

Antagonizing the PTH:-

- As Ca^{2+} rises the secretion of Parathyroid hormone falls while calcitonin rises.
- Calcitonin is a protein hormone ; about 32 amino acids.
- The activity of calcitonin resides in the middle of the amino acid chain.
- The calcitonin receptor is similar to the PTH receptor.
- Calcitonin antagonizes the action of PTH by decreasing Ca^{2+} level in a way.
- Calcitonin is produced by parafollicular cells in the thyroid gland.
- Calcitonin is also present in the nervous system as a neuromodulator similar to somatostatin.
- The activity of calcitonin is similar to the activity of PTH on the phosphate (decreases phosphate level in plasma).
- You may wonder that calcitonin normally is not that important, so when you remove the thyroid gland parafollicular cells will be removed ; therefore no calcitonin, but there will be no change in the Ca^{2+} level.

(Ca^{2+} level is not affected when calcitonin is absent).

Sometimes there is thyroid cancer leading to hyperactivity of parafollicular cell ; therefore more calcitonin will be secreted, but also Ca^{2+} levels will not change. ***(Ca^{2+} level is not affected when calcitonin is over secreted).***

- There is calcitonin from the salmon fish, it functions in a very good manner in humans. Therefore calcitonin is not that important hormone.
- Calcitonin functions both on kidney tubules and bone.(affecting both Ca^{2+} and PO_4^{3-}).

Similar to the growth and even more, many factors are involved in bone formation and Ca^{2+} metabolism.

Parathyroid, GH, Vit.D, Calcitonin, Cortisol, Somatomedin, TH, Insulin, Insulin like growth factor-1, estrogen, epidermal growth factor, platelet derived growth factor, fibroblast growth factor, osteoclast activating growth factor, prostaglandin.

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- **Phosphate**, 85% is in the bone. (*functions of PO_4^{3-} in the body?*)
 - 1- Part of intracellular buffer system.
 - 2- Constituent of the bone.
 - 3- Important constituent of variety of macromolecules such as (nucleic acids, phospholipids, metabolic intermediates and phosphoproteins).
- If phosphate decreases in plasma, first PTH is inhibited (because of increase in Ca^{2+} and decrease in PO_4^{3-}) Second, activation of enzyme in the kidney (1-alpha hydroxylase) to produce 1,25-(OH)₂ D₃ acts on the intestines and also on the bone to increase the absorption of both Ca^{2+} and PO_4^{3-} .
- Metabolism, of Ca^{2+} , PO_4^{3-} and Mg^{2+} are essential for life.
- Complex system acts to maintain normal body fluids content and ECF levels of these minerals to face environmental and internal changes.
- Organs and hormones that are important in the homeostasis of Ca^{2+} , PO_4^{3-} and Mg^{2+} (PTH, Vit. D, Calcitonin and other hormones) (organs : GIT, kidney, liver and skin).
- **Rickets**, very rare nowadays ,occurs mainly in children as a result of Ca^{2+} and PO_4^{3-} deficiency in the plasma (due to lack of Vit. D rather than a dietary lack of Ca^{2+} or PO_4^{3-})
- Occurs usually in spring months.
- Daily requirement for Vit. D is very minimal
- deficiency of Vit. D is very rare.
- Sometimes your body stops functioning and building Vit. D, you need several years to appear with symptoms of osteomalascia (similar to rickets but in adults).
- You have contents of Vit. D sufficient for several years , because a lot Vit. D is present in adipose tissue.
- **Osteomalasia or adults rickets** : Serious deficiency of both Vit. D and Ca^{2+} occasionally occurs as a result of steatorrhea (failure to absorb –a kind of diarrhea-).
- Vit. D is fat soluble and Ca tend to form insoluble salt with fat consequently in steatorrhea both Ca^{2+} and Vit. D tend to pass into the

feces under these conditions an adult occasionally has such poor calcium and phosphate absorption that adult rickets can occur, though this almost not proceed to tetany - but often it's a cause of severe bone disability . so almost similar to rickets in children but the cause is different , because there is no time for the absorption of Ca^{2+} and Vit. D due to steatorrhea.

- The most important or the most common of all bone diseases in adults is **osteoporosis** especially in old age and in women. It differs from osteomalacia and rickets, it results from diminished organic matrix rather than abnormal bone calcification.
- Usually in osteoporosis the osteoblastic activity in the bone is less than normal. Mineralization is less in osteoporosis and they don't know exactly what is the cause!!!
- Probable causes of osteoporosis:-
 - 1- Lack of physical stress on the bone because of the inactivity.
(Why inactivity causes osteoporosis? We don't know)
 - 2- Lack of Vit. C.
 - 3- Malnutrition to the extent that sufficient protein matrix can't be formed.
 - 4- Postmenopausal lack of estrogen secretions.
 - 5- Old age in which many of the protein anabolic functions are poor.
 - 6- cushing syndrome: because massive quantities of glucocorticoids cause decrease deposition of proteins.
 - 7- Acromegaly because of excess adrenocortical hormones and Lack of insulin because of diabetogenic effect of GH.

Drugs used to prevent the development of osteoporosis:-

- Estrogen is the best drug till now used against osteoporosis.
 - 1- Estrogen (have other advantages especially for ladies after menopause) >> the best.
 - 2- Calcitonin, this is synthetic (or taken from salmon fish) ; 10 times stronger than the human calcitonin.
 - 3- Biophosphonates , becoming popular nowadays ; potent inhibitor of bone resorption.

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- 4- PTH (available as injectable treatment by stimulating osteoblastic formation, also decrease the rate of fractures).
- 5- Vit. D and Ca^{2+} .