**Vitamin D & Calcium

-**Vitamin D3 (Cholecalciferol), is mainly produced through the skin, yet it also can be obtained from outside natural sourceslike cod, halibut, liver, eggs and fortified milk.
Vitamin D2 (Engocalciferol) is obtained only from the diet; richly found in fresh vegetables.
-Other than Vit D3 and D2, more than 15 other metabolites of Vitamin D are found in plasma. However, the 1,25-dihydroxycholecalciferol is the main active form.-Vitamin D3 and D2 are almost identical, with a minor difference in the structure.

**Vitamin D metabolism**

* Both Vit D3 and Vit D2, are eventually transferred and concentrated in the liver to give 25- hydroxycholecalciferol, which is not very active. This new derivative is then transferred to the kidney to be converted either to
24, 25- dihydroxycholecalciferol OR 1,25-dihydroxycholecalciferol, according to the body needs of Vitamin D.(1,25-dihydroxycholecalciferol is produced when in need, while 24,25-dihydroxycholecalciferol is produced when not in need)
{This makes 25- hydroxycholecalciferol similar to T4; a Prohormone}
* When there is deficiency in Vitamin D, Calcium or phosphate, or in the presence of PTH >> 1,25dihydroxycholecalciferol is produced by the action of
1α hydroxylase enzyme
* When there is enough 1,25dihydroxycholecalciferol, in blood and there is excess calcuim and phosphate >> 24, 25 dihydroxycholecalciferol is produced by the action of 24-hydroxylase enzyme.
* All three metabolites of Vit D are functional, yet they differ in their potency.
(1,25$(OH)\_{2}$-D is the most potent and the most active)
* Vitamin D is lipid soluble.

 **Effect of 1,25 dihydroxycholecalciferol**

* Increases the concentration of plasma phosphate and plasma Calcium, by:

Clarification for point (1): “Vitamin D plays important roles in both bone absorption and bone deposition. The administration of extreme quantities of vitamin D causes absorption of bone. In the absence of vitamin D, the effect of PTH in causing bone absorption is greatly reduced. The mechanism of this action is a result of the effect of 1,25-dihydroxycholecalciferol in increasing Ca transport through cellular membranes.”

1. increasing bone resorption from what's **around** the texture of the bone, specifically speaking from around the synovial fluid. (same effect of PTH, yet PTH is more concerned with normalizing Ca levels in the blood). If resorption takes place at the texture, this would cause bone softening (pathalogical).
2. increasing Calcium and Phosphate absorption in the intestine
3. increasing Calcium and Phosphate Reabsorption in the Kidneys

* Notice the difference between the effect of PTH and Vit D on calcium and phosphate levels. VitD increases the concentration of both blood Calcium and Phosphate, unlike PTH which increases blood calcium yet decreases blood phosphate.
* PTH and VitD function **synergistically**. Why?
* Vitamin D and PTH aid each other in function; showing a synergistic effect.
While Vitmain D functions to mineralize bone (by increasing blood calcium and phosphate levels), PTH functions to regulate/normalize the calcium levels in the blood (bringing it back to its normal level).

**Endocrine Modulation**

* Pituitary gland (through prolactin and growth hormone), pancreas (through insulin) and parathyroids ,all help in the regulation of the production of1,25$(OH)\_{2}$-D by directly activating the enzyme that produces it (1α hydroxylase).
* low Calcium and low Phosphate levels, have direct and indirect effects on stimulating the activity of the enzyme 1α hydroxylase.

\*\* check figure 8.41

**Vitamin D deficiency**

-People with Vitamin D deficiency are more at risk of developing Heart problems, Diabetes and hypertension.
-White people have twice as much Vitamin D as Black people
-Vitamin D is lipid soluble. Therefore, teenagers with excess fat at their abdominal area, have insufficient amounts of Vitamin D, as it dissolves in this fat, instead of escaping to blood.
\*\*Causes of deficiency of 1,25 dihydroxycholecalciferol are found in table 7.5 in the slides

 **Functions of Calcium**

* Essential to maintain normal Sodium permeability in nerves
(more sodium outside)
* Required for protein secretion (Example: release Acetylcholine at nerve endings into synaptic cleft)
* Needed in Excitation-contraction coupling in muscles.
* Serves as intracellular signal for some hormones. (Example: the release of Ca from ER by the action of IP3 which is produced when a ligand binds a receptor in some pathways)
* Some enzymes don't function without Calcium.
Example: Diacylglycerol, which is also produced when ligand binds receptor ( it activates enzymes) and does not function without the presence of Calcium.
* Essential for normal blood clotting
\*Note: a substance known as EDTA is used to prevent blood clotting (anticoagulant) in tubes, since it absorbs Calcium in blood.

**Note:**
\*99% of Calcium in body is situated in bone
\*Adipose tissue contains less water than bone tissue. (bone contains only 9% water)

**Calcium is either:**
**1**. Diffusable: ionized or complexed to hydrogen bicarbonate
(ionized Calcium is the type that stimulates PTH)

**2**. Non-diffusable: bound to albumin or globulin

**Effect of blood PH on Ionised Calcium levels:**
\* In acidosis, the concentration of hydrogen in blood increases. These ions bind preferably to albumin than calcium ions. Therefore the concentration of ionized calcium in blood increases. (little Ca is bound to proteins)
While the opposite happens in alkalosis, where the hydrogen ion concentration decreases, and more ionized Calcium bind to albumin, & the ionized Calcium levels in blood decreases.

\*\* The following slides were covered in this lec:

* Figure 38-5
* Figure 36.9
* “Vit.D”
* Figure 8.41
* Table 7.5
* “Functions of Ca”
* Table 27-4
* Table 21-1
* Figure 9-32

**بالتوفيق للجميع...إدعولنا :)**

