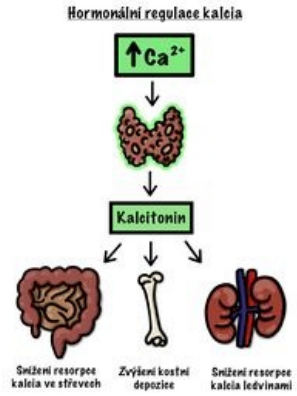
Disorders of Calcium And Phosphate Metabolism

Disorders of calcium phosphate metabolism are accompanied by abnormal levels of calcium and/or phosphorus and include disorders in the absorption, transport, storage and utilization of these minerals.

Calcium phosphate metabolism



Hormonal upregulation of calcium

99% of calcium is stored in mineralized bone mass and 1% is part of the body's internal environment in the form of calcium ions. **Calcemia is** mainly regulated by **vitamin D** and **parathyroid hormone** , and to a lesser extent by **calcitonin** .

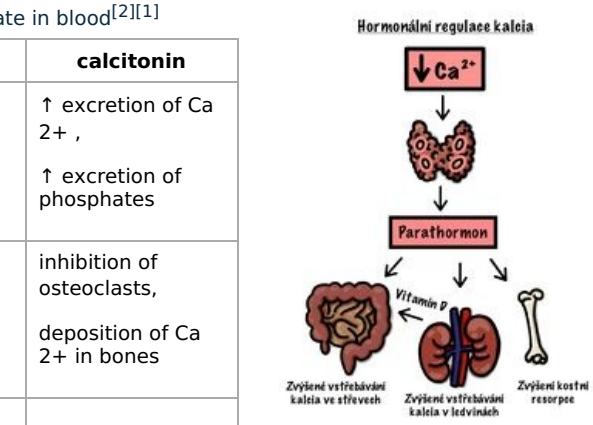
The exogenous source of vitamin D is mainly fish, and the endogenous source is 7-dehydrocholesterol , which is transformed in the skin by the effect of UV radiation into cholecalciferol (vitamin D 3) → in the liver to calcidiol (25(OH)D 3) → in the kidneys to calcitriol (1 ,25(OH) 2 D 3), the most effective metabolite.

Parathyroid hormone (PTH) is a peptide hormone produced by the parathyroid glands. Synthesis and secretion is controlled by a simple feedback loop – during **hypocalcemia, the release of PTH** into the blood increases.

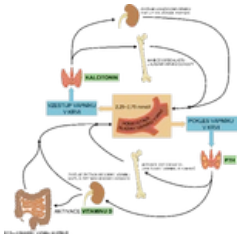
Calcitonin (thyrocalcitonin) is a peptide hormone produced by the parafollicular (C-cells) of the thyroid gland; the concentration of calcitonin increases with hypercalcemia, so it has a hypocalcemic effect.[1][2]

The influence of individual hormones on the level of calcium and phosphate in blood[2][1]

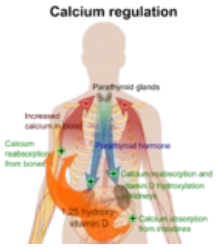
	Vitamin D	Parathyroid hormone	calcitonin
Kidney	↑ reabsorption of Ca 2+ and phosphates	↑ resorption of Ca 2+ and excretion of phosphates, stimulates the production of calcitriol	↑ excretion of Ca 2+ , ↑ excretion of phosphates
Bone	**bone mineralization** high levels, on the other hand, decalcify	bone resorption (osteoclast activation), **calcemia** and phosphatemia rise	inhibition of osteoclasts, deposition of Ca 2+ in bones
Intestine	stimulates resorption of Ca 2+ and phosphates	stimulates the production of calcitriol → stimulates the resorption of Ca 2+ and phosphates	-



Hormonal Down-Regulation of Calcium



Cacium & Phosphate metabolism



Calcium Regulation

See Calcium-Phosphate Metabolism for more detailed Information

Disorders of calcium phosphate metabolism in children

Hypocalcemia

- serum calcium < 2.0 mmol/l.[1]

Clinical manifestations:

- **acute**: apnea in newborns, tetany, convulsions (resemble epilepsy), muscle spasms, laryngospasm, dysarthria from spasm of the masseters, carpopedal spasms, prolonged QT interval on ECG
- **latent** tetany: Chvostk's sign (a tap on the face in front of the jaw joint at the site of the nervus facialis leads to a twitch in the face), Trousseau's sign (an inflated tonometer cuff on the arm causes the obstetric hand sign

within a few minutes)
- **chronic**: hair and nail growth disorders, possibly deposition of calcium in soft tissues → cataract, basal ganglia calcification, nephrocalcinosis, subcutaneous calcification in places of hematomas and minor trauma.

Differential diagnosis

- reduced secretion or reduced effects of **PTH**: hypoparathyroidism (DiGeorge syndrome , activating mutation of the calcium sensing receptor, autoimmune destruction – autoimmune polyglandular syndrome type I , iatrogenic damage during thyroid surgery), pseudohypoparathyroidism (target organ resistance to PTH), hypomagnesemia
- **vitamin D** deficiency or dysfunction: vitamin D deficiency rickets , vitamin D-dependent rickets type I and II;
- hyperphosphatemia : chronic renal insufficiency , cytostatic treatment, excessive supply of phosphates;
- malabsorption syndrome.[1]

Hypercalcemia

- serum calcium > 2.6 mmol/l.

Clinical manifestations

- reduced motility of the gastrointestinal tract, constipation, loss of appetite, nausea, vomiting,
- neurological symptoms: muscle weakness, somnolence, confusion, hallucinations, coma,
- cardiovascular symptoms: hypertension, tachycardia, ECG changes.

Differential diagnosis

- **hyperparathyroidism** : adenoma of the parathyroid gland (the most common cause of hypercalcemia), inactivating mutation of the calcium sensing receptor;
- increased resorption of calcium by **the intestine** and/or **kidneys** : phosphate deficiency (premature children), treatment with thiazide diuretics, vitamin D, A intoxication, sarcoidosis ;
- increased resorption of calcium **from bone** : thyrotoxicosis , immobilization, malignancies, bone metastases, paraneoplastic secretion of PTH or PTH-related protein.[1]

Rickets

- bone mineralization disorder due to lack of vitamin D or calcium or disorders of their metabolism:
- **vitamin D deficiency rickets** (children) / osteomalacia (adults)
  - it arises when there is a lack of vitamin D and/or calcium;
  - risk groups: fully breastfed dark-skinned children whose parents do not provide vitamin D, dark skin, strict vegetarian (vegan) diet, malabsorption syndromes with impaired fat absorption, cystic fibrosis , other pancreatic exocrine disorders, bile secretion disorders, untreated celiac disease ;
  1. phase: ↓ calcium → ↑ parathyroid hormone → normalization of calcium, phosphaturia, stimulation of calcitriol formation → ↑ osteoclast activity → ↑ alkaline phosphatase ;
  2. phase: bone resorption (parathyroid hormone+calcitriol) → classic clinical symptoms of rickets and typical X-ray picture of the skeleton (craniotabes, delayed closure of the large fontanelle, caput quadratum, rachitic rosary, Harrison's furrow, pectus carinatum, genua valga, genua vara, delayed eruption of milk dentition , enamel defects, tooth decay);
  3. phase: depletion of calcitriol reserves, without which PTH cannot break down bone → ↓ calcium despite pronounced hyperparathyroidism → clinical symptoms of hypocalcemia (spasmophilia, tetany, laryngospasm, convulsions) and vitamin D deficiency (frequent and more serious ongoing respiratory infections);
  - laboratory findings: Ca 2+ at the lower limit, then decreased, phosphate increased → normal → decreased, ALP high, parathyroid hormone increased, 25-OH-vitamin D decreased;
  - treatment: vitamin D (cholecaciferol im eventual. po), calcium; with manifest tetany 10% calcium gluconicum iv
- **vitamin D-dependent rickets type I** – AR hereditary defect of renal 25-OH-D α-hydroxylase → blocked calcitriol synthesis → clinical manifestations of rickets in the 2nd trimester → lifelong calcitriol substitution;
- **vitamin D-dependent rickets type II** – AR hereditary receptor defect that causes resistance of target organs (gut and skeleton) to calcitriol → lifelong substitution of very high doses of calcitriol, difficult to treat;
- **familial hypophosphatemic vitamin D-resistant rickets** – X-linked disorder of reabsorption of phosphates in the proximal tubules of the kidneys → high losses of phosphates in the urine (“phosphate diabetes”) → manifestations after the start of walking: deformation of the lower limbs, growth retardation → substitution of phosphates and calcitriol.[1]

See Rickets Page for more information

Osteoporosis

- systemic metabolic disease of the skeleton, characterized by a disorder of the mechanical resistance of the bone, increasing the risk of fractures;
- diagnostic criteria in children: clinically significant history of fractures and abnormal densitometry (two-photon X-ray absorptiometry, peripheral quantitative computed tomography);
- primary osteoporosis (rare in children): osteogenesis imperfecta , idiopathic juvenile osteoporosis, etc.;
- secondary osteoporosis in oncological diseases (leukemia treated with chemotherapy), systemic diseases with high-dose corticosteroid treatment (JIA), endogenous overproduction of cortisol (Cushing's syndrome ,

Cushing's disease) and neuromuscular diseases (spina bifida , muscular dystrophy), anorexia nervosa , untreated celiac disease or immobilization;
- therapy: bisphosphonates;
- prevention: adequate physical activity and nutrition, vitamin D and calcium.[1]

See the Osteoporosis page for more detailed information

Familial disorders of calcium phosphate metabolism

- Familial hypocalciuric hypercalcemia (FHH) – mutation in the calcium receptor,
- neonatal hyperparathyroidism,
- hypercalciuric hypocalcemia,
- hereditary hypophosphatemic rickets.[3]

Links

Related Articles

- Osteoporosis • Osteogenesis imperfecta
- Rickets
- Indicators of Bone Remodeling
- Metabolic bone disease

Reference

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2. SILBERNAGL, Stefan and Agamemnon DESPOPOULOS. *Atlas of Human Physiology: 6th Edition, Completely Revised and Expanded.* 3rd edition. Prague: Grada, 2004. pp. 290-293. ISBN 80-247-0630-X .
3. ŽOFKOVÁ, I. *Familial hypercalcemia and hypophosphatemia and their importance in the differential diagnosis of calcium-phosphate metabolism disorders* [online]. ©2010. [feeling. 2011-04-17]. < https://www.prolekare.cz/casopysi/vnitrni-lekarstvi >.