◉Sheet ○Slides

Subject :	Vitamins
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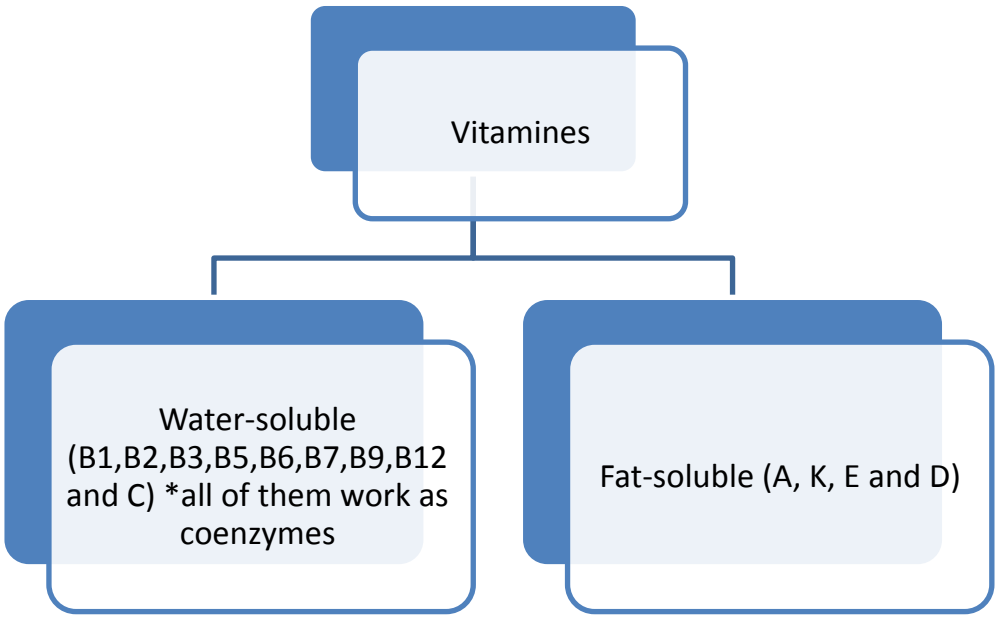
Number :	36(last one)

Vitamins

Vitamins are (1)***organic compounds*** that are(2) ***required in small amounts*** as a vital nutrient, and (3)***the body cannot synthesize them***.

The source of vitamins can be from the diet, or from the body itself (so *actually the body cannot synthesize them* --there are no specific pathways in the body to make vitamins, *but they can be synthesized in the body*, from irrelevant pathways and processes-like sunlight or microflora-).
*sometimes we can get the inactive form of the vitamin and activate it inside the body.

Classification:



Note: Fat soluble vitamins don't function as coenzymes, except for **Vitamin K**, which can work as a coenzyme.

Here you will find the **water soluble vitamins**. The doctor didn't say anything about them but they are mentioned in the slide.

Water-soluble vitamins

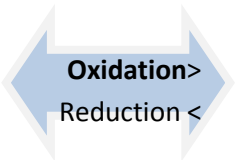
Vitamin	Coenzyme	Consequences of deficiency
Thiamine (B_1)	TPP	
Riboflavin (B_2)	FAD	Angular stomatitis (mouth lesions)
Nicotinic acid (niacin) (B_3)	NAD^+	
Pantothenic acid (B_5)	CoA	
Pyridoxine (B_6)	PLP	
Biotin (B_7)		
Folic acid (B_9)	TH4	Megaloblastic anemia
Cobalamin (B_{12})	5′-Deoxyadenosyl cobalamin	Megaloblastic anemia
Ascorbic acid (C)		Scurvy

Fat-soluble vitamins have long hydrocarbon chain to gain their lipophilicity, this also means that they can't move freely in the blood and they have to be coupled to proteins (transporters). Their ultimate storage site therefore will be the fat tissue. So people who go on severe diets eventually will face hypervitaminosis (less storageàhigher level) We'll talk about these 4 vitamins (***ADEK***) in details here.

Vitamin A

Is a group of chemically related molecules called **retinoids** (retinal, retinol, retinoic acid and β-carotene)

They involve *cis* and *trans* molecules



Oxidation

- Retinal and retinol are found in equilibrium (both the Oxidase and the reductase are present). The equilibrium is shifted to one of them when needed, but once the retinal is oxidized to retinoic acid it is

irreversible (no reductase present) ... that's why retinol and retinal have common functions different from retinoic acid (different func.)

- B-carotene is the **parent compound** that is broken from the middle in the intestinal mucosal cells, each segment is oxidized to give a retinal molecule. It's found in carrot, fruits and vegetables that have pigments (deep green, yellow, orange and red).

Mode of ingestion:

The absorption in the intestinal cells is either as **β-carotene** itself or as **retinol**. Retinol is usually coupled with a fatty acid. In the lumen, the bond breaks and retinol is freed. After entering the cell, it is re-coupled with a fatty acid again to produce retinyl-esters. B-carotene (after it's absorbed) is broken to yield two retinal molecules inside the cell, which are reduced back to retinol molecules, which are coupled to fatty acids to produce retinyl esters. From the intestine, these fat-soluble molecules reach the liver by ***chylomicrons***. In the liver they have two options: (1) storage in the liver or (2) coupled to Retinol binding protein (RBP) to reach other destinations (mainly the Retina of the eye).

*****The visual cycle:**

Retinal or Retinol (which reach the retina)àconverted to the active form (11-cis retinal) which is bound to opsin protein to form Rhodopsin (the visual pigment of the rod cells). When light hitsàdissociation of Rhodopsin and conversion of 11-cis retinal to all-trans retinal, this generates a nerve impulse that's transmitted to the brain. Now, all-trans retinal is reduced to all-trans retinol, esterified, isomerized to 11-cis retinol that is oxidized to 11-cis retinalàbind to opsin and the cycle continues.

*Retinal and Retinol therefore are responsible for **vision** and also **spermatogenesis**. And a high deficiency in vitamin A can lead to blindness.*

Retinoic acid is responsible for the maturation of the epithelial tissue and growth of cells. If it's needed, it also binds to RBP in the plasma and goes to epithelial tissues where it is inserted inside the cell by leaving the plasma RBP to bind with **cellular** RBP, and in the cell itself it enters the nucleus to work as a **transcription factor**. Retinoic acid works as a

RESET for the normal function of the keratin gene (Vitamin A is a good therapy if there's a disturbance in keratin (over/under production of keratin), acne or psoriasis).

Look at this example: a rat is given only retinoic acid (it cannot be converted to retinal and retinol), this rat was infertile and blind.

Deficiency

*Mild deficiency in vitamin A: night blindness (العشى) (elevation of vision threshold, so if weak lightàno vision). And it includes cell injury.
*Moderate deficiency: fibrous tissue, **irreversible** loss for certain cell
*Prolonged and severe deficiency: xerophthalmia, scar formation in the eye and may lead to early childhood blindness. (This thing is not rare- 0.5 million child/year develop xerophthalmia due to severe Vit.A deficiency).
*Acne and Psoriasis.

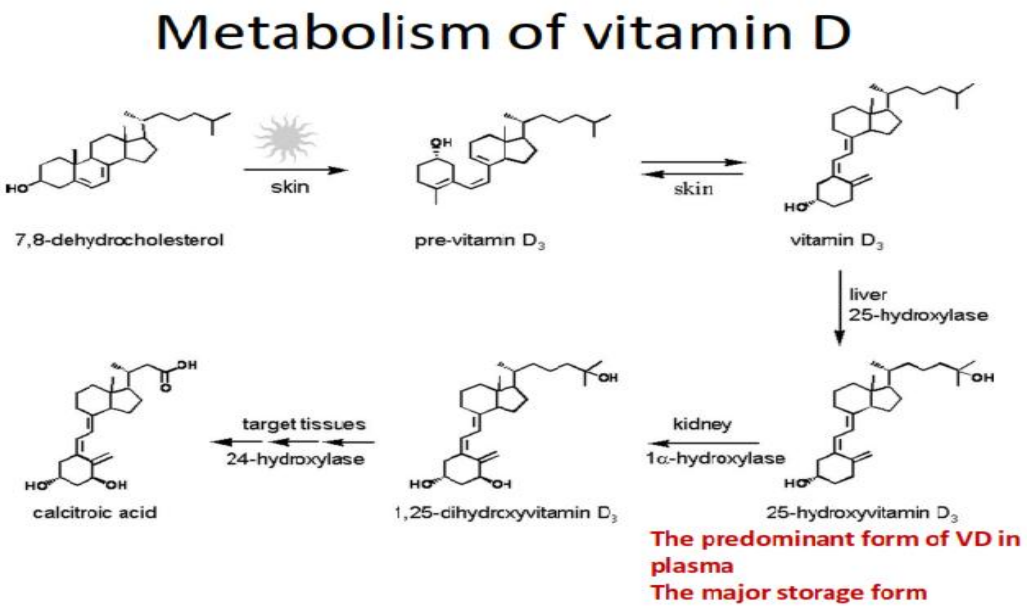
Toxicity

Excess of vitamin A: **hypervitaminosis A** which mainly affects the skin, liver and the nervous tissue.
This situation is not a big issue and **can be recovered**, but it's a problem if it's in a pregnant woman, because it can lead to **teratogenesis**.

Vitamin D

Is a group of molecules (some active and others not)

Its main function is to maintain adequate plasma level of calcium by:
1- increase the absorption of calcium in the **intestine**
2- decrease the secretion and increase the re-absorption in the **kidney**
3- stimulate **bone** resorption from the bones when needed.



Vitamin D3 (cholecalciferol) is made in the **skin**, from precursor (7-dehydrocholesterol) by the action of sun light or UV light.

If we don't get exposed to the sun, we can take it from supplements, plants ergocalciferols, animal sources (cholecalciferol)...

Vitamin D3 goes to the liver where it is converted to 25-hydroxyvitamin D3 (25-hydroxycholecalciferol) by **25-hydroxylase**, then it leaves to the kidney where its converted to *the active form*, 1,25-dihydroxyvitamin D3 (1,25-dihydroxycholecalciferol) by the enzyme **1- hydroxylase**.
*Note: if we take a blood sample, the form with highest concentration in the blood is 25-hydroxycholecalciferol (25-hydroxyvitamin D3).
Since the last enzyme produces the active form of vitamin D, this enzyme must be ***highly regulated (***turn between active and inactive forms) by (Ca+2, phosphate and parathyroid hormone)
Note: high calciumàlow phosphate and vice versa.

- When do we give vitamin D?
  1-Nutritional rickets (due to deficiency, result in massive bone resorption, bone now can't withstand the weightàfractures)
  2- Renal rickets (renal failure and excess loss of Vit.D)
  3- hypoparathyroidism

Keep in mind that not all the deficiency of vitamin D3 can lead to (symptomatic) problems but the results can be disastrous in some cases! And this field is an open space for research.

Toxicity:

*High doses (100,000 IU for weeks or months) can cause loss of appetite, nausea, thirst, and stupor.

* Enhanced calcium absorption and bone resorption results in hypercalcemia, which can lead to deposition of calcium in many organs, particularly the arteries and kidneys.

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Dietary sources of vitamin K

Vitamin K

It's a group of compounds that contains (Phylloquinone; K1 (plants)/ Menaquinone; K2 (bacteria)/ and Menadione; (synthetic) it leads to clotting by working as a coenzyme for the enzyme that converts Glutamate residues found on the surface of clotting factors (II,VII,IX and X) to Gamma-carboxyglutamate. The addition of the negative carboxylic group will attract calcium and recruit platelets. Platelets secret substances to convert pro-thrombin to thrombin which in turn converts fibronegen to fibrin. Fibrin is responsible for the clot formation.

Deficiency

The body cannot synthesize vitamin K, but it can be synthesized in the body by the **intestinal normal flora**. So the deficiency happens when the patient is given a broad spectrum antibiotic for a long time. Also it happens in newborns, because they are born sterile and the normal flora hasn't resided in the gut yet.

Breast feeders give their babies vitamin K but still not enough (20%), so sometimes vitamin k is given as a prophylactic shot.

Toxicity

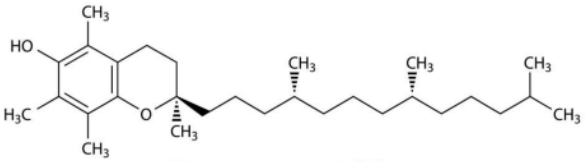
high levels of vitamin K affect the **liver** (break down of hepatocytes) causing jaundice and **RBCs** causing anemia.

Vitamin E

It's an ***antioxidant*** that has a ring structure (important for its function, because the free electron will keep rolling in the ring throughout all the resonance states possible).

All the antioxidants (unless they have a special pathway) must have a ring structure

Vitamin E is a group of molecules called **tocopherols** (type alpha is the **most active** one).



Alpha-tocopherol (E)

It has a long hydrocarbon chain which is inserted inside the membrane (hydrophobic) and the ring remains outside the cell for protection (the ring receives electrons from free radicals, protecting membrane fatty acids from damage).After accepting the electrons it passes them to vitamin C which passes them to glutathione, thus converting 2GSHàGSSG.

Deficiency in vitamin E is **rare**, and it's found in premature infants.
Vitamin E may be transmissible (not fully clear) from the mother to her baby during breast feeding, that's why premature babies (not breastfed yet) can have vitamin E deficiency

اللهم إنا نستودعك ما حفظنا و ما قرأنا و ما تعلّمنا
فردّه لنا عند حاجتنا إليه يا رب العالمين