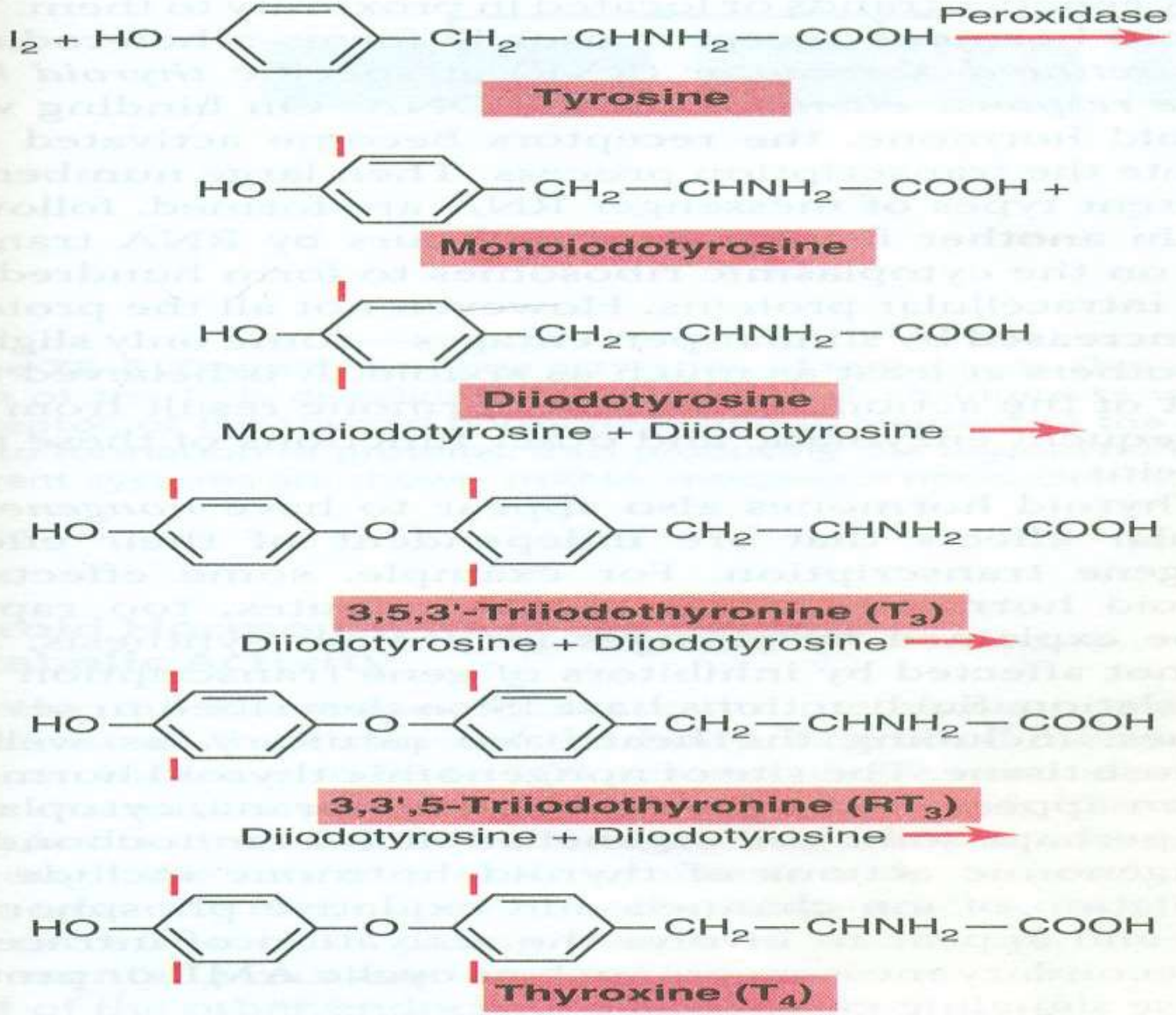

Figure 76-3 Chemistry of thyroxine and triiodothyronine formation.

Deficiency of Iodide

- Continual release of TSH
- Growth of the thyroid gland (goiter)
- Drop in the metabolic rate
- Cretinism
- Consumption of goitrogens (raw turnips, cabbage, cauliflower,) inhibits iodide metabolism

Toxicity of Iodide

- Thyroid hormone synthesis is inhibited
- “Toxic goiter” result
- Upper Level is 1.1 mg/day

abnormalities of thyroid function

- Three abnormalities associated with thyroid function are known .
- GOITER
- Any abnormal increase in the size of thyroid gland is known as goiter . Enlargement of thyroid gland is mostly to compensate the decreased synthesis
- of thyroid harmones and is associated with elevated TSH .
- Goiter is primarily due to a failure in the autoregulation of T 3 and T 4 synthesis . This may be caused by deficiency or excess of iodide

SIMPLE ENDEMIC GOITER

- This is due to iodine deficiency in diet
- HYPERTHYROIDISM
- This is also known as thyrotoxicosis and is associated with over production
- Of thyroid harmones .
- Hyperthroidism is characterized by higher BMR ,nervousness , irritability ,
- Anxiety , increase heart rate , loss of weight ,despite increased appetite ,

- Weakness ,diarrhea , sweating ,sensitivity to heat and often protrusion of
- Eye ball (exophthalmos)
- Hyperthroidism is caused by GRAVE S disease . Graves disease is due to elevated thyroid stimulating IgG also known as long acting throid stimulator
- LATS which activates TSH and then increases thyroid harmone production
- DIAGNOSIS is by scanning and or estimation of T 3 , T 4 both elevated

- And TSH decreased in plasma
- TREATMENT
- Antithyroid drugs
- In severe cases thyroid gland is surgically removed

HYPOTHYROIDISM

- This is due to an impairment in the function of thyroid gland that often causes decreased circulatotory levels of T 3 and T 4 .
- Disorders of hypothalamus or pituitary also contribute to hypothyroidism
- Hypothyroidism is characterized by reduced BMR , slow heart rate ,weight
- gain , sluggish behavior , constipation ,sensitivity to cold . Dry skin .
- Hypothyroidism in children is associated with **cretinism**

- HYPOTHYROIDISM in adults is known as **myxoedemat**
- **TREATMENT**
- **Thyroid harmone administration**

SODIUM

- Sodium is the chief cation of the extracellular fluid.
- About 50% of the body sodium is present in the bones,
- 40% in the extracellular fluid and the remaining 10% in the soft tissues
- Sodium level is intimately associated with water balance
- In the body
- Sodium the extracellular fluid volume

DIETARY REQUIREMENTS

- For adults daily requirement is 1_ 3.5 g
- Infants need 0.1 _ 0.5 g and
- Children need 0.3 _ 2.5 g daily
- Sodium is mainly consumed as sodium chloride
- For persons with a family history of hypertension daily
- Intake should be less

SOURCES

- The common salt used in the cooking medium is the major source of sodium. The ingested food also contribute to sodium
- Other sources include bread whole grains leafy vegetables nuts egg and milk

PLASMA SODIUM

In the plasma the normal concentration of sodium is 135 - 145 mEq /l

Sodium is an extracellular cation therefore blood cells contain much less 35 mEq/l

ABSORPTION OF SODIUM

- Sodium is absorbed by sodium pump situated in the basal
- & lateral plasma membrane of intestinal and renal cells
- SODIUM PUMP
- The sodium potassium pump is found in many cell membranes
- The process moving sodium and potassium ions across the cell membrane is an active transport process involving the hydrolysis of ATP to provide the necessary energy .It involves an enzyme reffered to as Na /K ATPase

Na pump is an enzyme , Na _k ATPase

- It is a glycoprotein composed of 2 alpha and 2 beta chains.
- Its activity requires ATP and Mg ions as cofactor
- Hydrolysis of ATP releases energy to transport three 3 Na
- Ions outside and simultaneously two K ions inside across
- The cell membrane

FORMS OF SODIUM PUMP AND MECHANISM

- Na –K ATPase exists in two forms E 1 and E 2
- The E 1 form presents its ion binding and phosphate binding sites on the cytoplasmic surface of the membrane
- Three sodium ions from the cytoplasm bind with the ion
- Binding sites of E 1 . This leads to phosphorylation of E 1
- With the help of ATP and Mg
- This results in conformational change and E 1 becomes E 2

E 2 now exposes

Both ion binding and phosphate binding sites on the extra

- Cellular surface of the membrane . Lowers the affinity of the ATPase for Na and releases into the ECF
- Now the K ions from the extra cellular bind to the respective binding site of the pump .This lowers the affinity of E 2 for phosphate
- This dephosphorylation changes the conformation of E 2 to E 1 again and lowers its affinity for K ions
- This leads to release of K from ATPase into the cell

EXCRETION OF SODIUM

Kidney is the major route of sodium excretion from the body

Approx 25000mmol of sodium are filtered by the kidneys

Due to tubular reabsorption less than 1 % of the sodium appears in the urine

Approx 70 % of the filtered sodium is reabsorbed in the

Proximal tubules and further 20 % to 30% of filtered sodium

Is absorbed in the ascending loop of Henle

Functions

- 1 In association with chloride and biocarbonate ,sodium regulates the bodys acid base balance
- 2 Sodium is required for the maintenance of osmotic
- Pressure and fluid balance
- 3 Role in action potential
- During stimulation of nerve or muscle fibre a local
- Depolarisation is observed this rapidly increases it s
- Permeability to sodium causing transmembrane influx
- Of Na down its inward conc gradient

4 Sodium is involved in intestinal absorption of glucose

Galactose and amino acids

5 It is necessary for the normal muscle irritability and cell permeability

TWO MAJOR TYPES OF CLINICAL CONDITIONS

- HYPERNATREMIA
- HYPONATREMIA
- CAUSES OF HYPERNATREMIA
- 1 Cushing disease
- 2 Prolong cortisone therapy
- 3 In pregnancy steroid harmone causes sodium retention in the body
- 4 In dehydration when water is predominantly lost,blood
- Volume is decreased with apparent increase sodium concentration

5 Exchange transfusion with stored blood

- 6 Primary hyperaldosteronism
- 7 Elderly patients with poor water intake and inability to
- Express thirst
- 8 Excessive intake of salt
- 9 Drugs
- Ampicillin
- Tetracycline
- Anabolic steroid
- Oral contraceptives
- Loop diuretics
- Osmotic diuretics

CAUSES OF HYPONATREMIA

- 1 Vomiting
- 2 Diarrhea
- 3 Burns
- 4 Addison disease (adrenal insufficiency)
- 5 Renal tubular acidosis (tubular reabsorption of sodium is defective)
- 6 Chronic renal failure nephrotic syndrome
- 7 Congestive cardiac failure
- 8 Hyperglycemia and ketoacidosis

9 Excess non electrolyte (glucose) iv infusion

- 10 SIADH and defective ADH secretion
- 11 Drugs
- ACE inhibitors
- Lithium
- NSAIDS
- Vasopressin and oxytocin

TREATMENT

- Treatment of hyponatremia depends on cause duration and severity
- In acute hyponatremia rapid treatment is possible
- But in chronic cases too rapid correction may increase mortality by neurological complications
- Treatment of hypernatremia is to be done with care to prevent overhydration and water intoxication

POTASSIUM

Potassium

Potassium is the principal intracellular cation. It is equally important in the extracellular fluid for specific function

Biochemical functions

- K+ maintains intracellular osmotic pressure
- It is required for the regulation of acid base balance and water balance in the cells.
- The enzyme pyruvate kinase (of glyocolsis) is dependent $_K$+ for optimal activity.
- K+ is required for the transmission of nerve impulse.
- Adequate intracellular concentration K+ is necessary for proper biosynthesis of proteins by ribosomes.
- Extracellular K+ influences cardiac muscle activity.

Dietary requirments

About 3-4 g/day

Sources

Banana , orange, pineapple, potato, beans, chicken, and liver. Tender coconut water is a rich source of potassium.

Absorption: The absorption of K+ form GIT tract is very efficient (90%) and very little is lost through feces.

Plasma potassium/ Excretion

The plasma (serum) concentration of K+ is 3.4-5.0 mEq/I.

Excretion: K+ is mainly excreted through urine the maintenance of body acid-base balance influences K+ excretion.

Disease States

Hypokalemia: Decrease in the concentration of serum K+ is observed due to overactivity of adrenal cortex (cushing's syndrome) prolonged cortisone therapy I/V administration of K+ free fluids treatment of diabetic coma with insulin prolonged diarrhea and vomiting.

The symptoms of hypokalemia includes irritability, muscular weakness, tachycardia, cardiomegaly and cardiac arrest.

Disease States

Hyperkalemia: Increase in the concentration of serum K+ is observed in renal failure, adrenocortical insufficiency (Addison's disease) diabetic coma, servere dehydration I/V administration of fluids with excessive potassium salts.

The manifestation of hyperkalemia include depression of central nervous system, mental confusion, numbness, bradycardia.

CHLORINE

Chlorine is a constituent of sodium chroride .

Metabolism of sodium and chloride are closely related

BIOCHEMICAL FUNCTIONS

- 1 Chloride is involved in regulation of acid base balance , fluid balance
- and osmotic pressure.These functions are carried out by interaction of chloride with sodium and potassium.
- 2 Chloride is necessary for the formation of HCL in gastric juice.
- 3 Chloride shift involves the active involvement of chloride.
- 4 The enzyme salivary amylase is activated by chloride.

DIETARY REQUIREMENT

- The daily requiremet of chloride as NaCl is 5- 10 g adequate intake of sodium will fulfill the requirement of chloride in the body .
- SOURCES
- Common salt whole grain leafy vegetables eggs
- ABSORPTION
- Chloride is absorbed in the gastrointestinal tract
- PLASMA CHLORIDE
- Plasma conc is 95 – 105 m Eq / l
- CSF fluid contains higher level of chloride .

EXCRETION

- Excess chloride is normally excreted in urine sweat , and bowels
- DISEASES
- HYPOCHLOREMIA
- A reduction of serum chloride is due to
- Vomiting diarrhea , respiratory alkalosis , Addison disease and excessive
- Sweating
- HYPERCHLOREMIA
- Dehydration . Respiratory acidosis and cushing syndrome