

PARATHYROID HORMON

Parathyroid Hormone provides a powerful mechanism for controlling extracellular calcium and phosphate concentrations by regulating:) intestinal reabsorption) renal excretion) exchange between the extracellular fluid and bone of these ions.

- **Excess activity of** the parathyroid gland causes rapid absorption of calcium salts from the bones, with resultant hypercalcemia in the extracellular fluid; conversely, hypofunction of the parathyroid glands causes hypocalcemia, often with resultant tetany.
- **Physiologic Anatomy of** the Parathyroid Glands. Each parathyroid gland is about 6 millimeters long, 3 millimeters wide, and 2 millimeters thick and has a macroscopic appearance of dark brown fat.
- **Contains • chief cells** (secrete most of the PTH). • oxyphil cells (absent in young humans) and oxyphil cells are modified or depleted chief cells that no longer secrete hormone.
- **Chemistry of Parathyroid** Hormone synthesized in the form of a preprohormone, cleaved to a prohormone, then to the hormone itself with 84 amino acids by the endoplasmic reticulum and Golgi apparatus, and finally is packaged in secretory granules in the cytoplasm of the cells.
- **Effect on Ca^{2+}** and Phosphate Concentrations in the ECF: suddenly infusing PTH) calcium ion concentration begins to rise and reaches a plateau in about 4 hours.) the phosphate concentration, however, falls more rapidly than the calcium rises and reaches a depressed level within 1-2 hours.
- **PTH ↑calcium** and phosphate absorption from the bone; PTH ↓excretion of calcium by the kidneys. PTH ↑renal phosphate excretion ** ** an effect that is usually great enough to override increased phosphate absorption from the bone.
- **PTH ↑calcium and** phosphate absorption from the bone
Second phase: Proliferation of osteoclasts
First phase: Activation of already existing osteocytes/osteoblasts
Activated osteocytes/osteoblasts send secondary signals to osteoclasts
Receptor proteins on osteocytes/osteoblasts that

bind PTH and activate calcium pump Osteoclastic absorption of bone itself Promote calcium and phosphate absorption

- **PTH ↓calcium excretion** & ↑ phosphate excretion from the kidneys θ Were it not for the effect of PTH on the kidneys to increase calcium reabsorption, continual loss of calcium into the urine would eventually deplete both the extracellular fluid and the bones of this mineral.
- **PTH increases intestinal** absorption of calcium & phosphate θ PTH greatly enhances both calcium and phosphate absorption from the intestines by increasing the formation in the kidneys of 1,25-dihydroxycholecalciferol from vitamin D.
- **after PTH** administration, the concentration of cAMP increases in the osteocytes, osteoclasts, and other target cells. θ This cAMP is responsible for osteoclastic secretion of enzymes and acids to cause bone reabsorption and formation of 1,25-dihydroxycholecalciferol in the kidneys.
- **Control of Parathyroid** Secretion by Calcium Ion Concentration θ decrease in calcium ion concentration in the ECF causes the parathyroid glands to increase their rate of secretion within minutes. θ decreased calcium concentration persists, the glands will hypertrophy, sometimes fivefold or more.
- **Control of Parathyroid** Secretion by Calcium Ion Concentration θ Conditions causing Enlarged parathyroid gland: } Rickets } Pregnancy } Lactation θ conditions causing reduced sized parathyroid gland } Excess calcium in diet } Increased vitamin D in diet } Bone absorption caused by factors other than PTH
- **increase in plasma calcium** concentration of about 10 per cent causes an immediate twofold or more increase in the rate of secretion of calcitonin, which is shown by the blue line in Figure.
- **Calcitonin θ peptide hormone** secreted by the thyroid gland, tends to decrease plasma calcium concentration and, in general, has effects opposite to those of PTH. θ Synthesis and secretion of calcitonin occur in the parafollicular cells, or C cells, lying in the interstitial fluid between the follicles of the thyroid gland.
- **Calcitonin θ The primary** stimulus for calcitonin secretion is increased plasma calcium ion concentration. θ calcitonin ↓ Ca⁺ plasma concentration } The

immediate effect is to decrease the absorptive activities of the osteoclasts }
 prolonged effect of calcitonin is to decrease the formation of new osteoclasts. }
 minor effects on calcium handling in the kidney tubules and the intestines } Effects
 are opposite to PTH , but of little important

- **Calcitonin** θ **Calcitonin Has** a Weak Effect on Plasma Calcium Concentration in the Adult Human. θThe effect of calcitonin in children is much greater because bone remodeling occurs rapidly in children θ In Paget's disease , in which osteoclastic activity is greatly accelerated, calcitonin has a much more potent effect of reducing the calcium absorption.
- **Disorders of PTH** θ **hypoparathyroidism** θ **Primary** hyperparathyroidism
 θSecondary hyperparathyroidism
- **Hypoparathyroidism** θ **↓PTH** θ **↓Ca⁺ reabsorption from** bone θ **↓ Ca⁺ level** in body fluids θ Bone remains strong θ If parathyroid glands are suddenly removed: } Ca⁺ levels fall from 9.4mg/dl to 6-7 within few days } Phosphate concentration may double } ↓Ca⁺ tetany θ Laryngeal muscles tetany θ obstructs respiration θ death
- **Hypoparathyroidism** θ **Treatment** } **hypoparathyroidism is usually** not treated with PTH administration. } large quantities of vitamin D daily } 1-2 grams of Calcium } 1,25-dihydroxycholecalciferol
- **Primary Hyperparathyroidism** θ **Tumor in** parathyroid glands (females mainly) θ excess PTH θ **↑Ca** concentration in ECF. **↓Phosphate** θ In severe hyperparathyroidism the bone may be eaten away entirely. θ Indeed, the reason a hyperparathyroid person seeks medical attention is often a broken bone.
- **Primary Hyperparathyroidism** θ **Radiographs** of the bone show extensive decalcification and, occasionally, large punched-out cystic areas of the bone that are filled with osteoclasts in the form of so-called giant cell osteoclast "tumors." θ The cystic bone disease of hyperparathyroidism is called osteitis fibrosa cystica
- **Primary Hyperparathyroidism** θ **Osteoblastic activity** in the bones also increases greatly in attempt to make up for the old bone absorbed by the osteoclastic activity. θ When the osteoblasts become active, they secrete large quantities of alkaline phosphatase. Therefore, one of the important diagnostic findings in hyperparathyroidism is a high level of plasma alkaline phosphatase.

- **Primary Hyperparathyroidism** **Effects of Hypercalcemia** in Hyperparathyroidism. Hyperparathyroidism can cause the plasma calcium level to rise to 12 to 15 mg/dl. The effects of such elevated calcium levels are:
 - } depression of the central and peripheral nervous systems,
 - } muscle weakness
 - } constipation
 - } abdominal pain
 - } peptic ulcer
 - } lack of appetite
 - } depressed relaxation of the heart during diastole
- **Parathyroid Poisoning and Metastatic Calcification** extreme quantities of PTH are secreted \uparrow Ca⁺, \uparrow phosphate \diamond CaHPO₄ crystals deposition in:
 - } alveoli of the lungs
 - } the tubules of the kidneys,
 - } the thyroid gland,
 - } the acid-producing area of the stomach mucosa,
 - } the walls of the arteries
 Calcium level in blood must rise above 17 mg/dl before there is danger of parathyroid poisoning. but once such elevation develops along with concurrent elevation of phosphate, death can occur in only a few days.
- **Kidney stones** **Mild hyperparathyroidism** leads to formation of kidney stones (calcium phosphate, calcium oxalate stones). Kidney stones are more common in alkaline urine (low solubility in alkaline media) \diamond treatment include acidotic diet & acidic drugs.
- **Secondary hyperparathyroidism** **high** levels of PTH occur as a compensation for hypocalcemia. this contrasts with primary hyperparathyroidism, which is associated with hypercalcemia. caused by vitamin D deficiency or chronic renal disease in which the damaged kidneys are unable to produce sufficient amounts of the active form of vitamin D.