Calcium (Ca): most abundant mineral in body.

- blood Ca^{2+} ⇒ 9 - 11 mg/dL

Dietary Source: milk & its products, millets, ragi

- Phytates (present in cereals) & oxalates (in green leafy vegetables) inhibit Ca absorption

RDA: Adult: 0.8 gm

Children: 0.8 - 1.2 gm

Pregnancy & Lactation: 1.5 gm

Absorption: absorbed in duodenum against conc. gradient

→ absorption requires Calcium Binding Protein (CBP)

Factors facilitating Ca absorption:

- Calcitriol (active form of vit. D) ⇒ induces CBP synthesis
- PTH (promotes synthesis of calcitriol)
- Lactose
- Lysine, Arginine
- Gastric Acidity (low pH)

Factors decreasing Ca absorption:

- Phytates (in cereals)
- oxalates (in green leafy vegetables)
- fatty acids
- high phosphate content in food
- alkaline condition

Chronic renal failure / Nephrosis Causes Decreased Ca^{2+} Absorption:

- Kidney is required for formation of Calcitriol required for CBP synthesis
- can be treated by administration of calcitriol.

Steatorrhea decreases Ca absorption:

- Steatorrhea occurs due to defective digestion & absorption of fat
- unabsorbed fatty acids inhibit Ca absorption

Calcium: Phosphate Ratio in Diet:

- Maximum ratio = 1:2 to 2:1
- Ideal ratio = 1:1

Storage: bones, teeth, muscles

Excretion: 500 mg/day in urine

Functions of Ca:

- **Bones & teeth formation:** Ca gives hardness & strength
- **Blood Coagulation**
- **Muscle contraction** - for excitation & contraction of muscle fibres
- **Transmission of nerve impulses** - in pre & post-synaptic region.
- **Neuromuscular excitability** - Ca decreases excitability
- **Hormone Action** - secondary messenger to some hormones
  eg - glucagon, adrenalin, vasopressin
- **Release of hormones** - insulin, PTH, calcitonin

Dietary Deficiency:

Children - impaired bone growth
- rickets like symptoms
- early occurrence of osteoporosis

Adults - osteoporosis
- hyperexitable state of nerves & muscles

Toxicity: unlikely to reach toxic amounts
- Increased risk of kidney stones
- decreased absorption of other minerals (Fe, Zn, P, Mg, etc.)

Calcium Homeostasis: blood Ca ⇒ 9-11 mg/dL

Vitamin D: hypercalcemic
- sites of action = intestine, kidney, bones

Intestine: Calcitriol induces CBP synthesis in mucosa

Kidney: increases calcium reabsorption

Bones: enhances osteoblastic activity, calcification (causes bone resorption during hypocalcemia)

Parathyroid Hormone (PTH): hypercalcemic

Intestine: PTH stimulates production of Calcitriol ⇒ increased intestinal absorption of Ca

Kidney: increased Ca reabsorption

Bone: demineralization (resorption) of bones (mainly during Ca deficiency)

Calcitonin: hypocalcemic

Kidney: inhibits Ca reabsorption by renal tubules

Bone: inhibits bone resorption by increasing activity of osteoblasts

PO_4^{2-} levels: Hypophosphatemia enhances hydroxylation of vit. D in kidneys to form Calcitriol ⇒ hypercalcemic effect

- Activation of some enzymes

→ As Ca-Calmodulin complex – Calmodulin is a CBP;
– It can bind with 4 Ca^{2+}

eg:- Adenylate cyclase, Ca dependent protein kinase

→ Direct action – pancreatic lipase, rennin

- Promotes & controls membrane integrity & cell permeability.
- Cell-to-Cell Contact

Hypocalcemia: < 9 mg/dL

Causes – vit. D deficiency
– hypoparathyroidism
– accidental surgical removal of parathyroid glands (during thyroidectomy)
– dietary deficiency
– Steatorrhea (due to accumulation of fatty acids, Ca absorption is inhibited)
– Chronic renal disease (impairment of Calcitriol formation)

Manifestations: increased neuromuscular excitability (mild tremors, tetany)
(Numbness of extremities, tightness, muscle spasms & cramps, convulsions, etc)

Positive Chvostek's sign & Trousseau's sign

Hypercalcemia: > 11 mg/dL

Causes - hypervitaminosis D
- hyperparathyroidism

Symptoms - increased excretion of urinary Ca leading to renal calculi
- bone deformities
- ectopic calcification of urinary bladder, renal tissue, pancreas
- anorexia
- muscle weakness
- depression

Phosphorus (P): adult body has about 1 kg P.

Sources: milk, eggs, cereals

- Phytates (in plant sources) inhibit P absorption

RDA: Adults: 800 mg

Children: 1000 mg

Lactation & Pregnancy: 1200 mg

Absorption: mainly from jejunum

↳ increased by Calcitriol & PTH

Storage: bones, teeth, muscles

Excretion: 500 mg / day

Functions:

- Formation of bones & teeth
- Production of high energy phosphates – ATP, GTP (for energy)
- Synthesis of nucleotide enzymes – NAD, NADP
- Nucleic acid synthesis in DNA & RNA. (phosphodiester bonds form backbone)
- Formation of phosphate esters → glucose-6-phosphate, etc.
- Enzyme activation (reversible covalent modification by phosphorylation & dephosphorylation)
- Buffer system in blood & cells.

Dietary deficiency: Rare

→ Causes – vit. D deficiency
– consumption of large amounts of antacid

→ may cause osteomalacia, growth retardation, etc.

Toxicity: unlikely

↳ may develop bone resorption

Phosphorus Homeostasis: normal serum level = 3-4 mg/dl in adults

children = 5-6 mg/dl

(Haemolysed blood specimens are not used for P estimation
∵ lysed RBCs release phosphate into plasma giving false higher value)

Vit. D: causes release of P from bones (by activating alkaline phosphatase)

PTH: decreases P reabsorption from renal tubules.

Hypophosphatemia: < 3 mg/dl

Causes: vit. D deficiency, hyperparathyroidism

Hyperphosphatemia: > 4 mg/dl

Causes: hypervitaminosis D, hypoparathyroidism, renal failure

Magnesium (Mg):

- 25g in body
- normal plasma level: 2-3 mg/dL

Sources: milk, green leafy vegetables, sea foods, cereals

RDA: Adult ♂ = 350mg

Adult ♀ = 300mg

Absorption: increased Ca & P decrease Mg absorption

↳ absorbed with the help of a specific carrier

Function: • Constituent of bone & teeth

- Cofactor for enzymes: hexokinase, fructokinase, PFK, enolase, ALA synthase, alkaline phosphatase
- Proper Neuromuscular function: decreases neuromuscular excitability
  ↳ along with Ca, Mg acts as a relaxant during activity, after contraction
- Insulin Sensitivity: Mg deficiency leads to decreased insulin dependent uptake of glucose
- Activates Amino acids for protein synthesis
- Synthesis & maintenance of genetic material

Dietary deficiency: Rare

→ manifests only in combination with protein-energy malnutrition (PEM), alcoholism, persistent diarrhoea.

Symptoms: muscle weakness, cramps, hypertension, etc.

Toxicity: unlikely

Cause: renal insufficiency being treated with supplementation

Symptoms: nausea, vomiting, diarrhoea.

Cu: Total body Cu = 100mg.

Sources: liver, fish, meat (milk is a poor source)

RDA: 2-3 mg

Absorption: from duodenum

↳ transport protein = metallothionein

→ phytates, zinc, molybdenum decrease Cu uptake

Functions: Formation of many enzymes – ALA synthase, cytochrome oxidase, dopamine oxidase

- Mobilisation of Iron – Fe^{2+} $\xrightarrow{\text{ceruloplasmin } (Cu^{2+})}$ Fe^{3+}
- Synthesis of Hb – Cu is a constituent of ALA synthase
- Formation of Collagen, Elastin – constituent of lysyl oxidase
- Synthesis of melanin – constituent of tyrosinase
- Catecholamine synthesis – constituent of dopamine β-hydroxylase
- Antioxidant function – as a component of SOD (Superoxide dismutase)
- Role in ETC – constituent of complex IV – cyt. oxidase

Dietary Deficiency: microcytic anemia (∵ Cu is needed for mobilisation & utilisation of Fe)

↳ defective collagen formation (osteoporosis, fragile capillaries)

Toxicity: by contamination of food cooked in copper vessels

↳ vomitting, diarrhea, etc.

Wilson's Disease / Hepatolenticular Degeneration:

→ autosomal recessive disease

→ defect in ceruloplasmin synthesis

(defect in hepatic excretion of Cu into bile & renal absorption of Cu)

Manifestation: low blood Cu

→ Excessive deposition of Cu in liver & brain ⇒ cirrhosis, neurological disorders

→ deposition in kidney ⇒ renal damage

→ deposition in cornea ⇒ Kayser Fleisure ring (at margin of cornea)

Treatment: penicillamine (Cu chelating agent)

Menke's Disease (Kinky / Steely Hair Syndrome):

→ X-linked disorder

→ defect in intestinal absorption of Cu (Cu may be trapped by metallothionein in intesti

Symptoms: decreased plasma & urine Cu.

→ anemia → growth failure

→ mental retardation

→ depigmentation of skin & hair (kinky / steely hair)

→ usually fatal in infancy.

Fe: Total body iron = 3-5 g

Sources: Rich – organ meat, jaggery

good – leaf vegetables, fish

poor – milk, polished rice, wheat

→ Phytates, oxalates, phosphates inhibit Fe absorption

RDA: Man & post-menopausal woman: 10-20 mg

Premenopausal women: 20-40 mg

children: 15-30 mg

Pregnancy & lactation: 20-40 mg

Absorption: upper part of duodenum mainly

Factors influencing Fe Absorption –

- Amount of iron – directly proportional
- Chemical form of iron: absorbed in Fe^{2+} form
- Physical form: heme iron is better absorbed than non-heme iron.

Dietary irons →
- Hem iron: absorbed into intestinal mucosal cells
- Non-heme iron: HCl in stomach releases Fe from non-heme proteins; this iron is in Fe^{3+} form; ∴ Fe^{3+} is reduced to Fe^{2+} by vitamin C, glutathione, HCl & then absorbed.

Factors Stimulating Fe absorption:

- HCl: $Fe^{3+} \rightarrow Fe^{2+}$ → absorption
- vit. C, cysteine, glutathione: $Fe^{3+} \rightarrow Fe^{2+}$ → absorption
- vit. A, amino acids: stimulate Fe absorption by forming soluble salts with Fe
- Calcium: forms complexes with iron inhibitors like oxalates, phosphates.

Factors Inhibiting Fe Absorption:

- Phytates, oxalates, phosphates: form insolumble complexes with Fe
- Fatty acids
- Tannic acid of tea

Regulation of Fe Absorption:

Mucosal Block Theory: Fe homeostasis is maintained at the level of absorption (not excretion).

→ during Fe deficiency – more iron is absorbed

→ during Fe overload – iron absorption decreases

→ iron absorption is regulated by the availability of apoferritin in intestinal mucosal cells.

→ Fe absorbe in Fe^{2+} form ; then converted to Fe^{3+}

$$Fe^{3+} + \text{apoferritin} \longrightarrow \text{ferritin}$$

→ Fe is slowly released from ferritin into plasma as per body requirement.

→ As long as iron is in ferritin, Fe absorption is reduced due to reduced availability of apoferritin.

→ If transferrin is saturated, any iron accumulation in the form of ferritin in mucosal cells is lost when intestinal cells are desquamated.

Transport: by transferrin in plasma

→ transferrin has 2 binding sites for Fe but can bind only to Fe^{3+} form

$$\therefore \quad Fe^{2+}\ (\text{absorbed}) \xrightarrow{\text{ceruloplasmin}} Fe^{3+}$$

→ absorbed Fe is mainly delivered to bone marrow for Hb synthesis & further incorporation into developing red cells.

Iron Utilization: Fe is required by all body tissues

↳ required more in bone marrow for Hb synthesis in developing erythrocytes.

Storage:

Ferritin: Fe is stored mainly in liver (90%); spleen, bone marrow, mucosal cells as ferritin

Hemosiderin: liver, spleen (mainly in iron excess conditions)

Functions: (Heme = Fe + Protoporphyrin IX)

Heme Proteins:
- for Hb & Mb
- for cytochromes (b, c, c_1, a_3, a)
- for cytochrome P450 (in liver; for detoxification)
- Catalases → destroy H_2O_2
- Peroxidases in neutrophils help in phagocytosis
- Enzymes → tryptophan pyrrolase, xanthine oxidase.

Non-heme proteins:
- ferritin & hemosiderin → for storage
- transferrin → for transport
- Fe S proteins / enzymes → NADH dehydrogenase (complex I of ETC), succinate dehydrogenase, ribonucleotide reductase
- Aconitase of Krebs Cycle

Iron Excretion: one-way element

↳ once it enters the body, it is utilized & reutilized

→ very little is excreted (< 1 mg/day)

→ menstruation is a major cause of loss of iron in premenopausal women.

Iron Deficiency Anaemia:

Causes – decreased iron intake
- lead poisoning (lead decreases Fe absorption)
- lack of absorption (steatorrhea, gastrectomy, achlorhydria)
- increased iron loss (in hook worm infestation, bleeding in urinary / genital tract, peptic ulcer, hemorrhoids, nephrosis)

Clinical Manifestations -

- Microcytic hypochromic anemia — Low Hb (< 12 g/dl) due to decreased Hb synthesis
- Atrophic glossitis
- Oesophagial web
- Dysphagia

} Plummer Vinson Syndrome

- Koilonchyia (spoon-shaped nails)
- Pica (craving for starch)
- Apathy (dull & sluggish due to decreased O_2 supply to tissues)
- fatigue • pallour • anorexia

Iron Toxicity (Hemochromatosis/Hemosiderosis):

1° hemochromatosis - increased iron absorption from intestine

2° hemochromatosis - may be due to increased iron absorption, repeated blood transfusions, thalassemia

Bantu tribes (in Africa) develop hemosiderosis (aka bantu siderosis) due to low phosphate in their staple diet corn [Phosphate favours iron absorption], cooking food & brewing alcohol in iron vessels.

Complications: excessive deposition of hemosiderin in liver, spleen, heart, pancreas (hemosiderosis)

→ deposition of hemosiderin in liver ⇒ liver cirrhosis
→ in pancreas ⇒ death of pancreatic cells ⇒ diabetes
→ bronze colouration of skin

} Bronze diabetes

Fluorine (F):

Distribution: teeth & bones as calcium hydroxy fluoro apatite

Sources: drinking water, fish, tea

RDA: Adults ⇒ 2-3 mg

→ Safe limit of fluorine in drinking water is 1 ppm

Functions: → Required for proper teeth development ⇒ fluoride gets incorporated into hydroxyapatite to form fluoroapatite

⇒ fluoroapatite (in enamel & dentine) is more resistant to destruction by bacterial acids & plaques, thus preventing dental caries & tooth decay

⇒ fluoride inhibits bacterial enzymes which produce acids that cause dental caries.

→ Required for proper bone development

→ fluoride is the inhibitor of enolase ∴ used during estimation of blood glucose level.

Deficiency: consumption of drinking water with less than 0.5 ppm of fluorine

→ dental caries

→ osteoporosis

Excess: fluorosis

Dental fluorosis: intake above 2ppm ⇒ mottling of enamel
⇒ discolouration of teeth (rough, yellow patches)

Skeletal fluorosis: intake above 20ppm ⇒ hypercalcification leading to increased bone density
⇒ ligaments of spine & collagen of bones get calcified

- In advanced stages, ligaments of spine get calcified
  ⇓
  Stiff spine ⇒ cripples the individual } Genu Valgum

Cobalt (Co):

→ Body contains about 1.1 mg cobalt

Function:

↳ cobalt is a constituent of corrin ring system of vit. B12 & their coenzymes

→ cobalt activates glycyl-glycine peptidase & ALA synthase.

→ stimulates the synthesis of erythropoietin (to promote erythropoiesis).

Deficiency: pernicious anemia (∵ cobalt deficiency causes cobalamin deficiency)

Toxicity: Cause ⇒ overconsumption

↳ polycythemia [increased RBCs in blood].

Iodine (I):

→ body contains ⇒ 25 mg ; 80% of this is stored in thyroid glands

Sources: drinking water, sea food, iodized salt

↳ fruits & vegetables grown on seashore

→ regions of high altitudes are deficient in iodine content in food cultivated in this soil.

∴ people of mountain regions have higher chances of developing iodine deficiency.

∴ Himalayan region = goiterous belt.

Goiterogens: substances which interfere with iodine utilization

↳ cabbage, cassava, cauliflower.

RDA: Adults : 100 – 150 µg

Pregnancy : 200 µg

Absorption: small intestine, skin & lungs

Storage: 80% of body iodine is stored as iodothyroglobulin in thyroid gland.

Functions: Formation of thyroid hormones

↳ synthesis of thyroxine (T_4) & triiodothyronine (T_3).

→ T_3 is functionally more active than T_4.

Synthesis of thyroid hormones:

- Tyrosine + I_2 $\xrightarrow{\text{thyroid peroxidase}}$ MIT (3-monoiodotyrosine)
- MIT + I_2 $\xrightarrow{\text{thyroid peroxidase}}$ DIT (3,5-diiodotyrosine)
- DIT + MIT ⟶ T_3
- DIT + DIT ⟶ T_4

→ synthesis takes place when tyrosine is still a part of thyroglobulin protein.

→ T3 & T4 are released from thyroglobulin by proteolytic breakdown.

Deficiency:

Simple endemic goiter: deficiency of iodine in food (mainly in geographical areas away from sea-coast)

Iodine deficiency disorder (IDD): hypothyroidism, cretinism, deaf-mutism, goiter, sub-normal intelligence

Excess: Toxic goiter: exophthalmic goiter.

Selenium (Se):

Sources: sea food, liver, kidney

RDA: 50 - 100 µg

Functions: • Antioxidant property – Selenium is an integral part of metalloenzyme glutathione peroxidase which destroys H_2O_2 & prevents it from causing oxidative damage of biological membranes

• Selenium has vit. E sparing action – vit. E & selenium (both antioxidants) work synergistically to reduce each other's requirement.

• Constituent of 5'- deiodinase – for conversion of T_4 to T_3.

Selenocysteine – 21st a.a ; coded by UGA

Keshan disease: endemic cardiomyopathy

↳ Selenium deficiency

→ name derived from ⇒ Keshan province in China, where soil is deficient in Se

Symptoms: – nausea
– dizziness
– anorexia
– muscle dystrophy
– enlargement of heart ⇒ cardiac failure.

Toxicity (Selenosis): Se is present in metal polishes & anti-rust compounds

∴ people handling these, generally develop selenosis

Symptoms: – loss of hair
– weight loss
– irritability
– diarrhea
– garlic odor to breath

Zinc (Zn):

→ total body Zn = 2mg

→ Prostrate gland is particularly rich in Zn.

RDA: 10 - 15 mg

Source: meat, milk, eggs, shell fish

Absorption: mainly absorbed in duodenum

→ metallothionein facilitates Zn absorption

→ ā·ā promote Zn absorption (ā·ā = amino acids)

Excretion: excreted through feces

↳ small amounts are excreted in bile

→ not normally excreted through urine

Function:

Formation of certain metalloenzymes: carboxy peptidase, RNA polymerase, Carbonic Anhydrase, alcohol dehydrogenase, cytosolic superoxide dismutase (SOD), retinal reductase

Participates in visual cycle: as a component of retinal reductase, it helps in regeneration of rhodopsin

Antioxidant role: as a component of SOD

Heme synthesis: as a component of ALA dehydratase

DNA & RNA formation, cell division

Zinc finger motif: → facilitate binding of certain transcription factors with specific regions of DNA

Insulin secretion: Zn is required for storage & secretion of Zn from pancreas

Immunity: Zn maintains integrity of immune system

Taste sensation: Zn containing protein Gustin (in saliva) plays an imp. role in taste

Wound healing

Normal reproduction: Zn is required for sexual maturation.

Deficiency:

Causes: common in children of developing countries due to lack of consumption of non-vegetarian food, high phytate content, diarrhea.

→ Zn deficiency of pregnant women ⟹ spontaneous abortion & congenital malformations.

Symptoms: poor wound healing
- anemia
- loss of taste sensation
- hypogonadism
- diarrhea
- growth failure

Acrodermatitis enteropathica: autosomal recessive condition
↳ defective Zn absorption
→ acrodermatitis is inflammation around mouth, fingers, nose, etc
→ diarrhea
→ ophthalmologic disorders
→ hypogonadism.

Toxicity: seen in welders due to inhalation of Zn-oxide fumes

Symptoms – nausea
- gastric ulcers
- pancreatitis
- pulmonary fibrosis
- vomiting
- anemia
- excessive salivation.

Molybdenum (Mo):

→ body contains about 9mg

RDA: 45 µg

Source: rich in cereals, legumes, green leafy vegetables, meat

Functions – Imp. role in RBC synthesis

- component of many enzymes ⇒ xanthine oxidase, sulfite oxidase, aldehyde oxidase, nitrate reductase
- Mo works with riboflavin to incorporate iron into Hb

Deficiency: Rare

↳ neurological symptoms – mental retardation

→ mouth & oesophageal cancer.

Manganese (Mn):

→ body manganese = 15 mg

Sources: cereals, nuts, fruits, tea

RDA: 5-6 mg

Functions: as an activator for enzymes — mitochondrial SOD, pyruvate carboxylase, arginase, squalene synthase

- Gluconeogenesis — pyruvate carboxylase
- Fatty acid synthesis — acetyl coA carboxylase
- Glycoprotein & chondroitin sulphate synthesis — glycosyl transferase
- Cholesterol synthesis — squalene synthase
- Inhibition of lipid peroxidation — SOD
- RNA polymerase activity

Deficiency: rare

↳ reported in case of protein-energy malnutrition (PEM), diabetes → pancreatic insufficiency

→ impaired growth, skeletal deformities

→ defective organic matrix of bone & cartilage

→ raised serum ALP levels

→ abnormal reproductive functions

Toxicity: overconsumption is unlikely

↳ can be caused on prolonged exposure to Mn dust in miners

→ excess Mn accumulates in liver & CNS.

→ severe neuromuscular symptoms (similar to those of Parkinson's disease).