Minerals

Principal Elements

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Of the large number of minerals in nature, only a few are essential for human beings

Some of these are required in relatively large quantities

These are known as principal elements or macronutrients

Some minerals are required in minute quantities

These are known as trace elements or micro-nutrients

The principal elements include:

1. Calcium
2. Phosphorus
4. Magnesium
4. Sodium
5. Potassium
6. Chlorine
7. Sulphur

The trace elements include:

1. Iron
2. Iodine
3. Copper
4. Zinc
5. Cobalt
6. Manganese
7. Molybdenum
8. Chromium
9. Selenium
10. Fluorine

Calcium

- The most abundant mineral in our body
- About 1,000 gm present in an adult
- Nearly 99% present in bones and teeth
- The rest in other tissues and body fluids

Muscles and nerves have relatively more calcium than other soft tissues

Calcium is present in bones mainly in the form of calcium phosphate

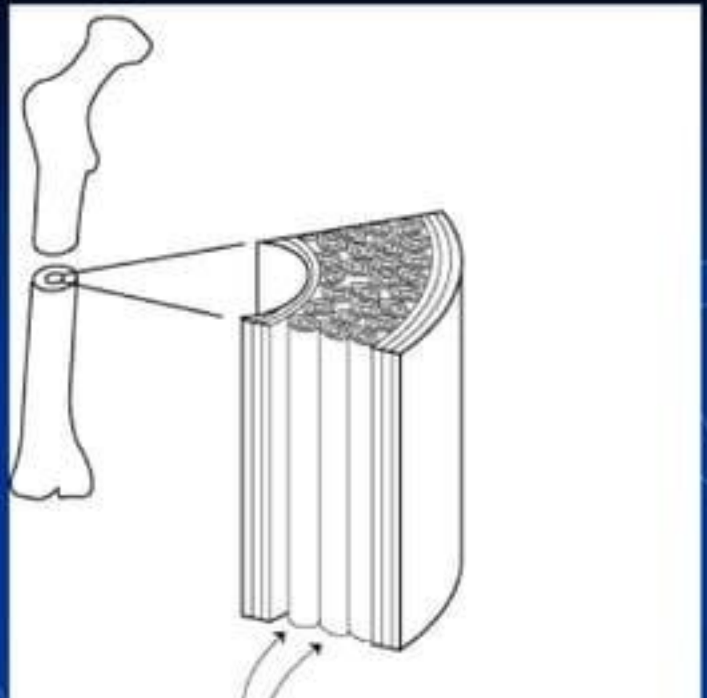
Small amounts of carbonate, hydroxide, fluoride, citrate etc are also present

Calcium phosphate is first deposited in an amorphous form

This is later converted into crystalline form

The crystalline form is hydroxyapatite, and its rough composition is $Ca_{10}(PO_4)_6(OH)_2$

The crystals are rod-shaped



There is a continuous exchange of calcium between bones and extra-cellular fluid

Concentration of calcium in intra- and extra-cellular fluids is delicately regulated

Concentration of calcium in plasma/serum is 9-11 mg/dl (4.5-5.5 mEq/L)

About 50% of this is bound to proteins, and can not diffuse through capillaries (protein-bound or non-diffusible calcium)

About 5% calcium is associated with organic anions, e.g. citrate, and is diffusible

The remaining 45% is free ionized calcium, which is freely diffusible

Almost all the physiological functions of calcium are performed by ionized calcium

Functions of calcium

- Formation of bones and teeth
- Excitability and conductivity of nerves
- Neuromuscular transmission
- Excitability and contractility of myocardium
- Coagulation of blood
- Action of hormones

Formation of bones and teeth

A major function of calcium is to form bones and teeth

Calcium phosphate is deposited around collagen fibres in the zone of ossification

It is deposited in an amorphous form which changes later into hydroxyapatite crystals

Osteoblasts deposit minerals in the bones

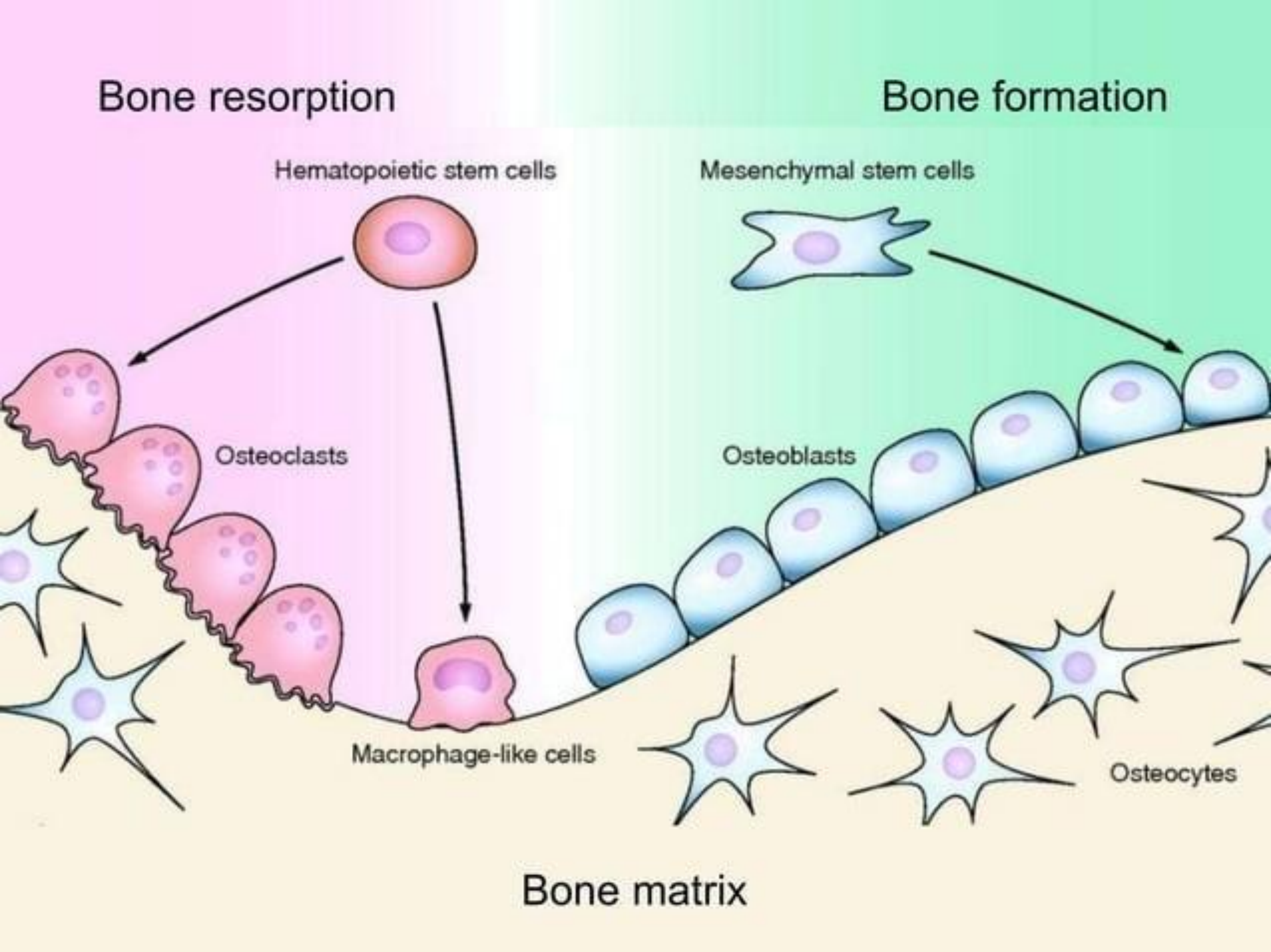
Osteoclasts remove minerals from bones

In growing age, osteoblastic activity is more than the osteoclastic activity

This leads to skeletal growth

In adults, osteoblastic and osteoclastic activities are balanced

This results in continuous remodeling of the bones


Bone resorption
Bone formation
Hematopoietic stem cells
Mesenchymal stem cells
Osteoclasts
Osteoblasts
Macrophage-like cells
Osteocytes
Bone matrix

Excitability and conductivity of nerves

Excitability of nerves depends upon a number of cations including Ca^{++}

A raised plasma Ca^{++} level decreases excitability of nerves

A lowered plasma Ca^{++} level increases the excitability of nerves

Transmission of impulses across synapses occurs due to release of neurotransmitters

This requires Ca^{++}

Neurotransmitters are present in the cell inside synaptic vesicles

There are two pools of synaptic vesicles, reserve pool and releasable pool

In the reserve pool, a synaptic vesicle is bound to actin filaments

Binding occurs through a protein, synapsin I (dephosphorylated)

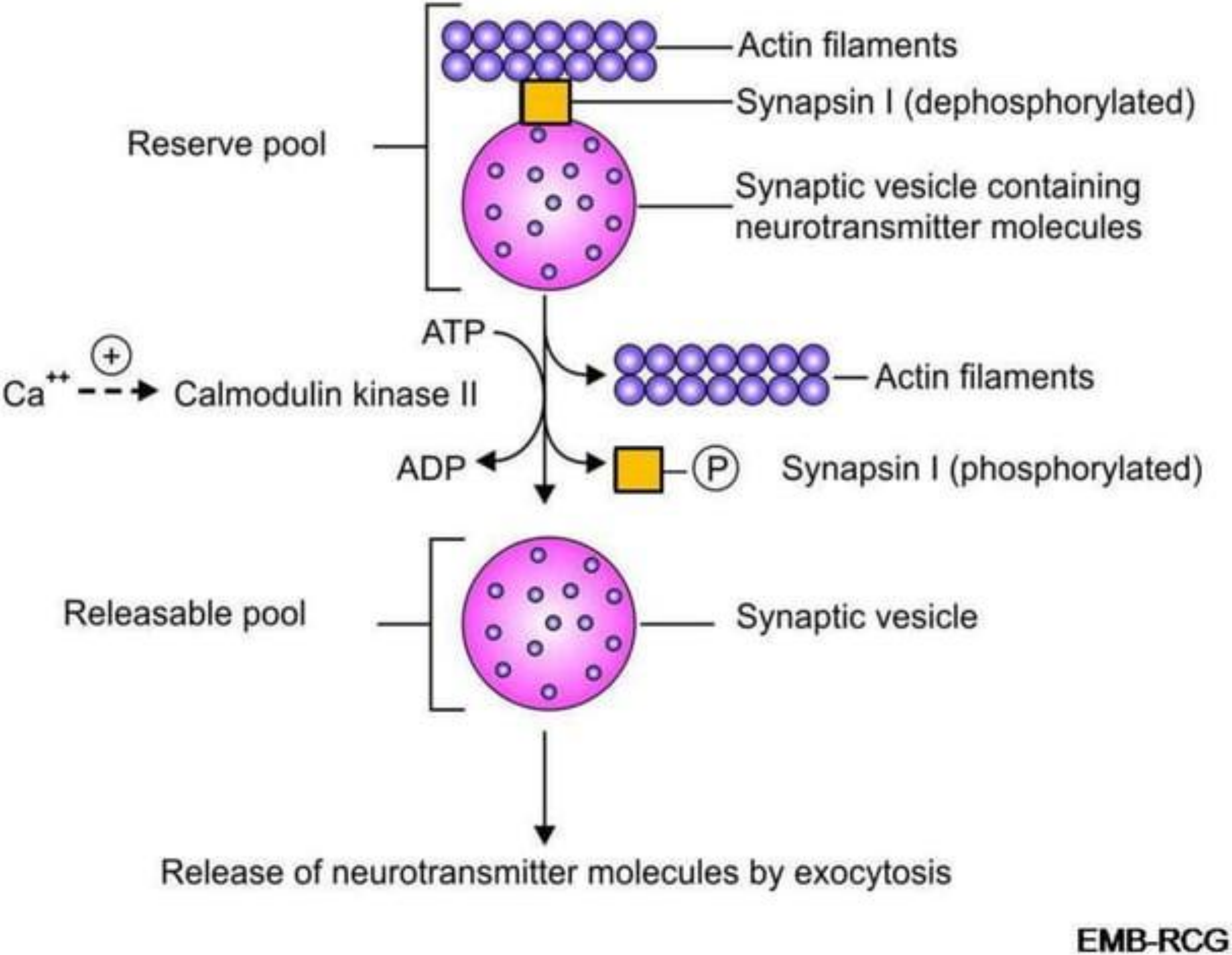
Release of Ca^{++} activates calmodulin (CaM) kinase II

CaM kinase II phosphorylates synapsin I

This leads to dissociation of the synaptic vesicle from actin filaments

Synaptic vesicle moves to releasable pool

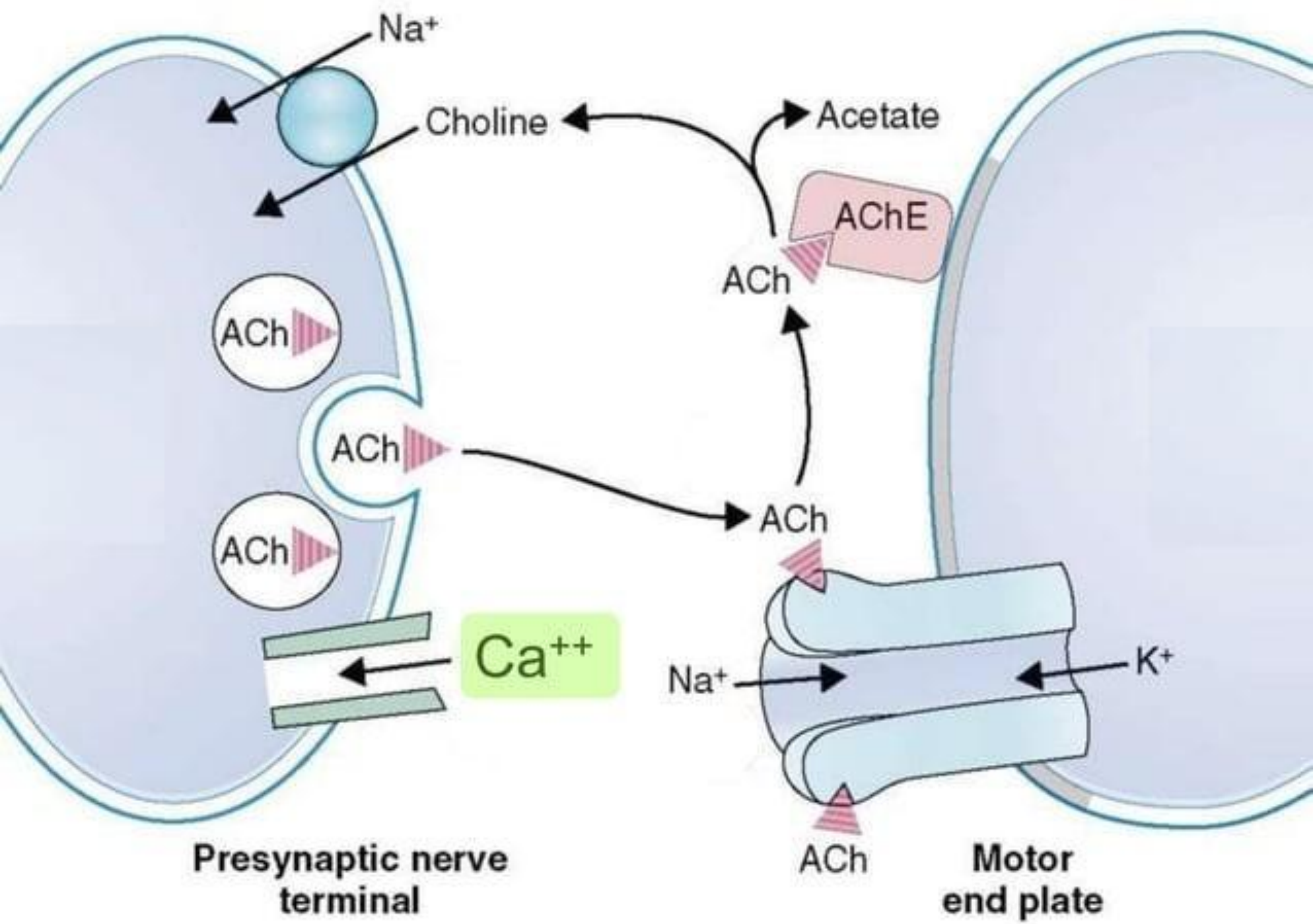
From there, it releases the neuro-transmitter molecules by exocytosis


Actin filaments
Synapsin I (dephosphorylated)
Reserve pool
Synaptic vesicle containing
neurotransmitter molecules
ATP
Ca++
Calmodulin kinase II
Actin filaments
ADP
P
Synapsin I (phosphorylated)
Releasable pool
Synaptic vesicle
Release of neurotransmitter molecules by exocytosis
EMB-RCG

Neuromuscular transmission

Neuromuscular transmission occurs upon release of acetylcholine from motor endplate

This occurs when calcium ions enter the presynaptic terminal



Na+
Choline
Acetate
AChE
ACh
ACh
ACh
ACh
ACh
Ca++
Na+
K+
ACh
Presynaptic nerve terminal
Motor end plate

Excitability and contractility of myocardium

Rhythmic generation of impulses in heart and contraction of myocardium require Ca^{++}

An increase in the concentration of Ca^{++} increases cardiac contractility and vice versa

Coagulation of blood

Ionized calcium is one of the coagulation factors

Coagulation of blood occurs by a cascade of reactions

Calcium ions are required in most of these reactions

Many anticoagulants are used to prevent in vitro coagulation of blood

These include oxalate, citrate, EDTA etc

All of them act by binding calcium ions


BD Vacutainer
Potassium Oxalate
5 mg/4 mg
REF 367921
2014-05
2.0
mL

Action of hormones

Ionized calcium acts as a second messenger for some hormones

Secretion of hormones which are stored in granular form also requires the presence of calcium ions

Absorption

Absorption of calcium occurs by active uptake in the upper part of small intestine

Normally, 10-20% of the dietary calcium is absorbed

The absorption is affected by:

- pH
- Calcium:phosphorus ratio
- Proteins
- Vitamin D and parathormone

pH

A relatively low pH increases solubility of calcium salts

This increases calcium absorption

Calcium:phosphorus ratio

Since calcium and phosphorus are absorbed together, they must be present in food in a proper ratio

The ideal ratio is 1:1 but absorption can occur satisfactorily as long as the ratio lies between 1:2 and 2:1

Proteins

Presence of amino acids together with calcium facilitates calcium absorption

As amino acids are present in proteins, dietary proteins promote calcium absorptions

Vitamin D and parathormone

Vitamin D and parathormone play an important role in calcium metabolism

Cholecalciferol is converted into 1,25-dihydroxycholecalciferol with the help of parathormone

1,25-Dihydroxycholecalciferol (calcitriol) is the active form of cholecalciferol

1,25-Dihydroxycholecalciferol acts on intestinal mucosa and induces the synthesis of:

- Calcium-binding protein
- Calcium-dependent ATPase
- Alkaline phosphatase

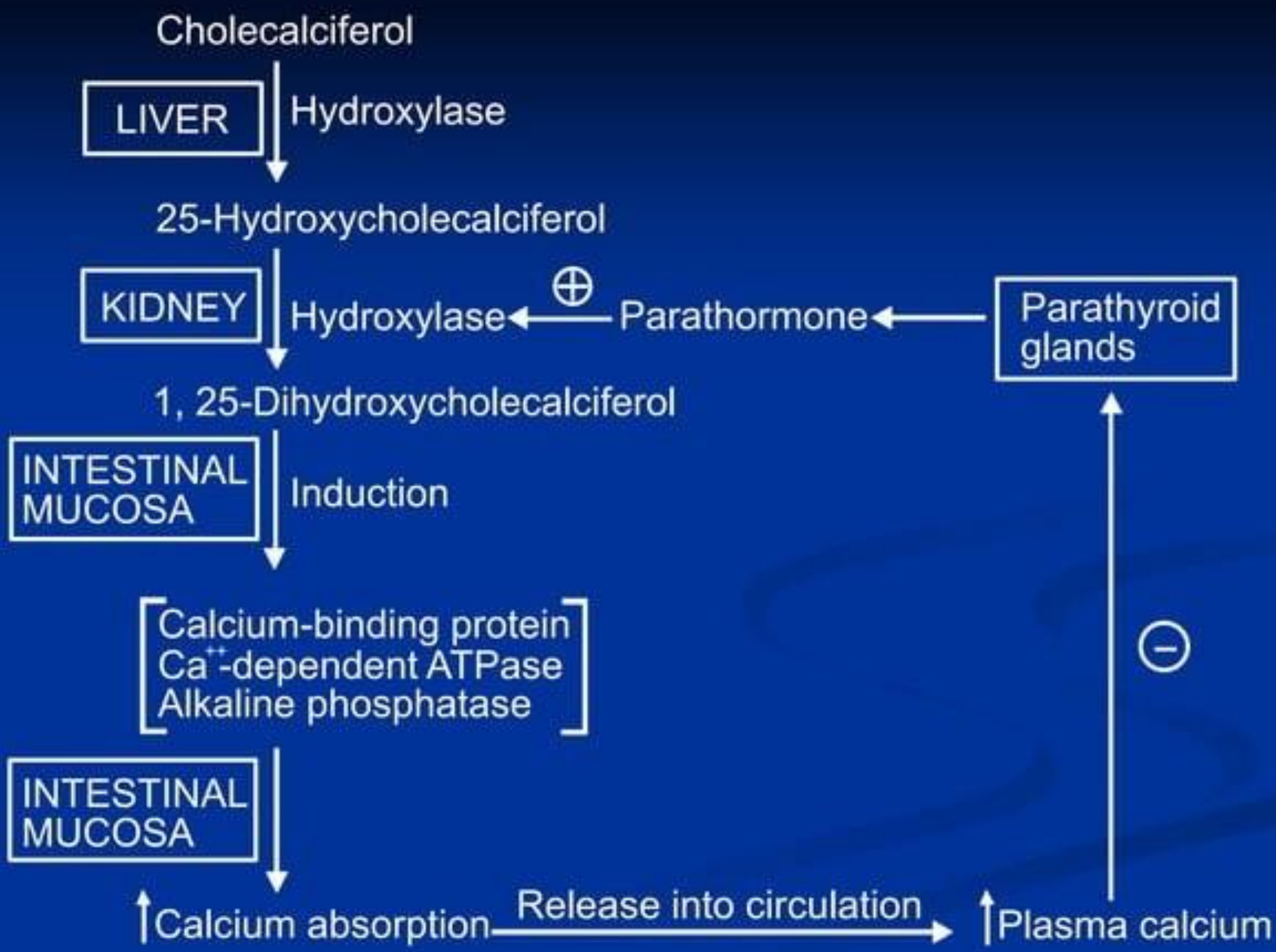
Calcium-binding protein, calcium-dependent ATPase and alkaline phosphatase are required for active absorption of calcium

As calcium is absorbed, plasma calcium level rises

When plasma calcium goes above normal, it causes feedback inhibition of parathormone secretion

This switches off activation of vitamin D

Thus, vitamin D and parathormone act together to regulate plasma calcium


Cholecalciferol
LIVER
Hydroxylase
25-Hydroxycholecalciferol
KIDNEY
Hydroxylase
⊕
Parathormone
Parathyroid glands
1, 25-Dihydroxycholecalciferol
INTESTINAL MUCOSA
Induction
Calcium-binding protein
Ca++-dependent ATPase
Alkaline phosphatase
INTESTINAL MUCOSA
↑Calcium absorption
Release into circulation
↑Plasma calcium
⊖

Daily requirement

Age	Requirement
Infants	400-600 mg/day
Children	800 mg/day
Adolescents	1200 mg/day
Adults	800 mg/day
Pregnant and lactating women	1200 mg/day


Milk
Cheese
Eggs
Nuts
Sources of calcium
Beans
Figs
Lentils
Cabbage

Abnormal serum calcium levels

Serum calcium level may rise or fall in some pathological conditions

An increase in serum calcium level is known as hypercalcaemia

A decrease in serum calcium level is known as hypocalcaemia

Hypercalcaemia occurs in:

- Hyperparathyroidism
- Hypervitaminosis D
- Bone cancer
- Multiple myeloma
- Leukaemia
- Polycythaemia
- Milk-alkali syndrome
- Sarcoidosis
- Idiopathic infantile hypercalcaemia

Hypocalcaemia occurs in:

- Hypoparathyroidism
- Rickets
- Osteomalacia
- Steatorrhoea
- Chronic renal failure
- Nephrotic syndrome

Prolonged elevation of serum calcium can cause deposition of calcium in soft tissues such as kidneys, liver, arteries etc

A sudden decrease in serum calcium may cause tetany (involuntary contraction of skeletal muscles)

Phosphorus

Next to calcium, phosphorus is the most abundant mineral in human beings

About 700 gm of phosphorus is present in an average adult

Nearly 80% of it is present in bones and teeth

The remaining 20% phosphorus is distributed all over the body

Nerves and muscles have relatively high amounts of phosphorus

Phosphorus is mainly an intracellular mineral

Serum inorganic phosphorus is 2.5-4.0 mg/dl in adults and 4-7 mg/dl in children

Serum calcium level (mg/dl) multiplied by serum inorganic phosphorus (mg/dl) is nearly constant

The product of these two is about 40 in adults and about 50 in children

Functions of phosphorus

- Formation of bones and teeth
- Formation of high-energy compounds
- Role in metabolism
- Formation of nucleic acids
- Formation of membranes
- Formation of nervous tissue
- Maintenance of pH

Formation of bones and teeth

Calcium phosphate is the principal salt in bones and teeth

Formation of bones and teeth is one of the major functions of phosphorus

Formation of high-energy compounds

Phosphorus is a constituent of most of the high-energy compounds in our body

These include ATP, creatine phosphate, phosphoenol pyruvate etc

Role in metabolism

Phosphorus is a constituent of co-enzymes e.g. FMN, FAD, NAD, NADP, TTP, pyridoxal phosphate and CoA

Phosphorus plays an important role in metabolic reactions in the form of these coenzymes

Phosphorus has a unique role in the metabolism of carbohydrates

Carbohydrates have to be phosphorylated before they can enter any metabolic pathway

Formation of nucleic acids

Phosphorus is required for the formation of nucleotides

These, in turn, form nucleic acids

Formation of membranes

Phospholipids are major constituents of membranes

Phosphorus participates in the formation of membranes in the form of phospholipids

Formation of nervous tissue

Phospholipids are a constituent of nervous tissue

Thus, phosphorus takes part in the formation of nervous tissue in the form of phospholipids

Maintenance of pH

Inorganic phosphorus exists as HPO_4^{-2} and $H_2PO_4^{-}$

These two constitute a buffer pair and help in the maintenance of pH

Phosphate buffer is more abundant in intracellular fluid

Absorption

Phosphorus is absorbed from the small intestine along with calcium

If absorption of calcium is normal, so will be that of phosphorus

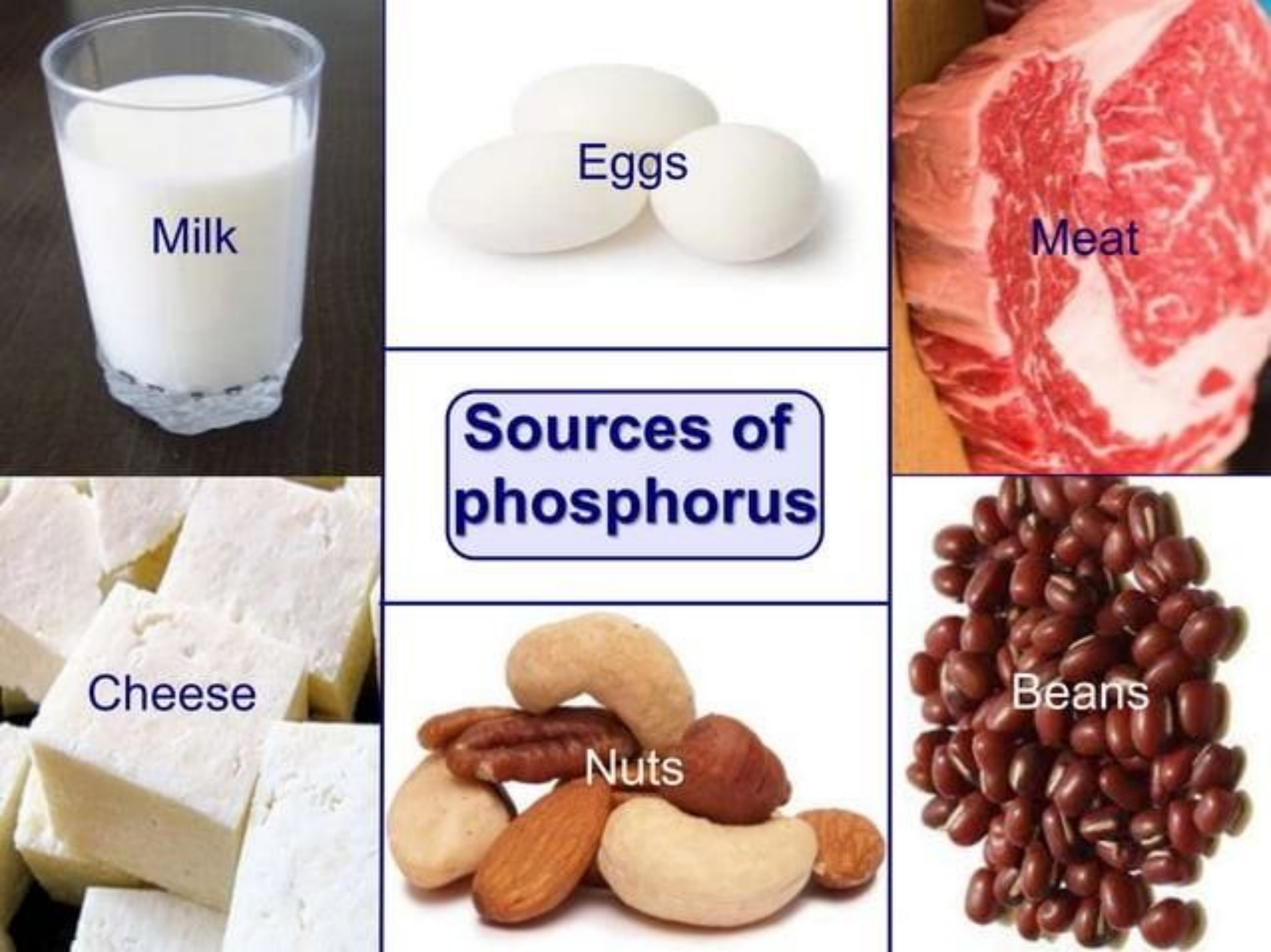
Daily requirement

Age	Requirement
Infants	250-400 mg/day
Children	800 mg/day
Adolescents	1200 mg/day
Adults	800 mg/day
Pregnant and lactating women	1200 mg/day

Dietary sources

Phosphorus is widely distributed in foodstuffs

If calorie and protein intakes are sufficient, a dietary deficiency of phosphorus is unlikely to occur


Milk
Eggs
Meat
Sources of phosphorus
Cheese
Nuts
Beans

Abnormal serum phosphorus levels

An increase in serum inorganic phosphorus level is known as hyperphosphataemia

A decrease in serum inorganic phosphorus level is known as hyperphosphataemia

Hyperphosphataemia occurs in:

- Chronic renal failure
- Hypoparathyroidism
- Hypervitaminosis D
- Acromegaly
- Diabetes mellitus

Hypophosphataemia occurs in:

- Rickets
- Osteomalacia
- Hyperparathyroidism
- Steatorrhoea
- Fanconi syndrome
- Familial hypophosphataemic rickets

Familial hypophosphataemic rickets is also known as renal rickets or vitamin D-resistant rickets

It is an inherited X-linked dominant disorder in which renal tubular reabsorption of phosphate is greatly decreased

Magnesium

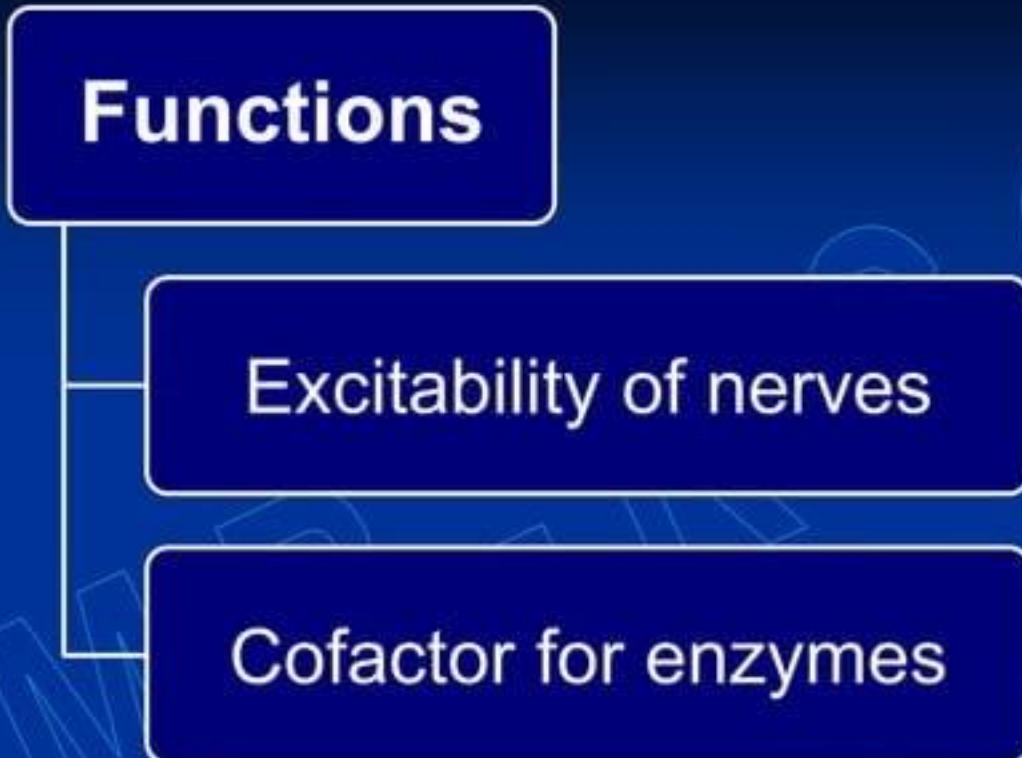
The total magnesium in an average adult is about 20 gm

Bones contain about 70% of the total body magnesium

The rest is present in other tissues and body fluids e.g. muscles, blood, CSF etc

Serum magnesium level is 2-3 mg/dl

Concentration in intracellular fluid is higher than that in extracellular fluid


Functions
Excitability of nerves
Cofactor for enzymes

Excitability of nerves

Together with some other cations, magnesium ions also affect the excitability of nerves

A low magnesium level increases the excitability, and a high magnesium level decreases the excitability

Cofactor for enzymes

Magnesium is a cofactor for all the enzymes requiring ATP

ATP participates in biochemical reactions as Mg^{++}- ATP complex

Magesium-dependent enzymes are involved in the metabolism of:

- Carbohydrates
- Lipids
- Amino acids
- Purines
- Pyrimidines

Examples of magnesium-dependent enzymes are:

- Hexokinase
- Phosphofructokinase
- Pyruvate kinase
- Thiokinase
- Mevalonate kinase
- Squalene synthetase
- Glutamine synthetase
- Carbamoyl phosphate synthetase
- PRPP synthetase

Absorption

Magnesium is absorbed from the small intestine

The extent of absorption depends on the magnesium content of the diet

It is independent of the requirement

On an average diet, about half of the ingested magnesium is absorbed

The degree of absorption increases on a low-magnesium diet

It decreases on a high-magnesium diet

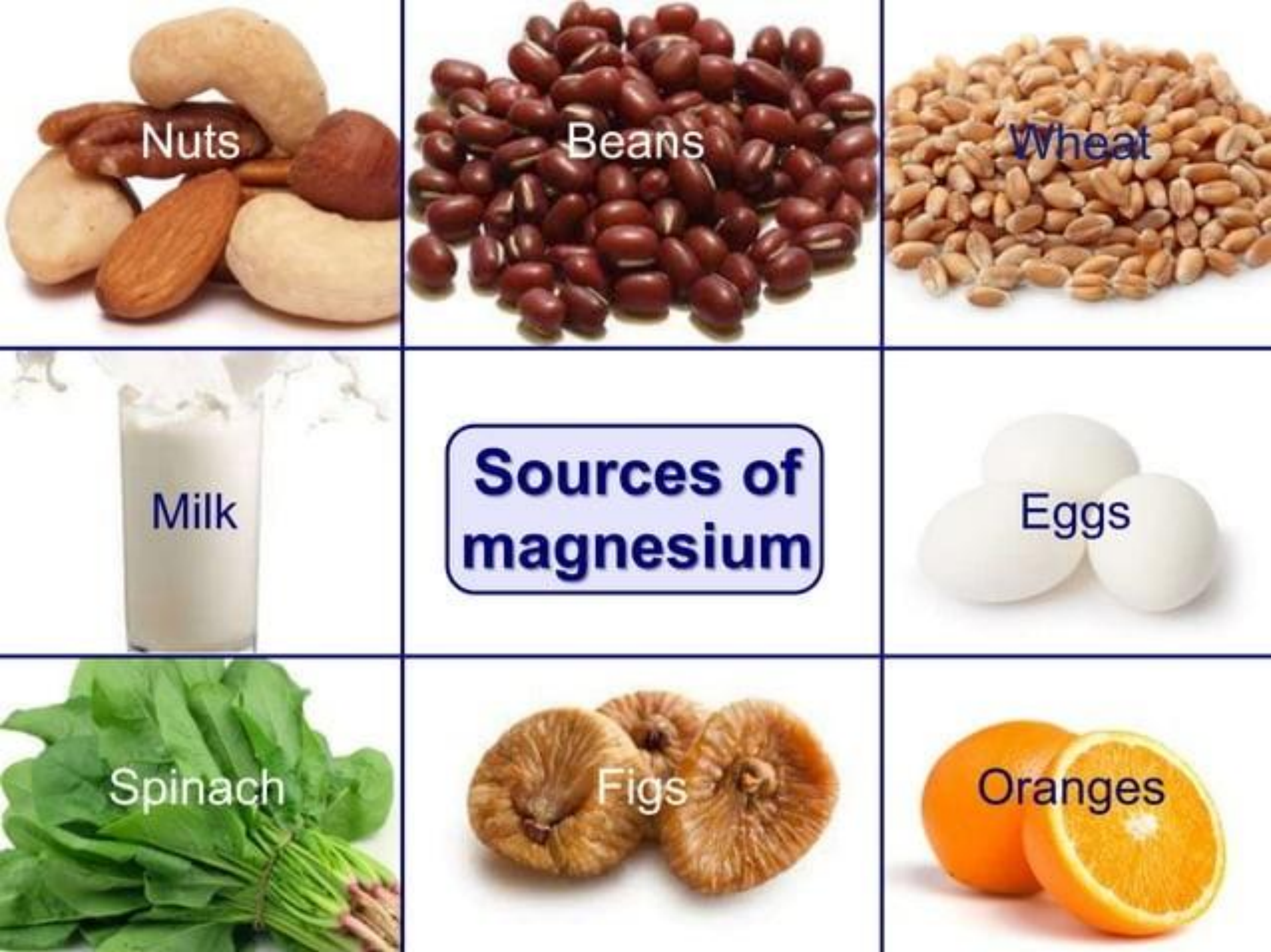
Regulation of magnesium balance is the function of kidneys

Aldosterone plays a role in the renal regulation

A high aldosterone level decreases the tubular reabsorption of magnesium

Daily requirement

Age and sex	Requirement
Infants	60-70 mg/day
Children	150-250 mg/day
Adult men	350 mg/day
Adult women	300 mg/day
Pregnant and lactating women	450 mg/day


Nuts
Beans
Wheat
Milk
Sources of magnesium
Eggs
Spinach
Figs
Oranges

Abnormal serum magnesium levels

Hypomagnesaemia occurs in chronic alcoholism, chronic diarrhoea, hyper-parathyroidism and aldosteronism

Hypermagnesaemia is commonly seen in renal failure

Sodium

Total amount of sodium in an average adult is about 60 gm

About 20 gm is present in bones

The rest is distributed in other tissues

Sodium is the major cation of the extracellular fluid (ECF)

Plasma sodium level is 136-145 mEq/L

Other extracellular fluids also have a high concentration

Intracellular fluid has only about 10 mEq/L

Functions

- Maintenance of osmotic pressure
- Maintenance of pH
- Nerve excitability and conduction
- Active transport

Maintenance of osmotic pressure

Osmotic pressure of ECF depends on sodium which is the major cation in ECF

Osmotic pressure depends upon the number of solute particles

Sodium ions outnumber all the other solute particles in extracellular fluids

Maintenance of pH

As $NaHCO_3$, sodium is a component of bicarbonate-carbonic acid buffer which is the major buffer of ECF

Renal excretion of H^+ in exchange for Na^+ is also important in maintaining the pH of body fluids

Nerve excitability and conduction

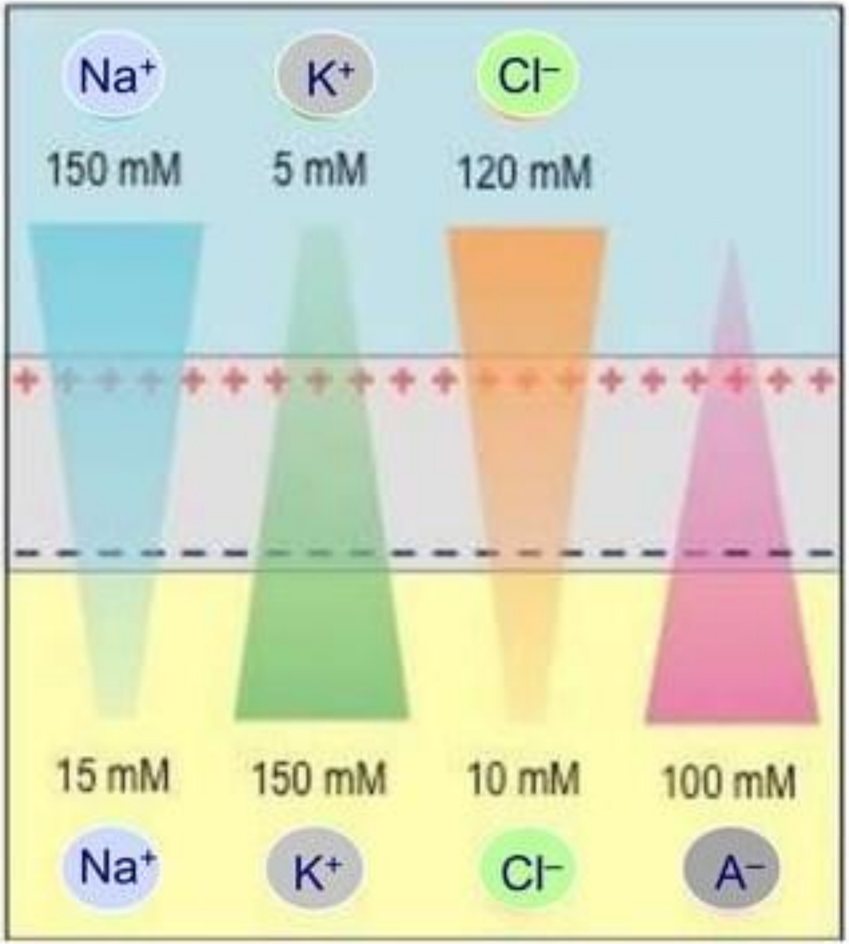
Sodium has a role in:

- Maintenance of excitability of nerves
- Conduction of nerve impulses

Specific distribution of cations and anions across nerve cell membrane creates a potential difference

The exterior of the membrane is slightly electropositive in relation to the interior

This potential difference is known as the resting potential



Resting potential

On stimulation of nerve, the stimulated area immediately becomes permeable to sodium ions

Sodium ions move into the interior of the nerve fibre

The interior becomes electropositive in relation to the exterior due to influx of sodium ions

This generates a nerve impulse

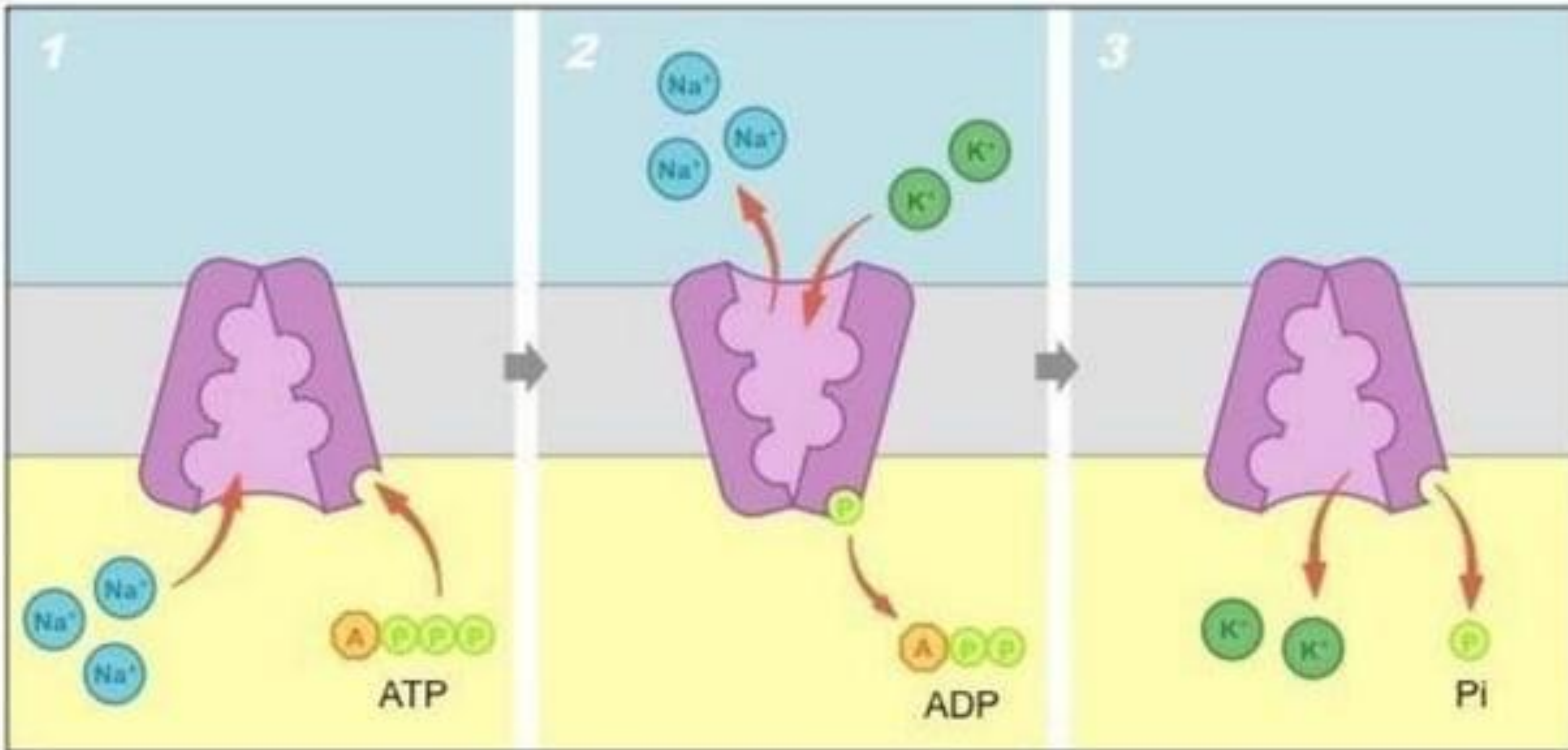
Nerve impulse is transmitted due to influx of sodium ions along the entire length of the nerve fibre

Active transport

Several compounds enter the cells against their concentration gradient by active absorption

Sodium pump ejects sodium ions from the interior of the cell to the exterior

This is linked with the active absorption of glucose, galactose and some amino acids



Sodium pump

Absorption transport

Sodium enters gastrointestinal tract through food and through digestive secretions

The latter is a far more abundant source as compared to dietary intake

Almost all the sodium is absorbed from the gastro-intestinal tract

The absorption occurs from the entire length of the small and large intestines

Sodium concentration in intestinal lumen is far greater than inside the mucosal cells

Sodium diffuses from the lumen into the cells down its concentration gradient

The intracellular sodium is actively transported into blood by the sodium pump

Pumping of Na^+ into blood keeps sodium concentration in mucosal cells at low level

More sodium diffuses from the intestinal lumen into the mucosal cells

Requirement

There has been considerable controversy about the daily requirement of sodium

The requirement depends upon daily loss of sodium

The loss depends upon the climate

The daily intake of elemental sodium recommended by ICMR (2010) is:

- 2.1 gm for adult men
- 1.9 gm for adult women

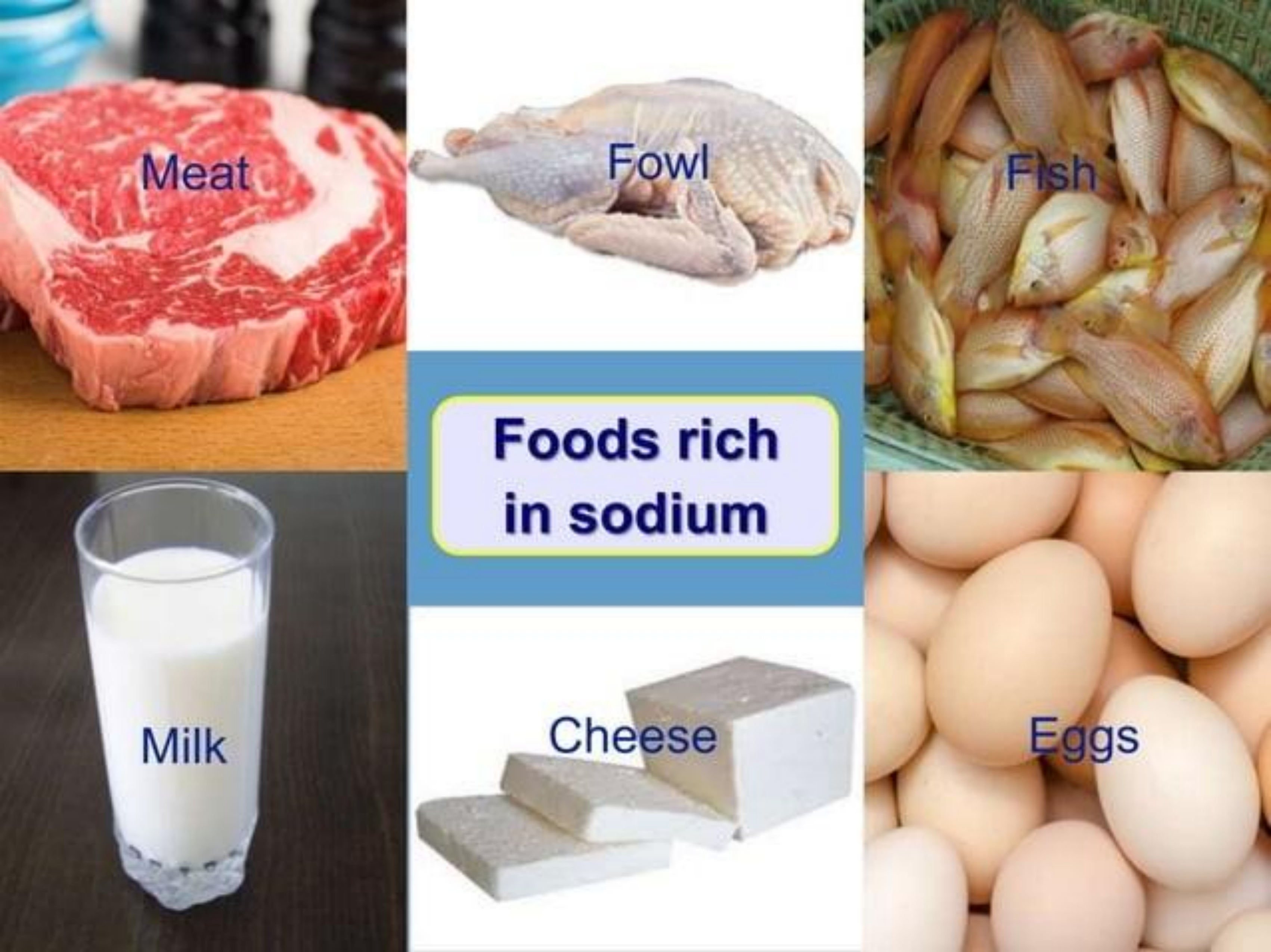
A direct relationship exists between excessive sodium intake and prevalence of hypertension

We have to guard against excessive intake rather than deficiency

Dietary sources

Table salt (sodium chloride) is the main source of sodium in our daily diet

Baking powder (sodium bicarbonate) can also contribute significant amounts


Meat
Fowl
Fish
Foods rich in sodium
Milk
Cheese
Eggs


Carrots
Radish
Cauliflower
Fair sources of sodium
Spinach
Legumes
Nuts

Abnormal serum sodium levels

Sodium metabolism is regulated by adreno-cortical hormones

Mineralocorticoids are the most potent in this regard

Glucocorticoids and sex hormones are less potent

Adrenocortical hormones cause retention of sodium and loss of potassium

Therefore, abnormal serum sodium levels occur in adrenocortical disorders

Excessive loss of sodium can also affect the serum sodium level

Hyponatraemia (low serum sodium level) occurs in:

- Adrenocortical insufficiency
- Severe diarrhoea
- Chronic renal disease
- Excessive sweating

Hyponatraemia may also occur due to haemodilution if dehydrated patients are rehydrated with salt-free fluids

Hypernatraemia (high serum sodium level) occurs in:

- Adrenocortical hyperactivity
- Prolonged steroid therapy
- Dehydration

Potassium

Total amount of potassium in an average adult is about 140 gm

Potassium is the chief cation of intra-cellular fluid, and is present in all cells

The potassium content of intracellular fluid is about 140 mEq/L

Potassium concentration in extracellular fluid is only about 5 mEq/L

Serum potassium level is 3.5-5 mEq/L

Functions

- Maintenance of osmotic pressure
- Maintenance of pH
- Nerve excitability and conduction
- Cofactor for enzymes
- Active transport

Maintenance of osmotic pressure

Potassium helps maintain osmotic pressure within the cells

Its role is similar to that of sodium in the extracellular compartment

Nearly half the osmolarity of intracellular fluid is due to potassium

Maintenance of pH

Potassium helps maintain the pH of intra-cellular fluid

It is a part of phosphate buffer in the form of KH_2PO_4 and K_2HPO_4

Nerve excitability and conduction

Potassium plays a role in excitability of nerves and nerve conduction

It has a role in excitability and contractility of muscles, particularly heart muscles

Abnormal serum potassium levels disturb the functioning of heart

Cofactor for enzymes

Potassium is a cofactor for some enzymes

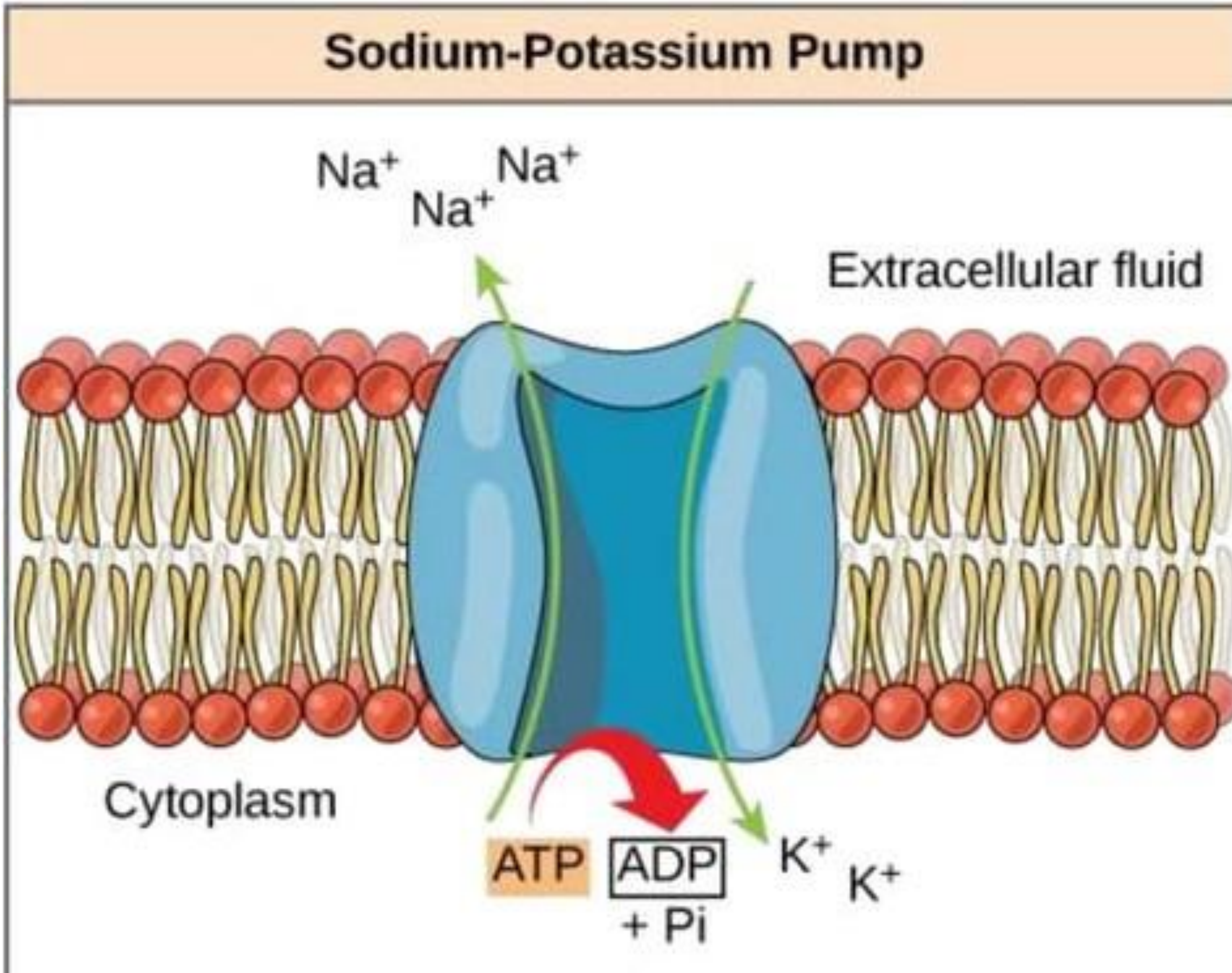
An example is pyruvate kinase

Active transport

Along with sodium, potassium is also involved in active transport

Sodium pump functions in active transport of glucose, galactose, amino acids etc

It is really a Na^+-K^+ pump as it causes efflux of sodium and influx of potassium


Sodium-Potassium Pump
Na+
Na+
Na+
Extracellular fluid
Cytoplasm
ATP
ADP
+ Pi
K+
K+

Absorption

Potassium is absorbed from small as well as large intestine

Potassium absorption occurs down its concentration gradient

Requirement

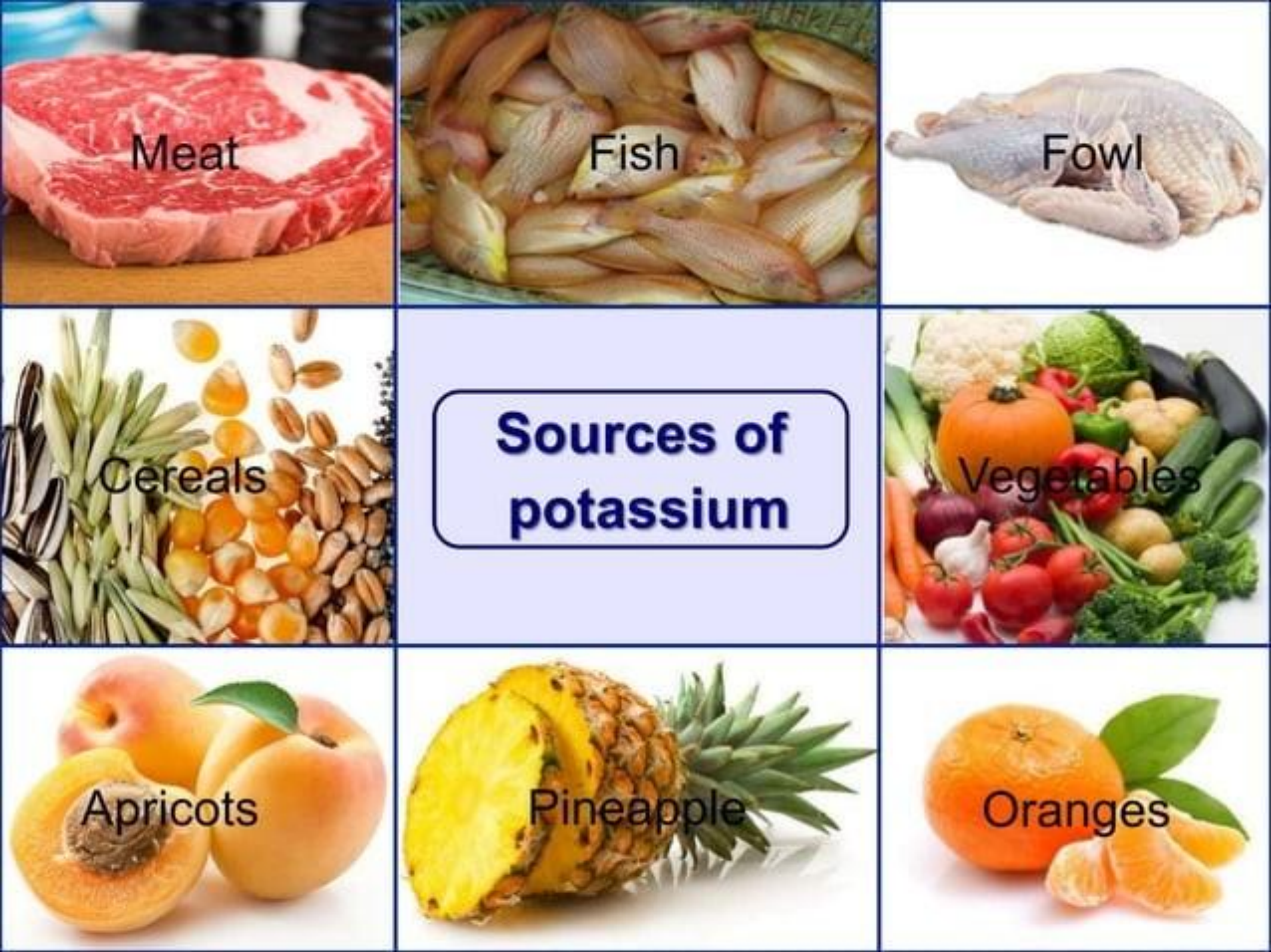
The exact potassium requirement is not known with certainty

A daily intake of 4 gm is sufficient to maintain potassium balance

Dietary sources

Potassium is very widely distributed in foodstuffs

It is present in animal foods as well as plant foods


Meat
Fish
Fowl
Cereals
Sources of potassium
Vegetables
Apricots
Pineapple
Oranges

Abnormal serum potassium levels

A decrease in serum potassium level is known as hypokalaemia

An increase in serum potassium level is known as hyperkalaemia

Both affect nervous system, heart and muscles

Hypokalaemia occurs in:

- Adrenocortical hyperactivity
- Prolonged steroid therapy
- Diarrhoea
- Wasting diseases
- Metabolic alkalosis
- Familial periodic paralysis
- After insulin injection
- Prolonged use of thiazide diuretics

Hypokalaemia can cause:

- Irritability
- Muscular weakness
- Tachycardia
- Cardiac dilatation
- Cardiac arrest

Hypokalaemia produces characteristic electrocardiographic changes:

- Flattened or inverted T waves
- Depressed ST segment

These changes are valuable in the diagnosis of potassium deficit

Hyperkalaemia occurs in:

- Adrenocortical insufficiency
- Renal failure
- Dehydration
- Indiscriminate intravenous potassium therapy

Hyperkalaemia causes:

- Mental confusion
- Numbness and tingling
- Muscular weakness and paralysis
- Bradycardia
- Peripheral circulatory failure
- Cardiac arrest

Electrocardiographic changes in hyperkalaemia are:

- Lengthening of P-R interval
- Widening of QRS complex
- Elevation of T waves

Chlorine

The total amount of chlorine in an average adult is about 80 gm

Chlorine, in the form of chloride ions, is the chief anion of extracellular compartment

Normal serum chloride level is 100-106 mEq/L (355-375 mg/dl)

The chloride content of cerebrospinal fluid is 120-130 mEq/L

The interstitial fluid contains about 110 mEq/L

The intracellular fluid contains only about 4 mEq/L

Functions

- Maintenance of osmotic pressure
- Maintenance of pH
- Formation of hydrochloric acid

Maintenance of osmotic pressure

Chloride ions are present in a high concentration in extracellular fluids

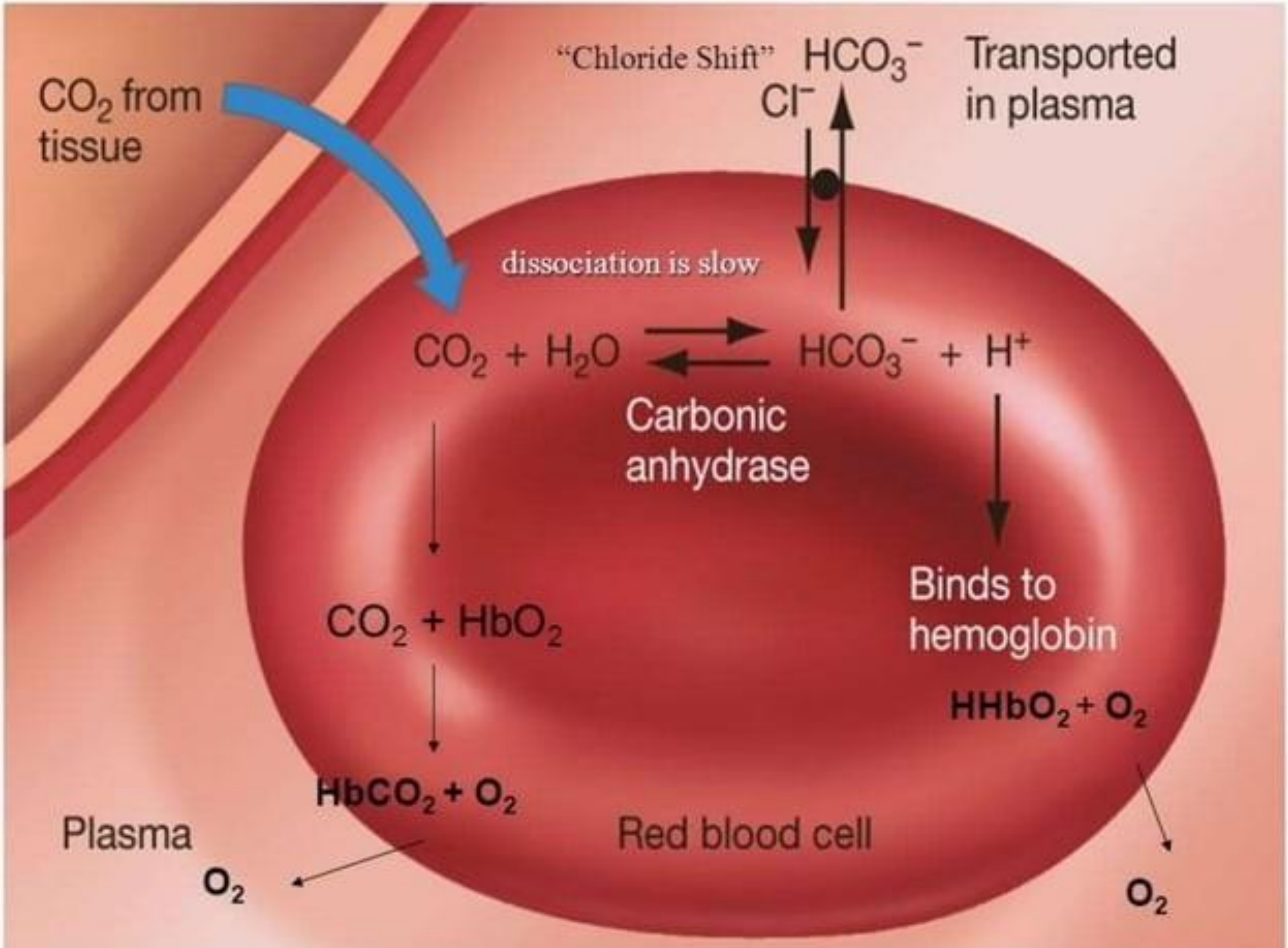
Along with sodium ions, they play an important role in maintaining the osmotic pressure of extracellular fluids

Maintenance of pH

Chloride ions help in maintaining the pH of blood by the mechanism of chloride shift

Entry of Cl^- into RBCs in exchange for HCO_3^- maintains HCO_3^- level in plasma

HCO_3^- is a component of bicarbonate-carbonic acid buffer



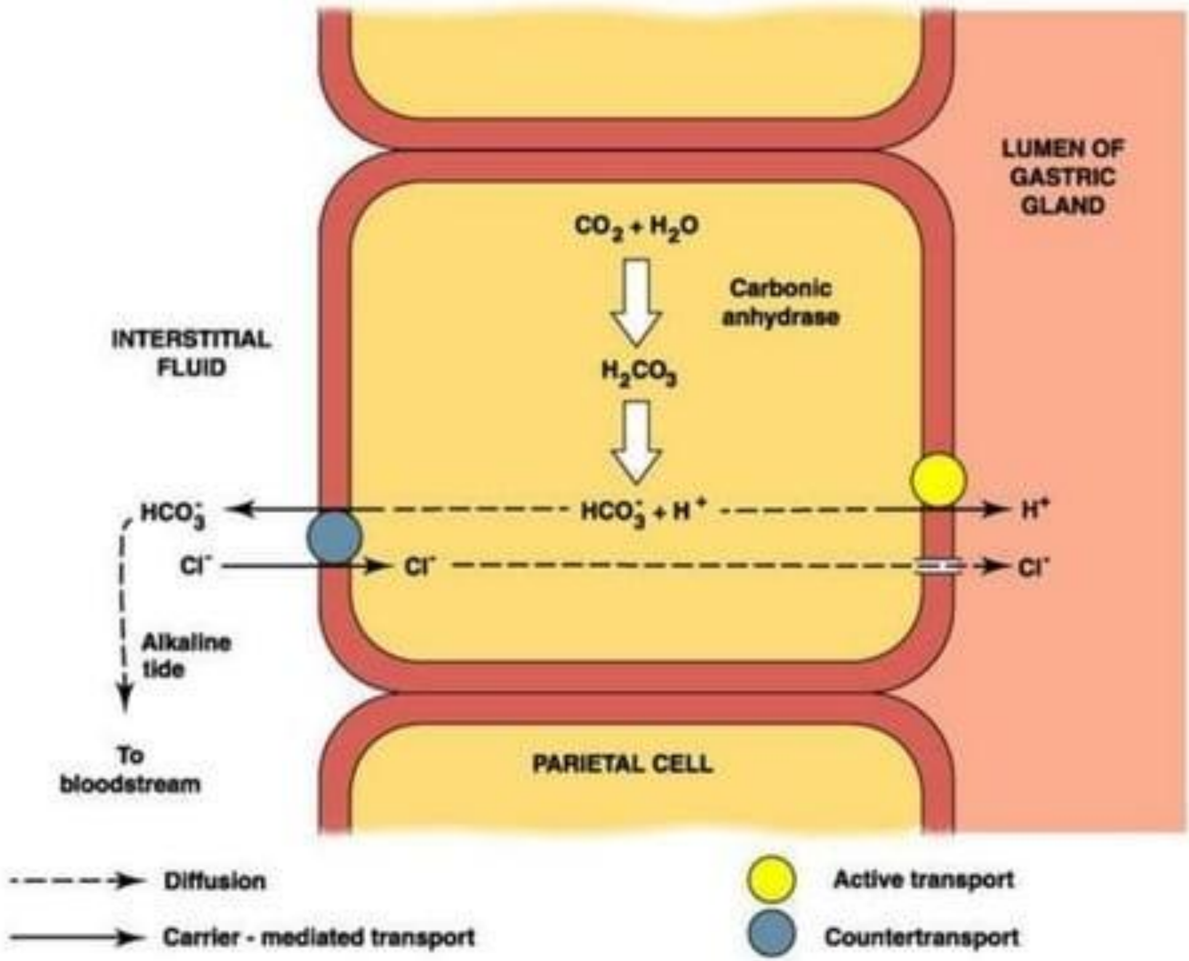
CO_2 from tissue
"Chloride Shift"
HCO_3^-
Cl^-
Transported in plasma
dissociation is slow
$CO_2 + H_2O \rightleftharpoons HCO_3^- + H^+$
Carbonic anhydrase
Binds to hemoglobin
$CO_2 + HbO_2$
$HHbO_2 + O_2$
$HbCO_2 + O_2$
Plasma
Red blood cell
O_2
O_2

Formation of hydrochloric acid

Hydrochloric acid is an important constituent of gastric juice

Formation of hydrochloric acid requires chloride ions

Hydrochloric Acid Production



Absorption

Chloride is absorbed passively down its concentration gradient in the proximal portion of small intestine

In distal ileum and colon, chloride ions are absorbed in exchange for bicarbonate ions

Requirement

Chloride is commonly present in food as sodium chloride

Therefore, sodium and chloride intakes are parallel

If daily requirement of sodium is met, so will be that of chloride

Dietary sources

Table salt is the most abundant source of chloride in our daily diet

Foods providing sodium also provide chloride e.g. meat, fish, fowl, eggs, milk, cheese, cereals etc

Abnormal serum chloride levels

A rise in serum chloride is known as hyperchloraemia

A decrease in serum chloride is known as hypochloraemia

Changes in serum chloride are generally parallel to those in serum sodium

Serum chloride level is raised in:

- Dehydration
- Respiratory alkalosis
- Metabolic acidosis
- Adrenocortical hyperactivity

Serum chloride level is decreased in:

- Severe vomiting
- Prolonged gastric suction
- Respiratory acidosis
- Metabolic alkalosis
- Addison's disease

Sulphur

About 100 gm of sulphur is present in an average adult

Organic sulphur is the predominant form of sulphur in our body

It is present in most proteins in the form of sulphur-containing amino acids

Functions

- Component of proteins
- Component of mucopolysaccharides
- Constituent of many vitamins
- Detoxification of harmful substances

Sulphur is a component of most of the proteins as part of cysteine and methionine

Disulphide bonds formed by –SH group of cysteine stabilize the structure of proteins

The –SH groups are also essential for the activity of many proteins e.g. enzymes

Mucopolysaccharides, e.g. heparin, chondroitin sulphate and keratan sulphate, contain sulphur

Sulphur is a constituent of many vitamins e.g. thiamin, biotin, lipoic acid etc

Coenzyme A and acyl carrier protein also contain sulphur

Detoxification of many harmful substances is done by conjugation reactions

Several such substances are conjugated with sulphate

Absorption

Sulphur is absorbed from the intestine mainly in the form of sulphur-containing amino acids

Absorption of inorganic sulphate is very poor

Requirement

The daily intake of sulphur is about 5 gm in average adults

Most of it is present in dietary proteins

If protein intake is adequate, it will provide sufficient sulphur as well

Dietary sources

Our sulphur requirement is met by the sulphur-containing amino acids in proteins

Therefore, protein-rich foods, e.g. eggs, milk, cheese, meat, fish, nuts and legumes, are the main sources of sulphur

Thank you