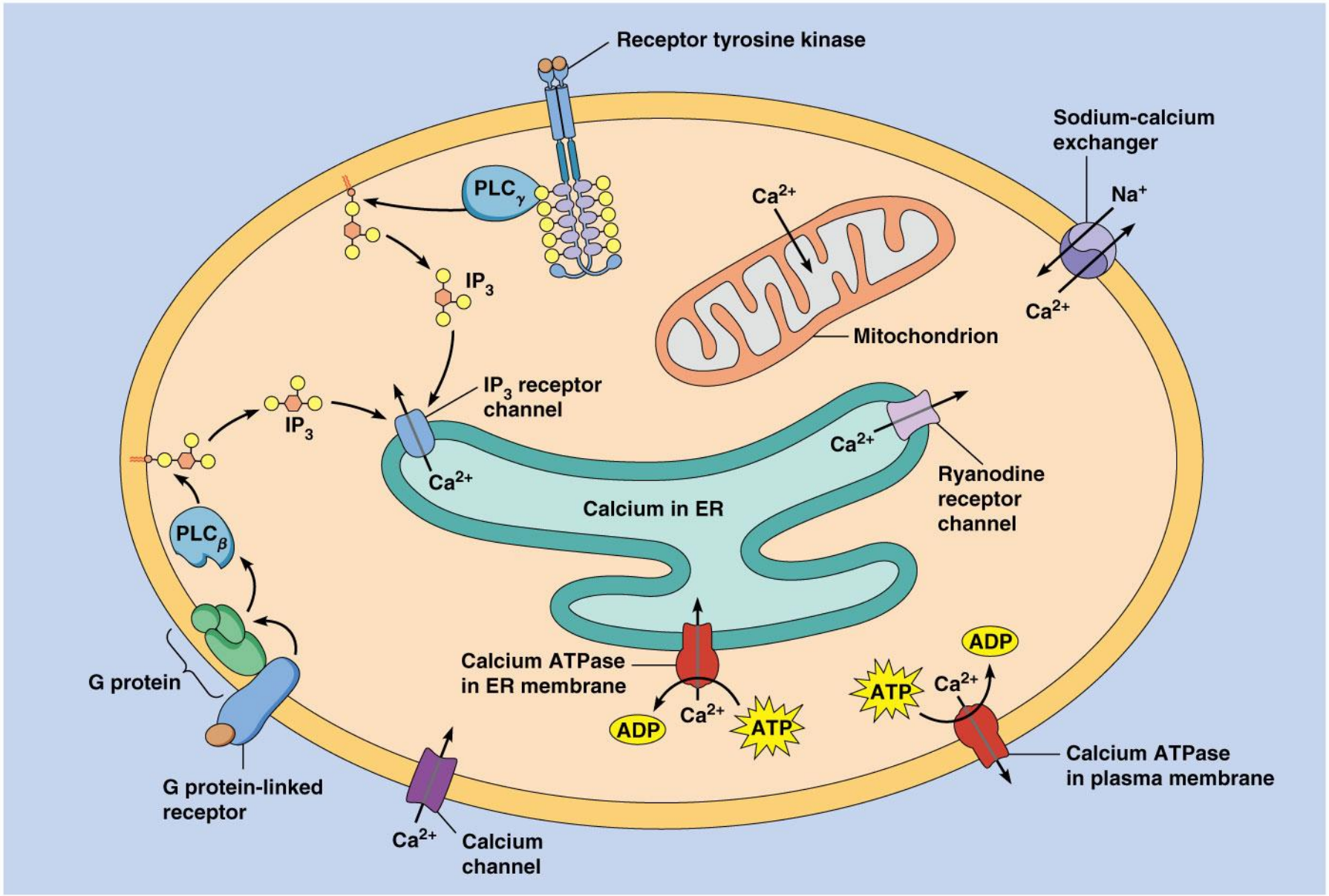
Metabolism of Calcium and Phosphate

8. week

Transport of intracellular calcium



Transport of intracellular calcium

Release of Ca^{2+} from intracellular stores
(ligand dependent calcium channels)

1. *„IP_3 receptor-linked“ channel* (endoplasmic reticulum) – receptors linked with Gp - proteins
2. *„ryanodine receptor-linked“ channel* (sarcoplasmic reticulum, signal – Ca^{2+})

Ca^{2+} channels in cell membrane

- various types: voltage-gated calcium channels
  binding of ligand dependent calcium channels
  covalent-modification dependent calcium channels

Transport of intracellular calcium

Restoration of low calcium levels in cytosol

Active transport of Ca^{2+} from cytosol

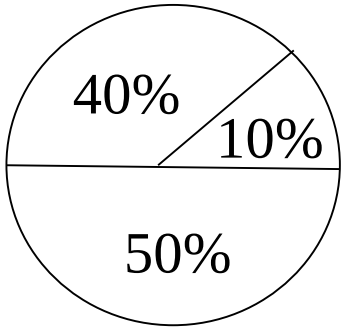
- **Ca^{2+} ATP-ase**
  - in plasma membrane
  - sarcoplasmic / endoplasmic retikulum

- **Na^{+}/Ca^{2+} exchanger**
  - exchange of 3 Na^{+} for 1 Ca^{2+} (antiport system)
  - restoration of Na^{+} gradient by Na^{+}/K^{+} ATP-ase
  - myocard, neurons

Calcium distribution

Three fractions of calcium in circulation:

1. Bound to proteins – **non-difusible** (biologically inactive)



2. Bound in complexes (citrate, lactate)

3. Ionized – free (biologically active; in body fluids)

Ca [circ]	= ionized Ca	+ Ca-proteins	+ Ca-complexes
2,2 – 2,6 mmol.L^{-1}	1,1 – 1,3 mmol.L^{-1}	0,9 – 1,0 mmol.L^{-1}	0,2 – 0,3 mmol.L^{-1}

Calcium absorption

- daily intake 0,5 – 1,0 g/day
- main absorption sites: duodenum, jejunum (25 - 40%)

- % of absorption is dependent on pH
- solubilization of insoluble components – acidic pH in stomach

Resorption from GIT:

- to the enterocytes: **facilitated diffusion**
- in enterocyte – transport protein - **CaBP**
- from enterocyte to the blood – **active transport** – Ca^{2+} ATP-ase located on the basolateral membrane of the enterocyte

Calcium excretion

• through urine (variable amount) and feces (0.8 g daily)

Kidney excretion:

• filtration in the glomeruli

• 60 – 65% passive reabsorption in the proximal tubule (depending on NaCl reabsorption)

• 15 – 20% reabsorption in the loop of Henle

• 5 – 10 % distal tubule (this fraction is regulated – by PTH, vitamin D, phosphates, etc.)

Ca^{2+} homeostasis in organism (blood plasma)

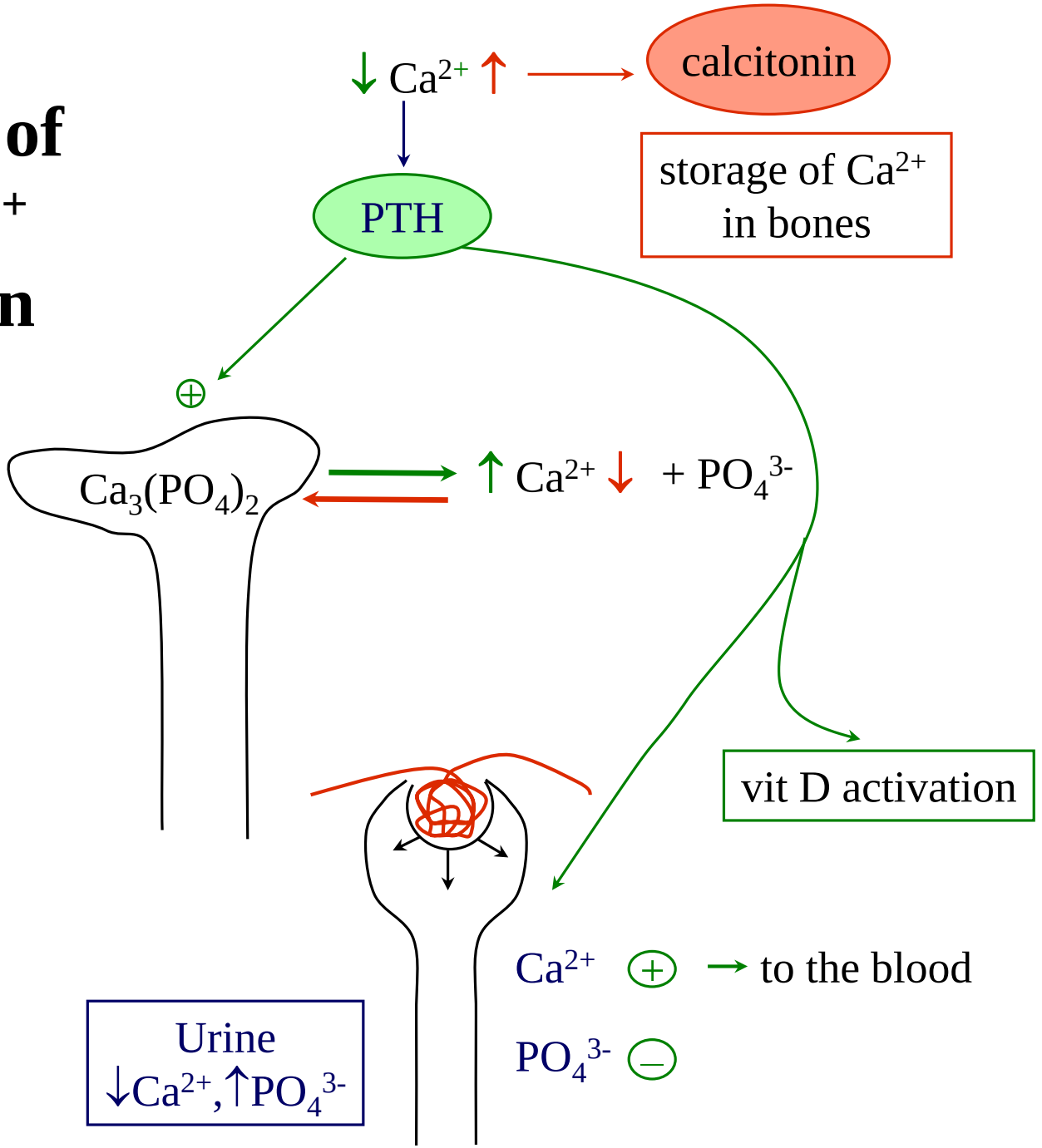
Calciotropic factors:

- **parathyroid hormone (PTH)**
  – chief cells of parathyroid glands

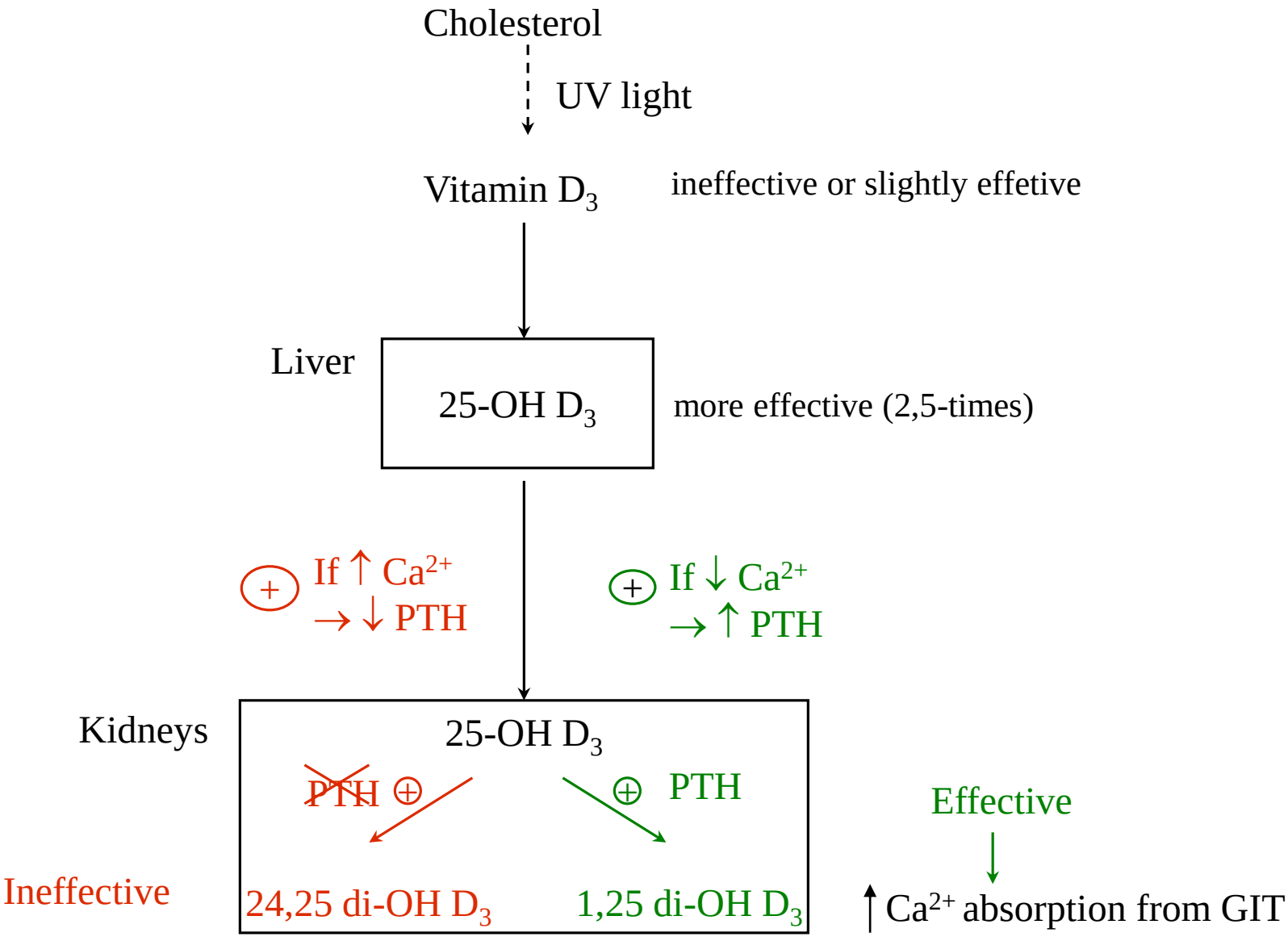
- **calcitonin**
  – thyroid parafollicular cells

- **calcitriol**
  – vit D derivative (1,25- dihydroxycholecalciferol)

Regulation of plasma Ca^{2+} concetration



Vitamin D activation

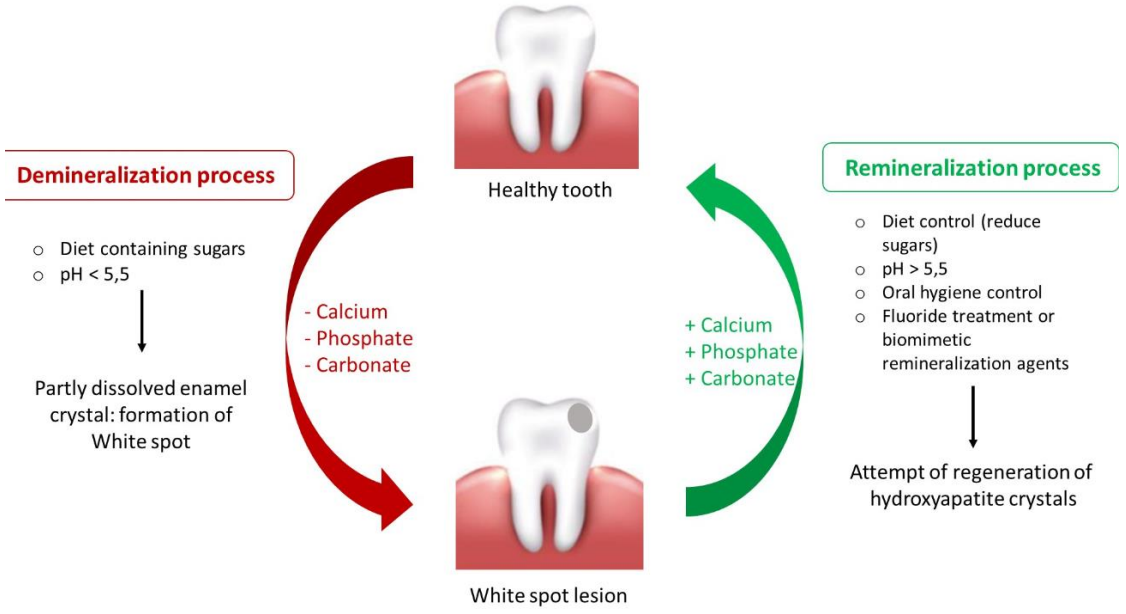


Calcium and phosphate in dentistry

- **Enamel**: main component - hydroxyapatite (the hardest part of the tooth)
- **Dentin:** contains hydroxyapatite to a lesser extent than enamel

  - higher proportion of collagen fibers, glycoproteins, proteoglycans
- **ALP:** essential enzyme for dentin/enamel mineralization

  highly expressed in dental hard tissues, local accumulation of Pi (re/mineralization)



Calcium metabolism disordes

Hypocalcemia

The most common etiological factors:

- absorption from intestine ↓
- PTH (hypoparathyroidism) ↓
- hypovitaminosis - vitamin D ↓
- renal disorders - reabsorption ↓

Other causes of hypocalcemia:

- pregnancy, lactation, acute pancreatitis, alkalemia, hypoalbuminemia

Clinical effect:

- increased irritability of muscles and nerves (tetany)

Calcium metabolism disordes

Hypercalcemia

- hyperparathyroidism
- excess of vitamin D
- increased absorption in the intestine

Increased mobilization of bone calcium:

- tumors, leukemia, multiple myeloma

  demineralization through OAF (osteoclasts activating factor)
- acute immobilization – skeletal atrophy from inactivity

Clinical effect:

- polyuria, polydipsia, long-term formation of urinary stones

Phosphate in the organism

600 g:

- 80% structure of bones and teeth
  (calciumphosphate, hydroxyapatite)
- 10% in serum - inorganic – buffering systems $HPO_4^{2-}/H_2PO_4^-$
  - organic – esterification - P-lipids, P-proteins
- 10% intracelullar (P-esters, macroergic molecules)
- 0.7 – 1.4 mmol/L in blood serum

Functions:

- maintenance of ABB (in blood serum and urine) $HPO_4^{2-}/H_2PO_4^-$
- NK, FL, creatine phosphate, coenzymes, phosphorylated molecules)

Phosphate metabolism disorders

Hyperphosphatemia

- physiological hyperphosphatemia during growth
- hypoparathyroidism – decreased function of the parathyroid glands
- renal failure (GF) – reduced urinary excretion
- bone demineralization
- fractures
- vitamin D intoxication

Hypophosphatemia

- vitamin D hypovitaminosis
- hyperparathyroidism – increased function of parathyroid glands
- resorption disorder in GIT