Parathyoid glands and PTH

They are four glands located behind the thyroid gland, each one from (20-50) mg in weight, and composed of two types of cells:
1. ***Cheif cells***: that produces PTH.
2-***oxyphil cells***: The function is uncertain until now ,but probably they are modified or depleted chief cells that no longer secrete PTH *in pathology oxyphil cells are not present in the young people ,even in some animals ,but in the human being it might develop later as a modified chief cells..

REGULATORS OF CA LEVEL IN THE BLOOD:

1- ***PTH***: functioning on kidney tubules, bones and intestines so as to normalize the Ca level >>11mg/100ml of plasma [Ca level must be maintained within a narrow range the same as PH].

*PTH has two types of receptors (sometimes three), and it uses either cAMP or [DAG and IP3].—**PTH related protein** has similar function to PTH [most probably this protein released from the parathyroid glands]
*The parathyroid glands develop at 5-14 weeks
Of gestation.
* PTH is a single chain protein (9600
Molecular weight) that contains 84 an1ino
Acids.
*The biologic activity of the hormone resides
·within a.a.l-34. [Within the first 34 a.a]
* PTH interacts with receptors on the surface
Of the target cells increasing the formation of
cAMP, IP & diacylglycerol.]
* PTH is free in plasma with half life 25 min.
* PTH is essential for life, without it Ca+·+·
Falls in plasma neuromuscular excitability increase
Tetany & death occurs.
* The dominant regulator of PTH secretion is
The plasma Ca++ level.
* Ca++ also regulates the size & the number of
Parathyroid cells.
* Hypomagnesemia stimulates PTH secretion_
such as Ca++ but less potent.
* Arise in plasma phosphate conc. indirectly cause transient increase in PTH secretion.
* 1, 25 (OH) 2 -D directly reduces PTH
Secretion.

..Function of the PTH: is to increase Ca plasma level, and to decrease the Phosphate plasma level. [Actually it is normalize rather than increase or decrease]

- On kidneys :increase Ca reabsorption and Phosphate excretion ,and the synthesis of V.D which will function on
- The intestines: increase Ca absorption.
- On bones :increase resorption of Ca and Phosphate [then phosphate will be excreted through the kidneys]

So generally, PTH function ***MAILNY* to normalize Ca level in order to function:
1-requeired for the- maintenance of normal‥ ⋯,
Sodium permeability in· nerves · 2. Involved in triggering the release of Acetylcholine from ·nerve endings at the
Neuromuscular junction [either the release will be deficient or absent depending on the degree of Ca deficiency] ·
3. Involved in excitation-contraction coupling
In muscle cells ·
4. Serves as an intracellular signal· for some
Hormones and enzymes [especially hormones that use DAG and IP3]
5. Required by some enzymes for normal
Activity.
6. Required for blood clotting to occur normally.
7-. Required for proteins secretion. [Such as insulin]. 8-constituent of the bones.

**THE UNDER ACTIVITY OF THE PTH: [because of atrophy or removal of the parathyroid during thyroidectomy]:
Decrease in the bone resorption, kidney reabsorption, intestine absorption of Ca...The result will be decrease in the Ca plasma level, if it reduces to (5-6) mg tetany will occur and if it reach to the respiratory system death occurs.

**THE OVER ACTIVITY OF PTH: [because of tumor]
1. Alot of Ca reabsorption the kidney tubules. 2. Alot of Ca absorbed by the intestines .3.alot of Ca resorped from the bones.
The result will be softening of the bones, and fragility a disease called [**osteitis fibrosa cystica].**

The second major regulator of the Ca level: [V.D] major regulator of Ca and phosphate [both of them]
*v.d sometimes considered a hormone produced in the body and released into the blood.
*v.d sometimes considered a vitamin taken from the ingested food.

In both cases .V.D has 2 sources firstly through the skin >>V.D3…then from the diet >>V.D2.

* Vitamins D3 & D2 are essentially prohormones that Undergo identical processing that converts them to Molecules with identical qualitative & quantitative Actions.

* Once vitamin D enters the circulation from the skin or the Gut, it is concentrated in the liver. There it is hydroxylated to 25-0H-D. this molecule is transported to the kidney where it undergoes alternative fates.[in the kidneys the most potent derivative will be formed >>1,25(OH)-D …and another derivative 24,25(OH)-D its potency is $1/20^{th}$ of the previous one .]

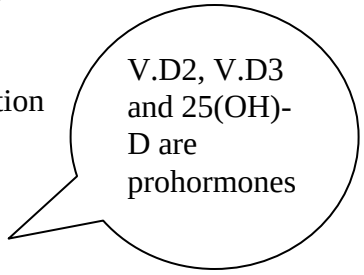
*24,25(OH)-D mainly serves to dispose of excess vitamin D.[it means that if there is need >>1,25 will be formed ….if there is less need 24,25will be formed .

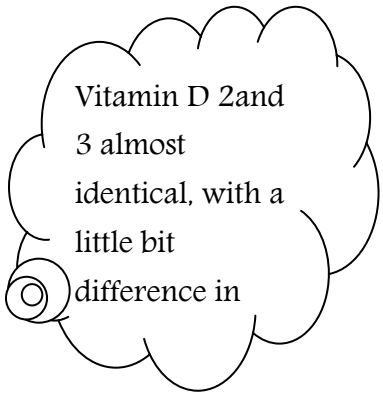
*Vitamin D, 25-0H-D & 1,25-(0H)-D circulate bound to a protein carrier.

*V.D3 has many natural sources like codfish, eggs, and 45-milk, in addition To the skin.

*BUT V.D2 can be obtained only from the diet.

*in addition to vitamin D2and 3 and their derivatives there are other 15 Metabolite without known function.





** Conclusion of V.D processing:

1-vitamin d will be transferred to the liver to become 25(OH)-D.>this comp. will be transferred to:

2-kidneys, either to become 1,25 OR 24,25 derivatives

##deficiency of (Ca, phosphate, V.D) and the PTH leads to formation of the 1, 25(OH)-D by 1-α hydroxylase enzyme.

##1,25(OH)-D ,,Ca and phosphate excess leads to the formation of 24,25 by 24-hydroxylase enzyme .

25 and 1,25 and 24,25 ALL are functioning derivatives but with varying degrees

	Plasma conc {µg/l}.	Plasma half life{days}	Production rate µg/day
1,25	0.03	1 to 3	1
24,25	2	15 to 40	1
25	20	5 to 20	10

SO vitamin D will:
1-increases reabsorption of Ca and phosphate in the kidneys.
2-increases absorption of both from intestines.
3-increases resorption of old bones...thus normalize the level of both {Ca and phosphate} unlike PTH which increases the Ca level but decreases phosphate level.

The main function of vitamin D is to MENERALIZE the new bones and if there is need for the other bones.

	%in the bones
Ca	99
Phosphate	85
Carbonate	80
Mg	50
Na	35
Water	9

***the tissue that has the least percentage of water even less then bones is **ADIPOSE TISSUE.**

The Americans (300 million) consume almost ½ of the world's proteins.
The Europeans (500 million) consume 50% of the other half .and the other 50%are consumed by the rest specially China and India.

**and now .we know that most of V.D in our bodies stored in the adipose tissue, and it cannot release it, SO teenagers who eat too much proteins are obese individuals mainly in the abdomen where the adipose tissue are concentrated, they are unable to release the vitamin thus will be exposed to her failure and heart attack,, hypertension and diabetes.

White individuals have normal V.D, while the black ones don't...and sometimes even the white Mexicans don't have much of the normal V.D.

**the modulators of V.D synthesis in kidneys:
Low Ca, low phosphate ,, PRL and GH(pituitary),, insulin(pancreas) ,, PTH (parathyroids)…..then V.D functions on bones ,kidneys ,,intestine ..and also can be transferred to mammary glands ,,placenta,, skin ,, Avian shell gland .

**the causes of deficiency of 1:25dihydroxycalciferol:
1. Failure to synthesize chole¢alciferol the skin (this occurred in the dark skinned people in temperature climate).
2. Dietary deficiency of cholecalciferol [relatively unimportant]
3. Failure to hydroxylate cholecalciferol in the 25 position (this· occurs in chronic liver disease; hepatic-osteodystrophy}
4. ·Rapid metabolism, of cholecalciferol and its· active metabolites {this occurs. 'when-hepatic.enzymes·are.induced and is seen in patients taking anticonvulsants) _
5. Failure to hydroxylate 25-cholecalcifernl in the 1position (this occurs in· patient-s with chronic renal failure; renal osteodystrophy)

Diffusible Ca	Distribution (mol/L) of calcium in normal human plasma.		
Ionized	1.18		
Complexed to HCO3 or citrate	0.16	total	1.34
Nondiffusible{protein bound}			
Bound to albumin	0.92		
Bound to globulin	0.24	total	1.16