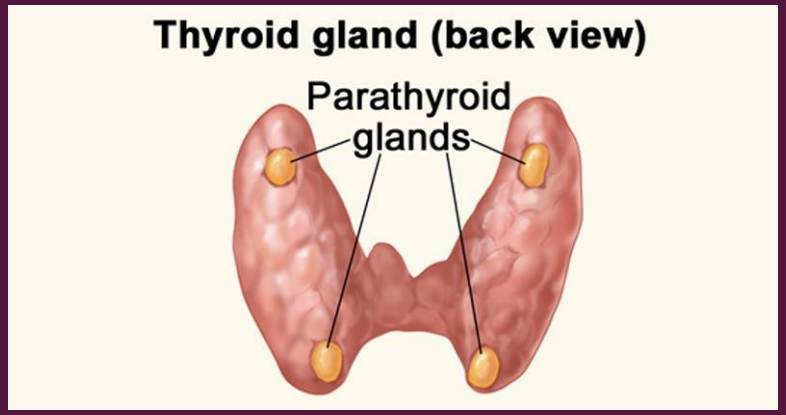
Parathyroid Hormone

The parathyroid glands are small endocrine glands in the neck of humans that produce parathyroid hormone



- PTH is secreted from the parathyroid glands in response to a low plasma concentration of ionized (free) calcium
- PTH immediately causes the transfer of labile calcium stores from bone into the blood stream
- PTH increases rates of dietary calcium absorption by the intestine indirectly via the vitamin D3 system activation of enterocyte activity

- Maintenance of calcium, phosphate and magnesium homeostasis is under the influence of two polypeptide hormones; parathyroid hormone(PTH), and calcitonin (CT), as well as a sterol hormone, 1,25 dihydroxy cholecalciferol (1,25 $(OH)_2D_3$.

- These hormones regulate the flow of minerals in and out of the extracellular fluid compartments through their actions on intestine, kidneys, and bones.

The PTH acts directly on the bones and kidneys and indirectly on the intestine through its effect on the synthesis of 1,25 $(OH)_2D_3$. Its production is regulated by the concentration of serum ionized calcium. Lowering of the serum calcium levels will induce an increased rate of parathyroid hormone secretion

CALCITONIN

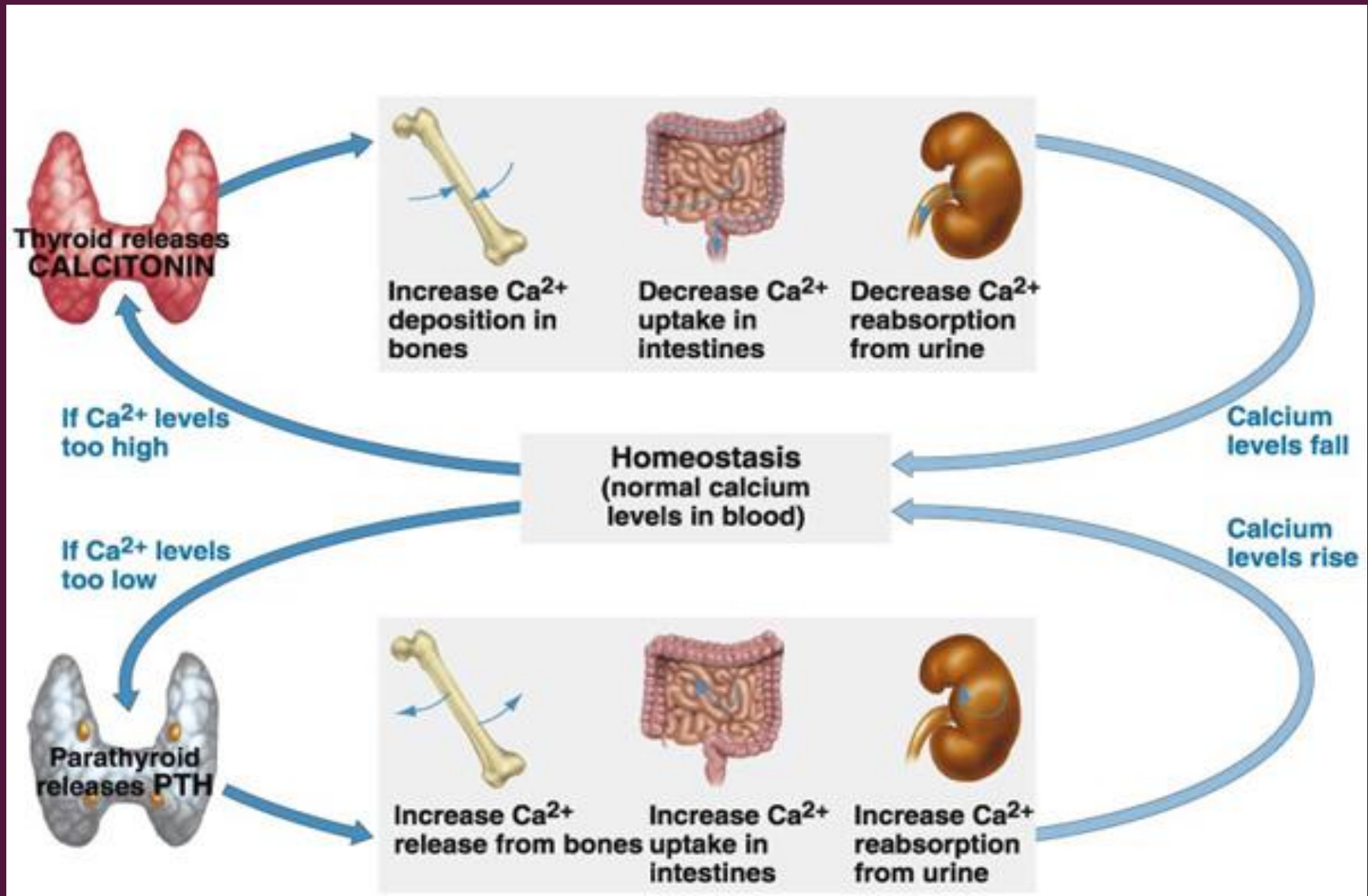
- Calcitonin release is normally stimulated by rising serum calcium levels and suppressed by hypocalcemia
- Calcitonin is released by the “C” cells (parafollicular cells in the thyroid gland)
- It acts on the kidney and bones to restore the level of calcium to just below a normal set point which in turn inhibits secretion of the hormone.

Calcitonin is the physiological antagonist of PTH. The two hormones act in concert to maintain normal concentration of calcium ion in the extracellular fluid.

VITAMIN D3 (CHOLECALCIFEROL)

Vitamin D3, through its active metabolite, 1,25- (OH)2D3, also plays an important role in maintaining calcium homeostasis by

- Enhancing intestinal calcium absorption,
- PTH-induced mobilization of calcium from bone,
- calcium reabsorption in the kidney


Thyroid releases CALCITONIN
Increase Ca^{2+} deposition in bones
Decrease Ca^{2+} uptake in intestines
Decrease Ca^{2+} reabsorption from urine
If Ca^{2+} levels too high
Calcium levels fall
Homeostasis (normal calcium levels in blood)
If Ca^{2+} levels too low
Calcium levels rise
Parathyroid releases PTH
Increase Ca^{2+} release from bones
Increase Ca^{2+} uptake in intestines
Increase Ca^{2+} reabsorption from urine

CLINICAL USES OF PARATHYROID HORMONE, CALCITONIN, VITAMIN D, AND BISPHOSPHONATES

Hyperparathyroidism

- Primary hyperparathyroidismis due to excessive production of PTH by one or more of hyperfunctioning parathyroid glands. This leads to hyprcalcemia which fails to inhibit the gland activity in the normal manner.
- The cause of primary hyperparathyroidism is unknown. A genetic factor may be involved. The clonal origin of most parathyroid adenomas suggests a defect at the level of the gene controlling the regulation and/or expression of parathyroid hormone.

Medical Treatment of the hypercalcaemia

In acute severe forms the main stay of therapy is adequate hydration with saline and forced diuresis by diuretics to increase the urinary excretion of calcium rapidly along with sodium and prevent its reabsorption by the renal tubules.

Other agents

- Glucocostiroids
  - In hypercalcaemia associated the hematological malignant neoplasms
- Mythramycin
  - A toxic antibiotics which inhibit bone resorption and is used in hematological and solid neoplasms causing hypercalcaemia.

Other agents

- Calcitonin
  - Also inhibit osteoclast activity and prevent bone resorption
- Bisphosphonates
  - They are given intravenously or orally to prevent bone resorption.
- Phosphate
  - Oral phosphate can be used as an antihypercalcaemic agent and is commonly used as a temporary measure during diagnostic workup.
- Estrogen
  - It also decrease bone resorption and can be given to postmenopausal women with primary hyperparathyroidism using medical therapy

Surgery

- Surgical treatment should be considered in all cases with established diagnosis of primary hyperparthyroidism.
- During surgery the surgeon identifies all four parathyroid glands (using biopsy if necessary) followed by the removal of enlarged parathyroid or 3 ½ glands in multiple glandular disease.

Hypoparathyroidism

Deficient secretion of PTH which manifests itself biochemically by hypocalcemia, hyperphospatemia diminished or absent circulating iPTH and clinically the symptoms of neuromuscular hyperactivity.

Hypoparathyroidism

Treatment:

The mainstay of treatment is a combination of oral calcium with pharmacological doses of vitamin D or its potent analogues. Phosphate restriction in diet may also be useful with or without aluminum hydroxide gel to lower serum phosphate level.

Osteoporosis

- Postmenopausal osteoporosis is the most common form of osteoporosis. In perimenopausal women, the greatest amount of bone density is lost during the first 5 year after onset of menopause
- Women going through menopause at a particularly early age are especially at risk for developing osteoporosis

Treatment

take some prophylactic regimen at the onset of menopause such as

- estrogen replacement therapy (ERT),
- calcium supplementation
- D3.
- However, the benefits of ERT, including increased bone density, decreased risk of colon cancer, and decreased vaginal atrophy,must be weighed against the slightly increased risk of breast cancer, endometrial cancer, stroke, and deep vein thrombosis.
- ERT appropriate combinations with a progestin negate such risk

Paget's Disease

- Paget's disease is an uncommon disorder of bone characterized

by mixed lytic and sclerotic bone changes.

- These individuals have areas of increased bone resorption

and other areas of abnormal new bone formation.

- The abnormal bone formation can result in pain, deformity,

and fracture of affected bones.

- The bisphosphonates and calcitonin are most commonly used in the

treatment of this disease

- the bisphosphonates are given in a cyclic pattern to treat Paget's disease. Because Long-term continuous use of

bisphosphonates can be associated with the induction of

osteomalacia through a direct impairment of new bone

formation.

Renal Osteodystrophy

- Patients with chronic renal failure develop hyperphosphatemia, hypocalcemia. The secondary hyperparathyroidism is due to hyperphosphatemia and decreased 1, 25-(OH)D2 formation.

Treatment

- Oral or intravenous 1,25-(OH)2 D3 (calcitriol) therapy along with oral phosphate-binding agents and calcium supplementation