Bone minerals

Lecture topics

* Type of bone minerals
* Calcium, Source, metabolism and Regulation
* Calcium Functions
* Vitamin D, Sources, Absorption, Transport and Activation of Vitamin D

Type of bone minerals

* Chemical Composition of Bone

-The majority of bone is made of the matrix.

-Bone, a calcified tissue composed of 60% inorganic component (hydroxyapatite), 10% water and 30% organic component (proteins).

-Inorganic components are Ca, Phosphate, Magnesium, Chloride and Fluoride.

-The organic component of bone comprises more than 30 proteins with type I collagen being the most abundant (>90%)

Calcium

* Calcium is the most abundant mineral in the body.
* The adult human body contains about 1.2 kg of calcium.
* About 99% the body's calcium is present in bone together with phosphate as the mineral hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$], with small amounts in soft tissue and extracellular fluid.

Source

* The main dietary sources of calcium are milk and dairy products, (half a liter of milk contains approximately 1,000 mg of calcium) cheese, cereal grains, legumes, nuts and vegetables.
* Recommended quantities per day, **Adults:** 800 mg/day, **Women during pregnancy**: 1200 mg/day, and **Infants**: 300–500 mg/day.

Metabolism and regulation

* Calcium metabolism is regulated in large part by the **parathyroid hormone (PTH)–vitamin D endocrine system**.
* The rapid release of mineral from the bone is essential to maintain adequate levels of ionized calcium in serum.
* During vitamin D deficiency states, bone metabolism is significantly affected as a result of reduced active calcium absorption.

* This leads to increased PTH secretion as the calcium sensing receptor in the parathyroid gland senses changes in circulating ionic calcium.
* Increased PTH levels induce enzyme activity (1α-hydroxylase) in the kidney, which converts vitamin D to its active hormonal form, calcitriol.
* calcitriol stimulates enhanced calcium absorption from the GIT.

Parathyroid Hormone (PTH)

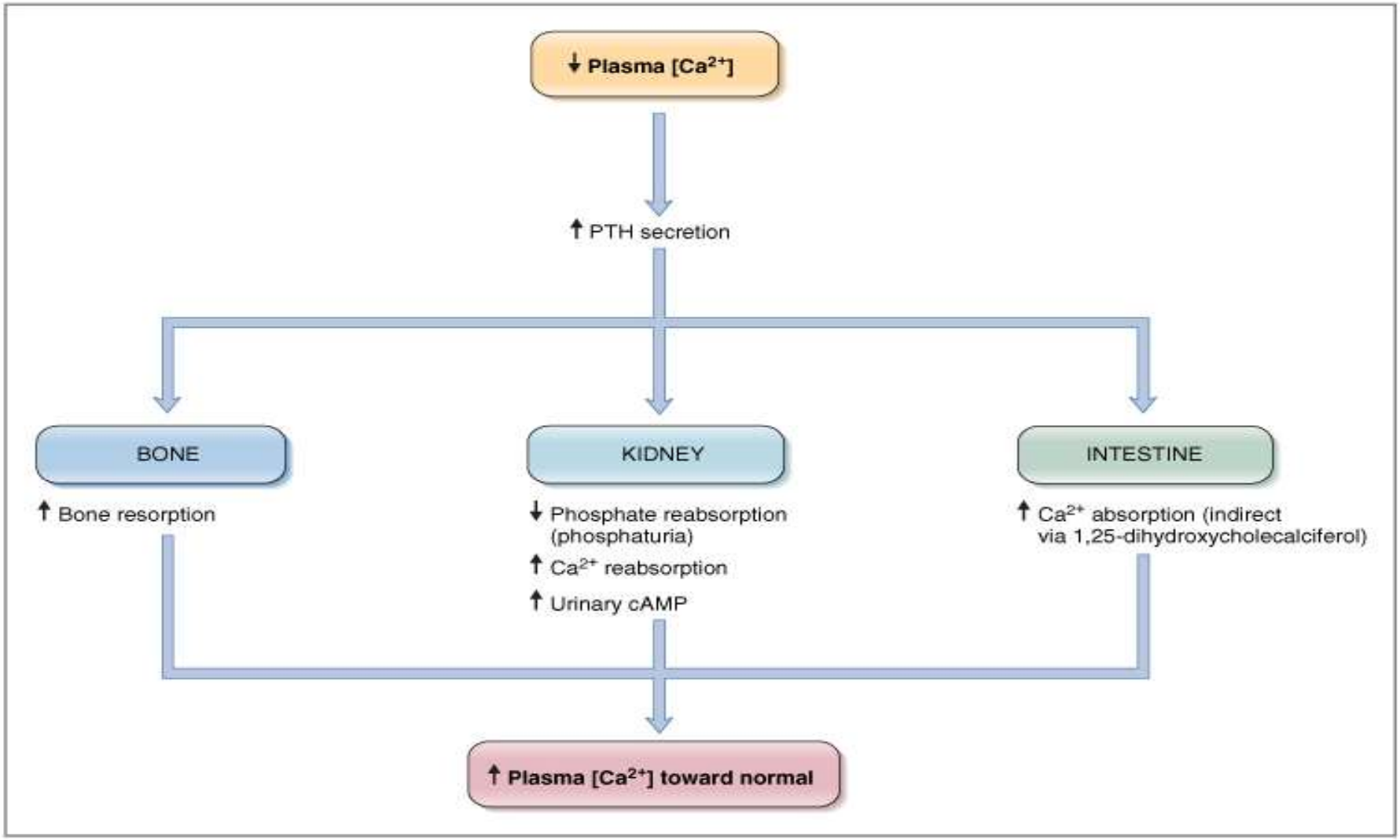


Figure 9-37 **Regulation of PTH secretion and PTH actions on bone, kidney, and intestine.** cAMP, Cyclic adenosine monophosphate; PTH, parathyroid hormone.

Factors affecting absorption

* Vitamin D stimulates absorption of calcium from intestine by inducing the synthesis of calcium binding protein, necessary for the absorption of calcium from intestine.
* Parathyroid hormone (PTH) stimulates calcium absorption indirectly via activating vitamin D.
* Acidic pH: Since, calcium salts are more soluble in acidic pH, the acidic foods and organic acids (citric acid, lactic acid, pyruvic acid, etc.) help the absorption of calcium from intestine.
* High protein diet favors the absorption of calcium (Basic amino acids, lysine and arginine derived from hydrolysis of the dietary proteins) increase calcium absorption.
* Lactose is known to increase the absorption of calcium, by forming soluble complexes with the calcium ion.

Calcium Functions

* Formation of bone and teeth: 99% of the body's calcium is located in bone in the form of hydroxyapatite crystal. The hardness and rigidity of bone and teeth are due to hydroxyapatite.
* Blood coagulations: Calcium present in platelets involved in blood coagulation, the conversion of an inactive protein prothrombin into an active thrombin requires calcium ions.
* Muscle contraction: Muscle contraction is initiated by the binding of calcium to troponin.
* Release of hormones: The release of certain hormones like parathyroid hormone, calcitonin, etc. requires calcium ions.
* Release of neurotransmitter: Influx of $Ca2+$ from extracellular space into neurons causes release of neurotransmitter.
* Regulation of enzyme activity: Activation of number of enzymes requires $Ca2^{+}$ as a **specific cofactor**. For example: Activation of enzyme glycogen phosphorylase kinase which then triggers glycogenolysis.

* Second messenger: Calcium acts as a second messenger for hormone action. For example, it acts as a second messenger for epinephrine or glucagon.
* Membrane excitability: Calcium ions activate the sodium channels. Deficiency of calcium ions lead to decreased activity of Na-channels, which ultimately leads to decrease in membrane potential so that the nerve fiber becomes highly excitable causing muscle tetany.
* Cardiac activity: Cardiac muscle depends on extracellular $Ca2^{+}$ for contraction. Myocardial contractility increases with increased $Ca2^{+}$ concentration and decreases with decreased calcium concentration.
* Membrane integrity and permeability: Calcium is required for maintenance of integrity and permeability of the membrane.
* Physiological calcium ($Ca2^{+}$) signaling has been found to be vital for the proper insulin-releasing function of β-cells. Calcium dysregulation events can have a dramatic effect on the proper functioning of the pancreatic β-cells.

Phosphate

* Phosphorus is an element that plays an important role in the body. In the body, almost all phosphorus is combined with oxygen, forming phosphate.
* Phosphate is one of the body's electrolytes, which are minerals that carry an electric charge when dissolved in body fluids such as blood, but the majority of phosphate in the body is uncharged.
* Bone contains about 85% of the body’s phosphate.
* The remaining phosphate is located primarily inside cells, where it is involved in energy production.

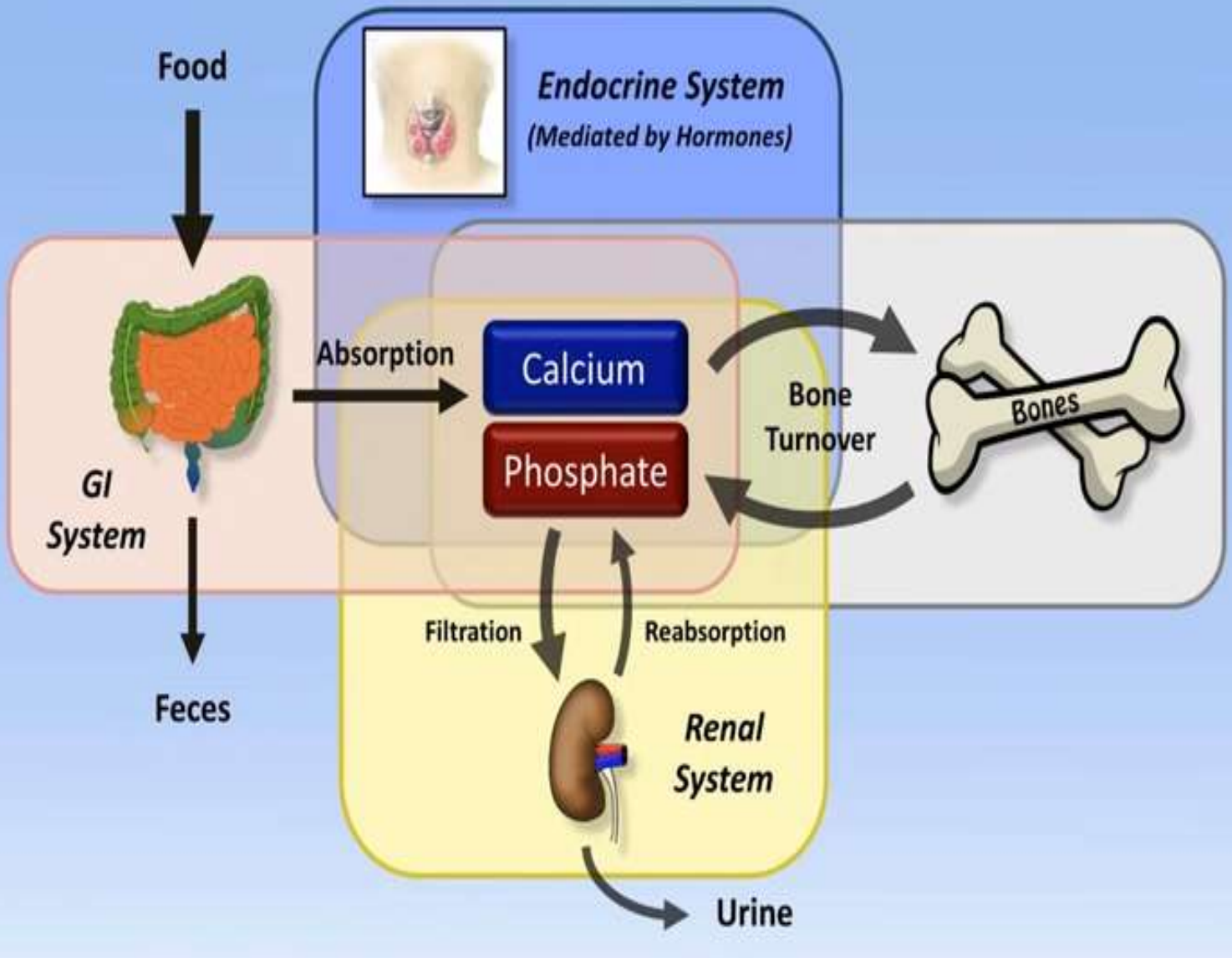
Functions

* Phosphate is necessary for the formation of bone and teeth.
* Phosphate is also used as a building block for several important substances, including those used by the cell for energy, cell membranes, and DNA (deoxyribonucleic acid).
* The body obtains phosphate from foods and excretes it in urine and sometimes stool. How much phosphate is in stool varies, depending on how much is not absorbed from food. Foods that are high in phosphate include milk, egg yolks, chocolate, and soft drinks.
* Intracellular phosphate is largely organic as a component of phospho-lipids, phospho-proteins.

Regulation of phosphate levels

* The kidney is a major regulator of Phosphate homeostasis and can increase or decrease its phosphate reabsorptive capacity to accommodate phosphate need.

Calcium Phosphate Homeostasis



Vitamin D

* Vitamin D is fat-soluble vitamin. It is essential for maintaining normal calcium metabolism.

Sources

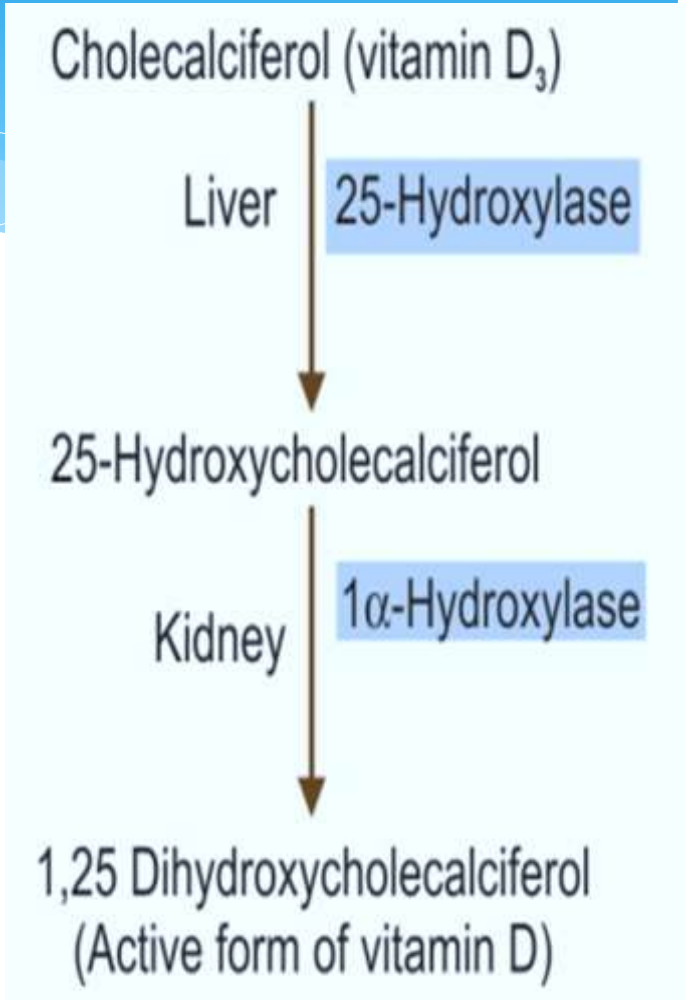
* Vitamin D can be synthesized by humans in the epidermis of the skin upon exposure to ultraviolet-B (UVB) radiation from sunlight, or it can be obtained from the diet.
* various fish species (salmon, sardines and mackerel, tuna, catfish), fish oil, cod liver, eggs, beef liver, mushrooms.

Absorption, Transport and Activation of Vitamin D

* Exogenous or dietary vitamin D is absorbed in the duodenum along with lipids. It is transported to the liver through chylomicron
* **Active Form of Vitamin D**

Cholecalciferol is an inactive form of vitamin D. It needs further metabolism to produce the active form of the vitamin.

1,25-dihydroxycholecalciferol also known as **calcitriol** is the active form of vitamin D.



Synthesis and Regulation of Calcitriol