Mineral metabolism

by

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Functions of Minerals

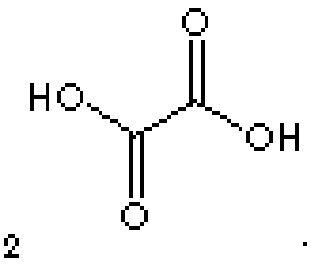
- Some participate with enzymes in metabolic processes (cofactors, e.g. Mg, Mn, Cu, Zn, K)
- Some have structural functions (Ca, P in bone; S in keratin)
- Acid-base and water balance (Na, K, Cl)
- Nerve & muscle function (Ca, Na, K)
- Unique functions: hemoglobin (Fe), Vitamin B_{12} (Co), thyroxine (I).

Classification

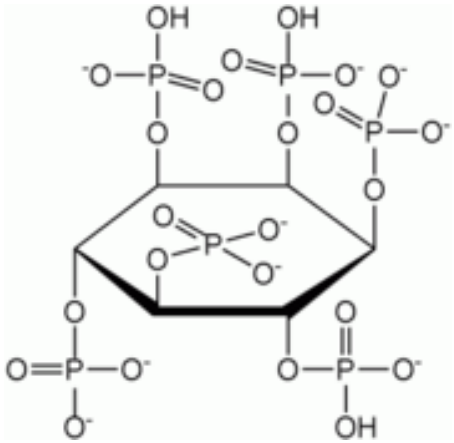
- **Macro or Major minerals**
  - Sodium (Na), potassium (K), magnesium (Mg), calcium (Ca), phosphorus (P), sulfur (S), chloride (Cl)
- Present in body tissues at concentrations >50 mg/kg
- requirement of these is >100 mg/d

- **Micro or Trace minerals** (body needs relatively less)
  - Manganese(Mn), iron(Fe), cobalt(Co), chromium(Cr), molybdenum(Mo), copper(Cu), zinc(Zn), fluoride(F), iodine(I), selenium(Se)
- Present in body tissues at concentrations <50 mg/kg
- requirement of these is < 100 mg/d

Minerals in Foods



Oxalate

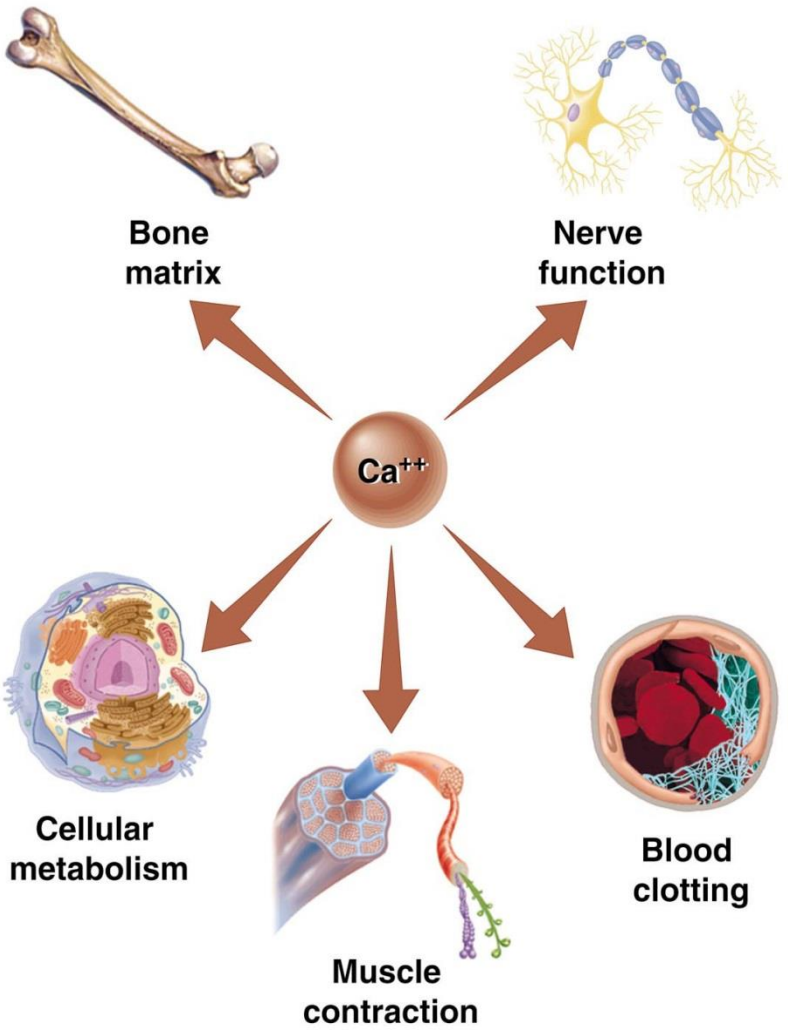


Phytate

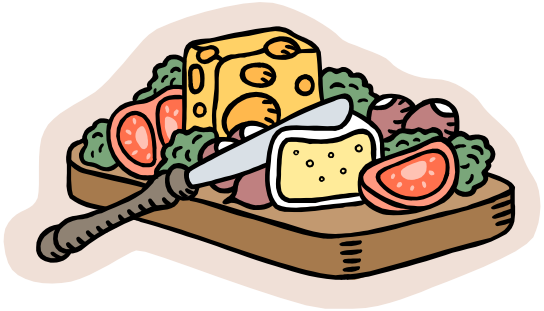
- Found in all food groups.
- More reliably found in animal products.
- *Often other substances in foods decrease absorption* (bioavailability) of minerals
  - *Oxalate,* found in spinach, prevents absorption of most calcium in spinach.
  - *Phytate,* form of phosphorous in most plants makes it poorly available

Calcium (Ca)

- *Most abundant mineral* in animal tissues
  - 99% Ca in skeleton
  - 1% Present in:
    - Blood & other tissues
- Lots of functions
  - Bone structure
  - Nerve function
  - Blood clotting
  - Muscle contraction
  - Cellular metabolism



Dietary requirements



- **Dietary requirements:**
  - Adult : 800 mg/day;
  - Women during pregnancy, lactation and post-menopause: 1.5 g/day;
  - Children (1-18 yrs): 0.8-1.2 g/ day;
  - Infants: (< 1 year): 300-500 mg /day
- **Food Sources:**
  - Best sources: milk and milk product;
  - Good sources: beans, leafy vegetables, fish, cabbage, egg yolk.

- **Absorption of calcium:**
  - in small intestine (duodenum), first half jejunum against electrical and concentration gradient, by an energy dependent active process, which influenced by several factors.

- **Mechanism**
  - Simple diffusion
  - An active transport involving Ca pump

Factor promoting Ca absorption

1. Vit.D induce the synthesis of Ca binding protein in the intestinal epithelial cells and promotes Ca absorption.
2. Parathyroid hormone (PTH) enhances Ca absorption through the increased synthesis of calcitriol.
3. Acidity (low pH) is more favorable for Ca absorption.
4. Lactose promotes calcium uptake by intestinal cell.
5. Lysine and arginine facilitate Ca absorption.

Factor inhibiting Ca absorption

1. Phytates and oxalates form insoluble salts and interfere with Ca absorption.
2. The high content of dietary phosphate results in the formation of insoluble Ca phosphate and prevent Ca uptake.
3. The free fatty acids react with Ca to form insoluble Ca soaps.
4. The alkaline condition (high pH) is unfavorable for Ca absorption.
5. High content of dietary fiber interferes with Ca absorption.
6. Low estrogen levels (postmenopausal women)

- **Plasma calcium:**

normal range: 9-11 mg% (2.25-2.75 mmol/L)

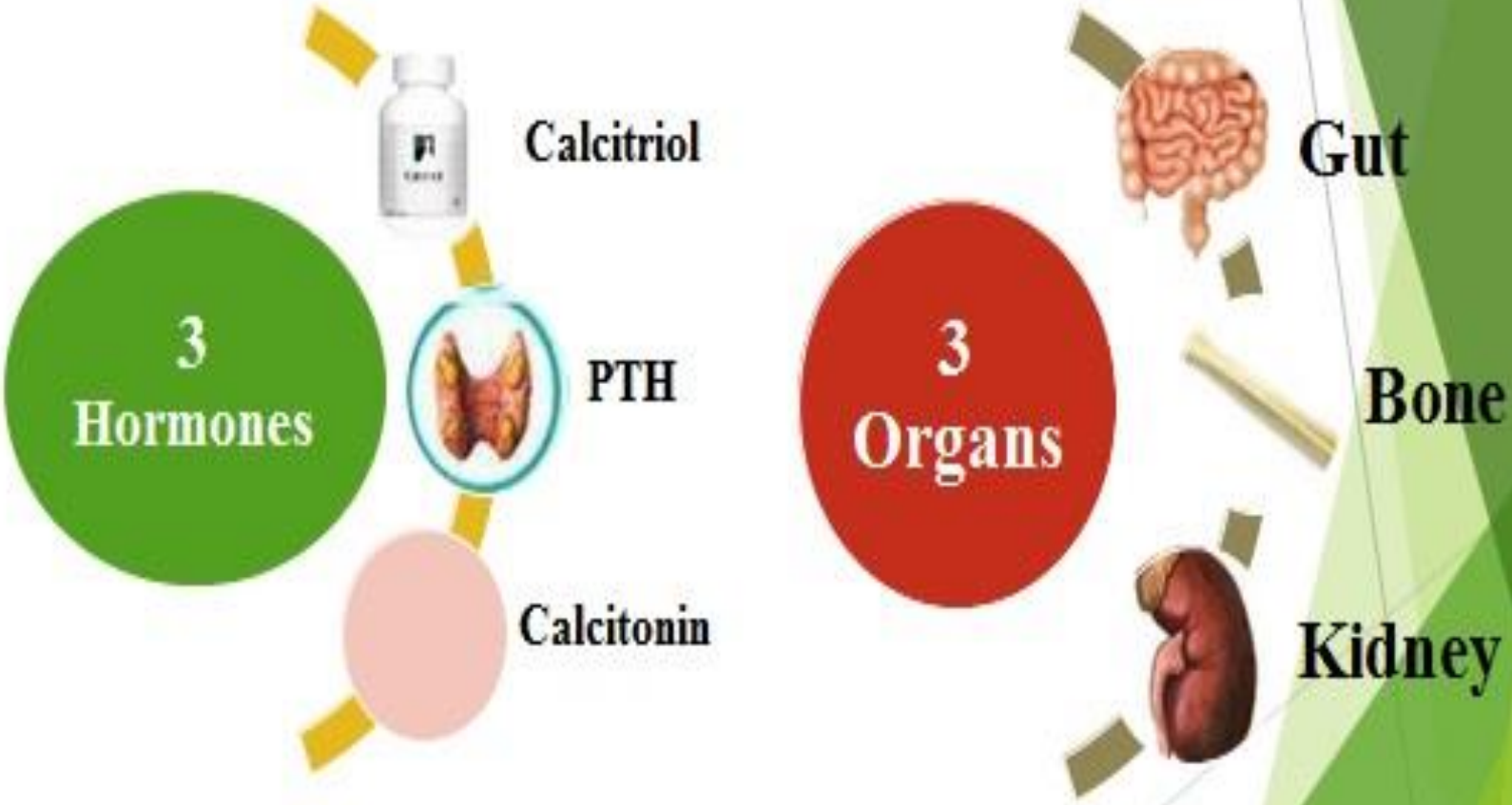
Three forms of plasma calcium:

① Ionized Ca (diffusible): **about 50% is ionized from which functionally the most active.**

② Complex Ca with organic acid (diffusible): **about 10% is found in association with citrate or phosphate.**

③ Protein bound Ca (non-diffusible): **about 40% is found in association with albumin and globulin.**

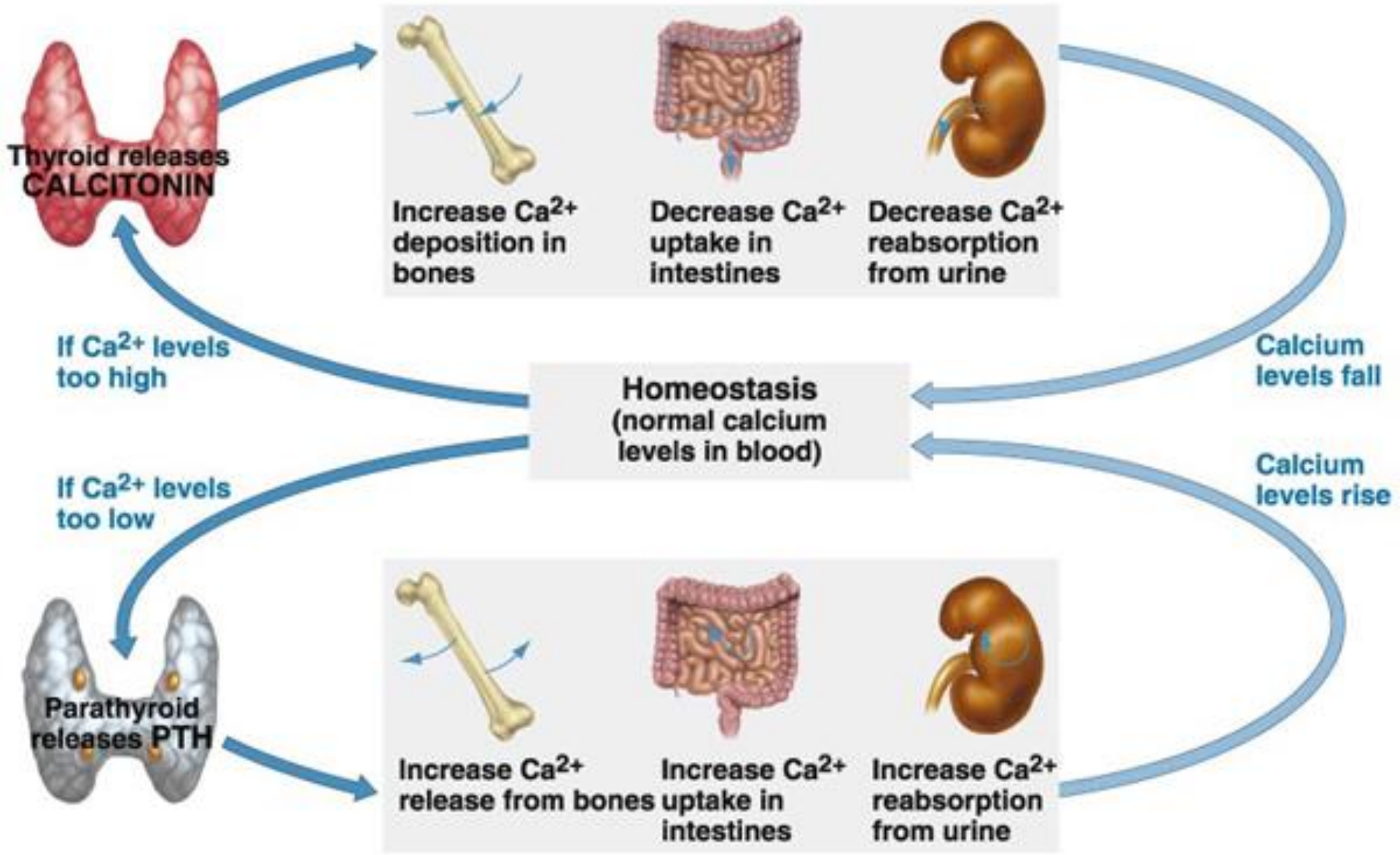
REGULATION OF PLASMA CALCIUM



Factors Regulating Plasma Ca Level

- Plasma Ca is regulated variable
- *Three hormones* involved in regulation
  - Calcitriol (1,25-$(OH)_2$ $VitD_3$, or 1,25 DHCC)
    - from kidney
  - Parathyroid hormone (PTH)
    - from parathyroid gland
  - Calcitonin(CT)
    - from thyroid gland
- *Vitamin D_3 and PTH* : *increase* plasma Ca↑
- *Calcitonin* : *decrease* plasma Ca↓

Regulation of Calcium Homeostasis



EXCRETION OF CALCIUM

Stools

Unabsorbed calcium in the diet

60 – 70%

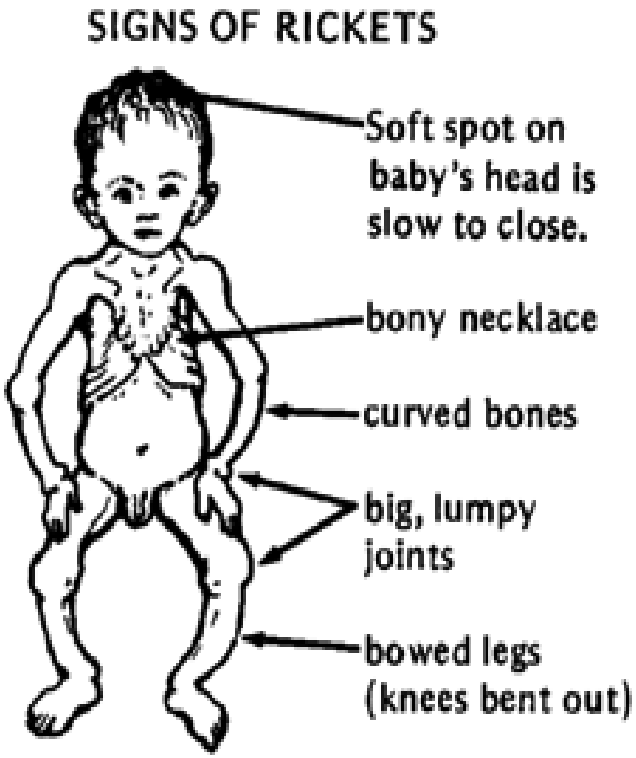
Urine

100-300mg/day

Sweat

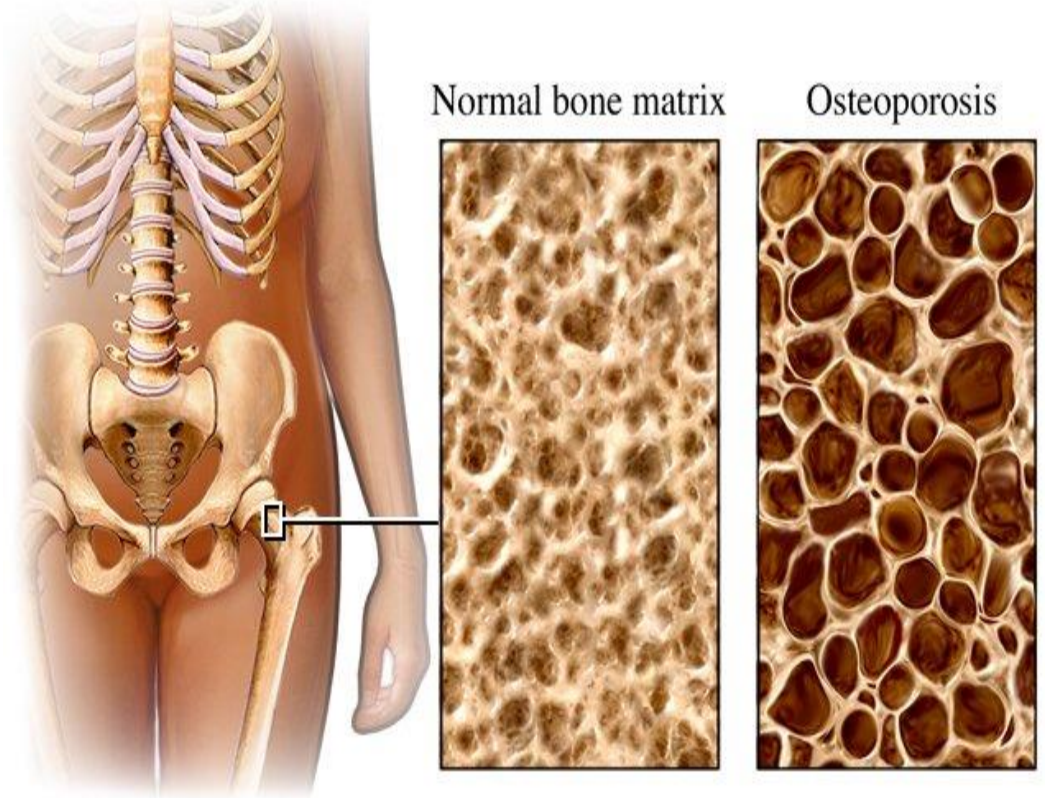
15mg/day

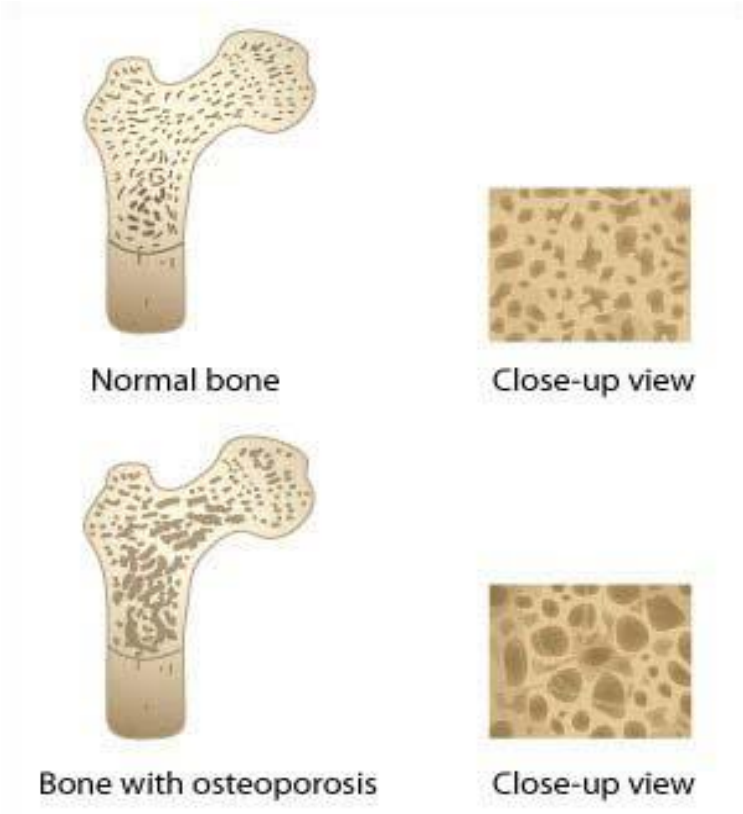
Calcium Deficiencies -*Rickets*



➢weakness and deformity of the bones that occurs from vitamin D deficiency or dietary deficiency of Ca and P in a growing person or animal.

Calcium Deficiencies -*Osteoporosis*





➢progressive loss of bone density, thinning of bone tissue and increased vulnerability to fractures in the elderly people of both sexes.

OSTEOPOROSIS

- Characterized by **demineralization of bone** resulting in the progressive loss of bone mass.
- After the age of 40-45, **Ca^{2+} absorption is reduced** & Ca^{2+} **excretion is increased**; there is a net negative balance for Ca^{2+}
- After the age of 60, osteoporosis is seen
- There is **reduced bone strength** & an **increased risk of fractures**.
- Decreased absorption of vitamin D & reduced levels of androgens/estrogens in old age are the causative factors.

Phosphorous (P)

- 80% of P occurs in combination with Ca in the bone and teeth.
- About 10% is found in muscles and blood in association with proteins, carbohydrate and lipids.
- The remaining 10% is widely distributed in various chemical compounds.

PHOSPHORUS – DISTRIBUTION

Human body contain about 840gm of phosphorus

- 80% present in bone and teeth
- 20% in other tissue

NORMAL RANGE- Serum phosphate level **3-4 mg/dl**

REGULATION OF PLASMA PHOSPHORUS

3HORMONES

- Calcitriol
- PTH
- Calcitonin

Functions of Phosphorus

- Essential for the development of bones and teeth
- Phospholipids, Phosphoproteins
- Component of:
  - DNA & RNA
  - ATP, NAD^+, $NADP^+$
- Energy metabolism: ATP, GTP
- Maintenance of blood pH: phosphate buffer system

Dietary requirements

- The recommended dietary allowance (RDA) of phosphate is *based on the intake of calcium*.
  - For adult, the ratio of Ca:P of 1:1 is recommended (800mg/day);
  - *For infant*, however, the ratio is around 2:1, which is ratio found in human milk.
- Sources:
  - milk, cereals, leafy vegetable, meat, eggs.

Absorption and Excretion

Absorption:

Phosphate absorption occur from jejunum

1. Calcitriol promotes phosphate uptake along with calcium.
2. absorption of P and Ca is optimum when the dietary Ca:P is 1:2-2:1.
3. acidity favors while phytate decreases phosphate uptake by intestinal cells.

Excretion:

About 500 mg phosphate is excreted in urine per day. The reabsorption of phosphate by renal tubules is inhibited by PTH.

Serum phosphate

blood: 40 mg/dl **serum: 3-4 mg/dl**

- **RBC and WBC have very high content of phosphate.**
- **The serum P may exist as *free ions* (40%) or in a *complex form* (50%) with cation as Ca^{2+}, Mg^{2+}, Na^{+}, K^{+}. About 10% is *bound proteins*.**

- **Importance of Ca:P ratio**
  - The ratio of plasma Ca:P is important for calcification of bones.
    - The product of Ca×P (in mg/dl) in child is around 50 and in adults around 40. This product is less than 30 in rickets.

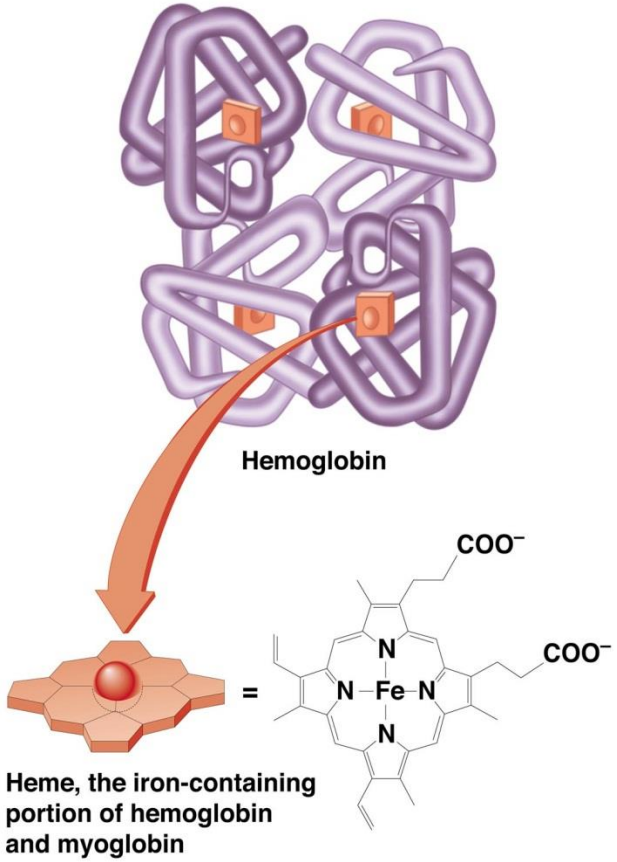
- **Phosphorus Deficiency**
  - Rickets, osteomalacia, osteoporosis

Iron

- The total content of iron in an adult body is 3-5 g.
  1. About 70%: in the erythrocytes of blood as a constituent of Hb.
  2. At least 5%: in Mb of muscle.
  3. Heme is the most predominant iron containing substance: e.g. Hb, Mb, cytochromes.
  4. Non-heme iron: e.g. transferrin, ferritin.

Functions

- O_2 and CO_2 transport via hemoglobin
  - Thus, necessary for ATP production!
- Essential component of many enzymes
- Immune function
- Brain function
  - Iron deficiency/toxicity thought to slow mental development in kids.



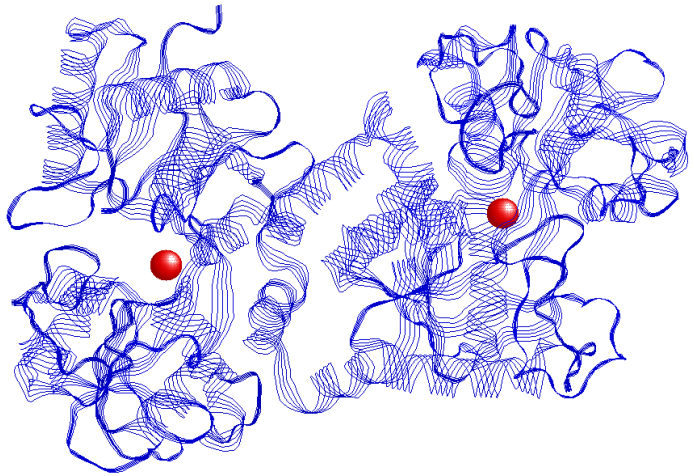
Dietary requirements

- **Dietary requirements:**
  - Adult man: 10 mg/day
  - Menstruating woman: 18 mg/day
  - Pregnant and lactating woman: 40 mg/dl
- **Sources:**
  - Rich source: organ meats (liver, heart, kidney).
  - Good source: leafy vegetables, pulses, cereals, fish, apple, dried fruits, molasses.
  - Poor sources: milk, wheat, polished rice.

Iron absorption

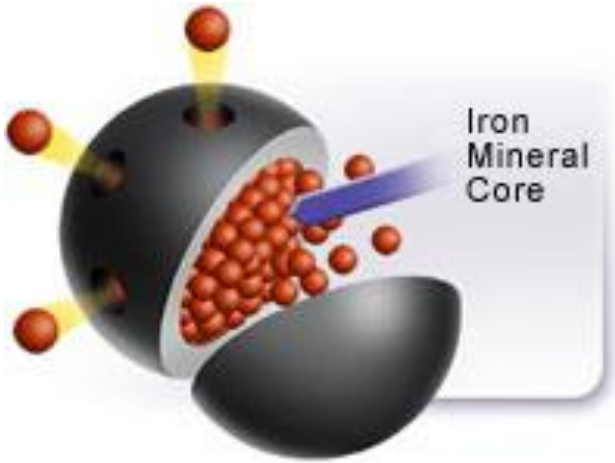
- Iron is mainly absorbed in the stomach and duodenum.
  - mostly found in the food in ferric form (Fe^{3+}), bound to protein or organic acid.
  - In the acid medium provided by gastric HCl, the Fe^{3+} is released from food.
  - Reducing substances such as *ascorbate (Vitamin C)* and *cystein reduces ferric form (Fe^{3+}) to ferrous form (Fe^{2+}).*
  - Iron in ferrous form (Fe^{2+}) is soluble and readily absorbed.
- How much do we absorb?
  - We absorb iron from the diet only when we need it
  - In normal people, about 10% of dietary iron is usually absorbed.
  - Those with LOW stomach acid secretions absorb less.

- **Iron transport in the plasma**
  - The iron enters the plasma in ferrous state (Fe^{2+}), then oxidized to ferric form (Fe^{3+}) by a copper-containing protein, ceruplasmin.
  - Fe^{3+} binds with a specific iron binding protein, namely transferrin. Each transferrin molecule can bind two atoms of ferric iron.

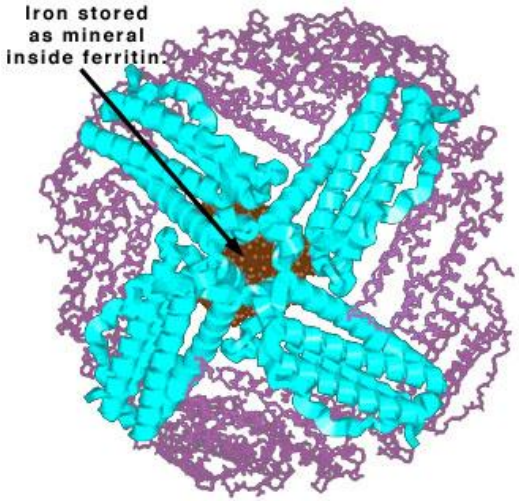


Transferrin

- **Iron storage**
  - Iron can be stored by **ferritin** (a protein) or **hemosiderin**
    - Stored in liver, bone marrow (why here?), intestinal mucosa, and spleen
    - A apoferritin molecule can combine with 4,000 atoms of iron.



Ferritin



Ferritin

Disease states

1. Iron Deficiency Anemia: The most common dietary deficiency worldwide is iron, affecting half a billion persons. However, *this problem affects women and children more*.

a) *A growing child* is increasing the RBC mass and needs additional iron.

b) Women who are menstruating require double the amount of iron that men do, but normally the efficiency of iron absorption from the gastrointestinal tract can increase to meet this demand.

c) *A developing fetus* draws iron from the mother, totaling 200-300 mg at term, so extra iron is needed in pregnancy.

2. **Hemosiderosis:** this is less common disorder and due to excessive iron in the body.
   - It is commonly observed in subjects receiving repeated blood transfusions over the years, e.g. patients of hemolytic anemia, hemophilia.
3. **Hemochromatosis:** this is rare disease in which iron is directly deposited in the tissue (liver, spleen, pancreas and skin).
   - Bronzed-pigmentation of skin, cirrhosis of liver. pancreatic fibrosis are the manifestations of this disorder.

MINERAL	FUNCTIONS	SOURCES	RESULTS OF DEFICIENCY
Calcium (Ca)	Formation of bones and teeth, blood clotting, nerve conduction, muscle contraction	Dairy products, eggs, green vegetables, legumes (peas and beans)	Rickets, tetany, osteoporosi
Phosphorus (P)	Formation of bones and teeth; found in ATP, nucleic acids	Meat, fish, poultry, egg yolk, dairy products	Osteoporosis, abnormal me tabolism
Sodium (Na)	Fluid balance; nerve impulse conduction, muscle contraction	Most foods, especially processed foods, table salt	Weakness, cramps, diarrhe dehydration
Potassium (K)	Fluid balance, nerve and muscle activity	Fruits, meats, seafood, milk, vegetables, grains	Muscular and neurologic disorders
Chloride (Cl)	Fluid balance, hydrochloric acid in stomach	Meat, milk, eggs, processed foods, table salt	Rarely occurs
Iron (Fe)	Oxygen carrier (hemoglobin, myoglobin)	Meat, eggs, fortified cereals, legumes, dried fruit	Anemia, dry skin, indigestio
Iodine (I)	Thyroid hormones	Seafood, iodized salt	Hypothyroidism, goiter
Magnesium (Mg)	Catalyst for enzyme reactions, carbohydrate metabolism	Green vegetables, grains, nuts, legumes	Spasticity, arrhythmia, vasodilation
Manganese (Mn)	Catalyst in actions of calcium and phosphorus; facilitator of many cell processes	Many foods	Possible reproductive disorders
Copper (Cu)	Necessary for absorption and use of iron in formation of hemoglobin; part of some enzymes	Meat, water	Anemia
Chromium (Cr)	Works with insulin to regulate blood glucose levels	Meat, unrefined food, fats and oils	Inability to use glucose
Cobalt (Co)	Part of vitamin B12	Animal products	Pernicious anemia
Zinc (Zn)	Promotes carbon dioxide transport and energy metabolism; found in enzymes	Meat, fish, poultry, grains, vegetables	Alopecia (baldness); possibly related to diabetes
Fluoride (F)	Prevents tooth decay	Fluoridated water, tea, seafood	Dental caries