

Vitamins

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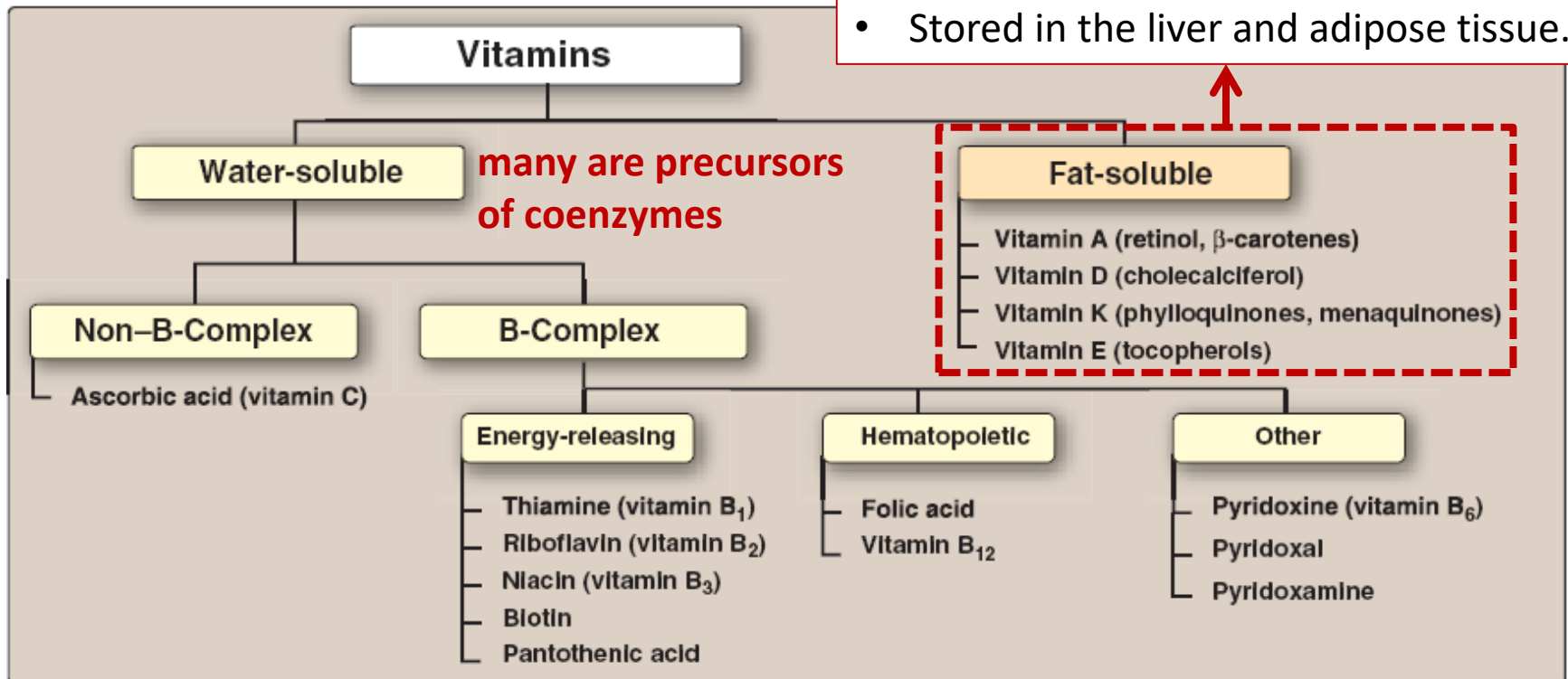
DDS, MSc, PhD

What are vitamins?

- They are chemically unrelated organic compounds that are required by an organism in tiny amounts as a vital nutrient.
- They cannot be synthesized in adequate quantities by humans and, therefore, must be supplied by the diet.
- They are compounds that are convertible to the active form of the vitamin in the body.

Classification

- Released, absorbed, and transported with the fat of the diet.
- Not readily excreted in the urine
- Stored in the liver and adipose tissue.



Water-soluble vitamins

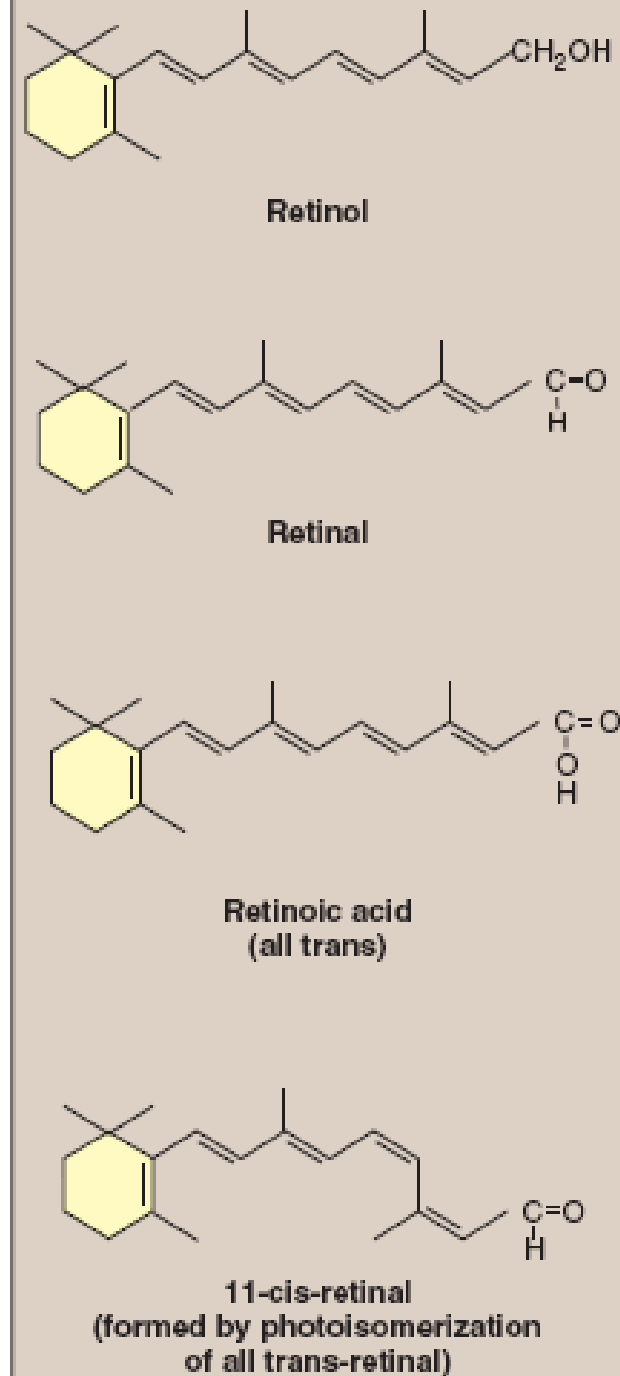
Vitamin	Coenzyme	Consequences of deficiency
Thiamine (B ₁)	TPP	
Riboflavin (B ₂)	FAD	Angular stomatitis (mouth lesions)
Nicotinic acid (niacin) (B ₃)	NAD ⁺	
Pantothenic acid (B ₅)	CoA	
Pyridoxine (B ₆)	PLP	
Biotin (B ₇)		
Folic acid (B ₉)	TH ₄	Megaloblastic anemia
Cobalamin (B ₁₂)	5'-Deoxyadenosyl cobalamin	Megaloblastic anemia
Ascorbic acid (C)		Scurvy

Fat-soluble vitamins

Vitamin	Main function	Deficiency
A	Roles in vision, growth, reproduction	Night blindness, cornea damage
D	Regulation of Ca^{+2} & phosphate metabolism	Rickets (children), Osteomalacia (adults)
E	Antioxidant	RBCs fragility
K	Blood coagulation	Subdermal hemorrhaging

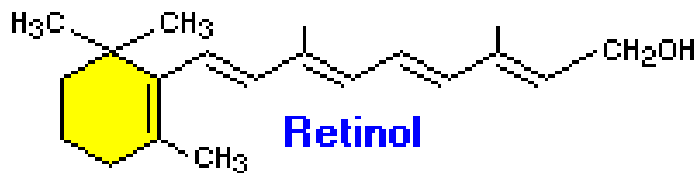
Vitamin A

- Vitamin A: a collective term for several related biologically active molecules.
- The retinoids, a family of molecules that are related to retinol (vitamin A), are essential for vision, reproduction, growth, and maintenance of epithelial tissues.
- Retinoic acid, derived from oxidation of dietary retinol, mediates most of the actions of the retinoids, except for vision, which depends on retinal, the aldehyde derivative of retinol.

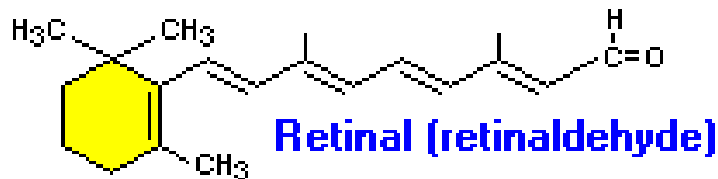


Forms of vitamin A

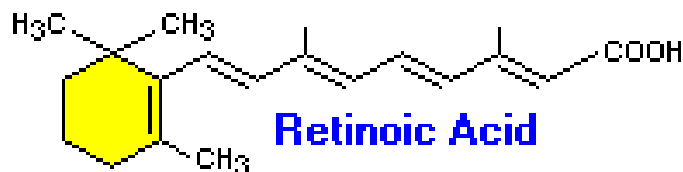
Retinol: A primary alcohol containing a ring with an unsaturated side chain; found in animal tissues as a retinyl ester with long-chain FAs.



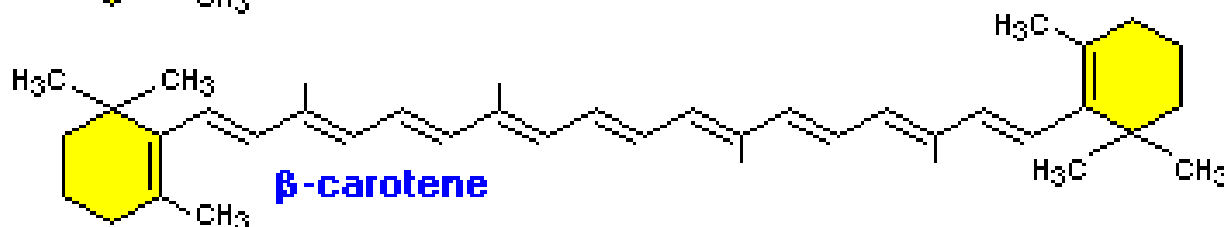
- **Retinal:** An aldehyde ; derived from the oxidation of retinol; Retinal and retinol can be interconverted.



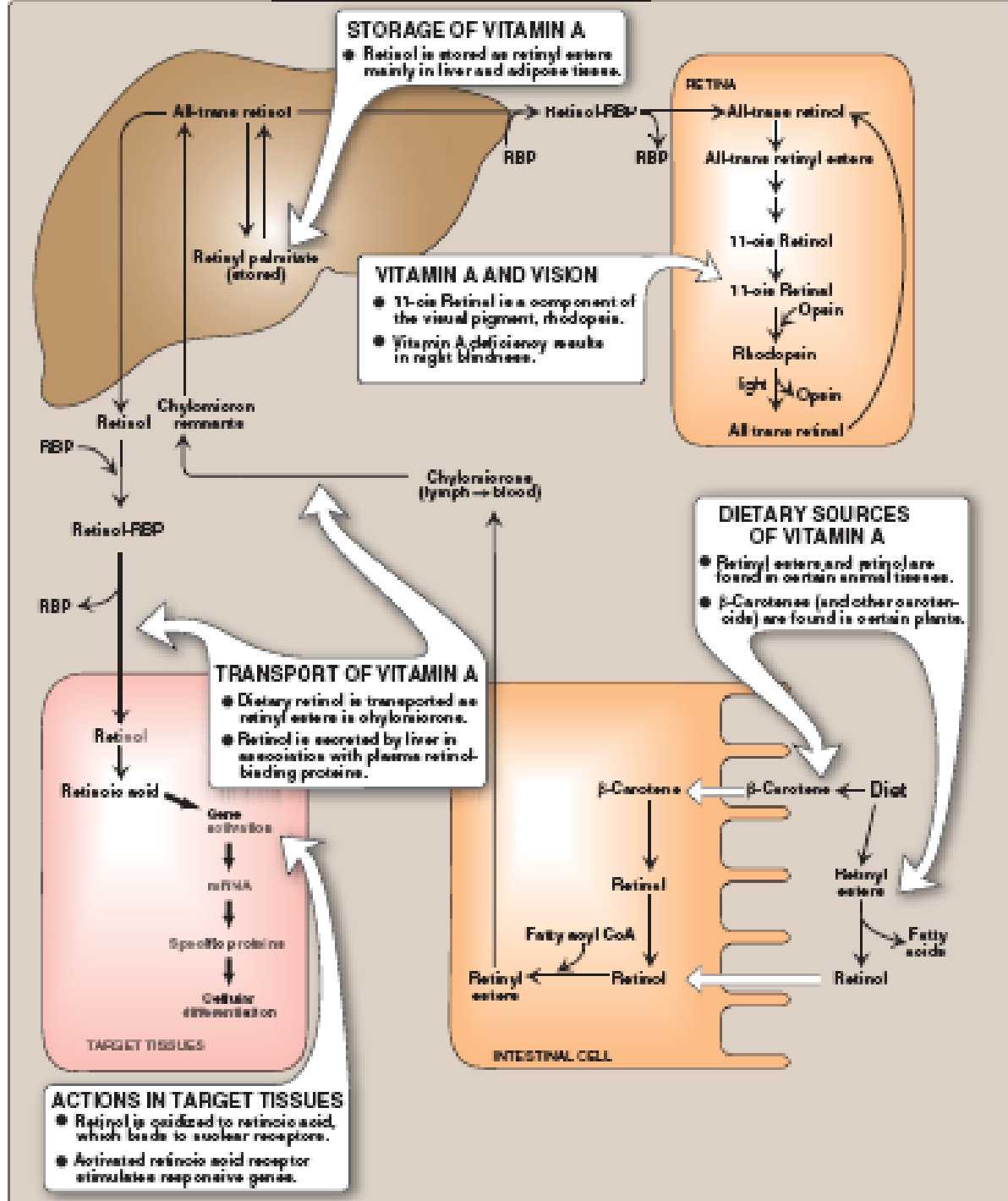
- **Retinoic acid:** An acid derived from the oxidation of retinal; cannot be reduced into retinal or retinol.



- **β-Carotene:** Cleaved in the intestine to yield two molecules of retinal.

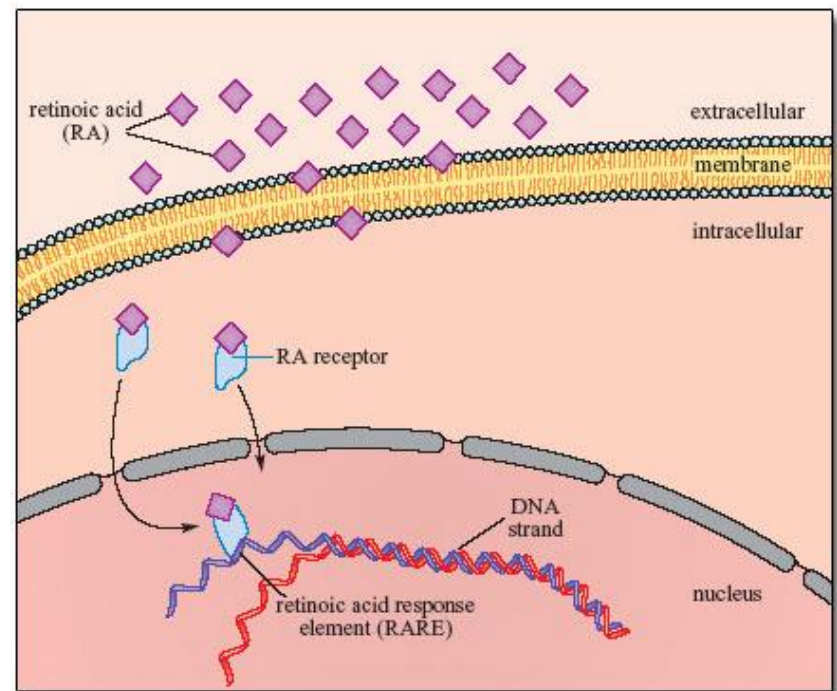


Cellular RBP →
nuclear receptors
(steroids), RNA,
proteins (keratin
expression)



Mechanism of action of vitamin A

- Retinol is oxidized to retinoic acid, which binds to a specific nuclear receptor.
- The complex regulates gene expression (RNA synthesis)
 - Retinoids control the expression of keratin in most epithelial tissues of the body.

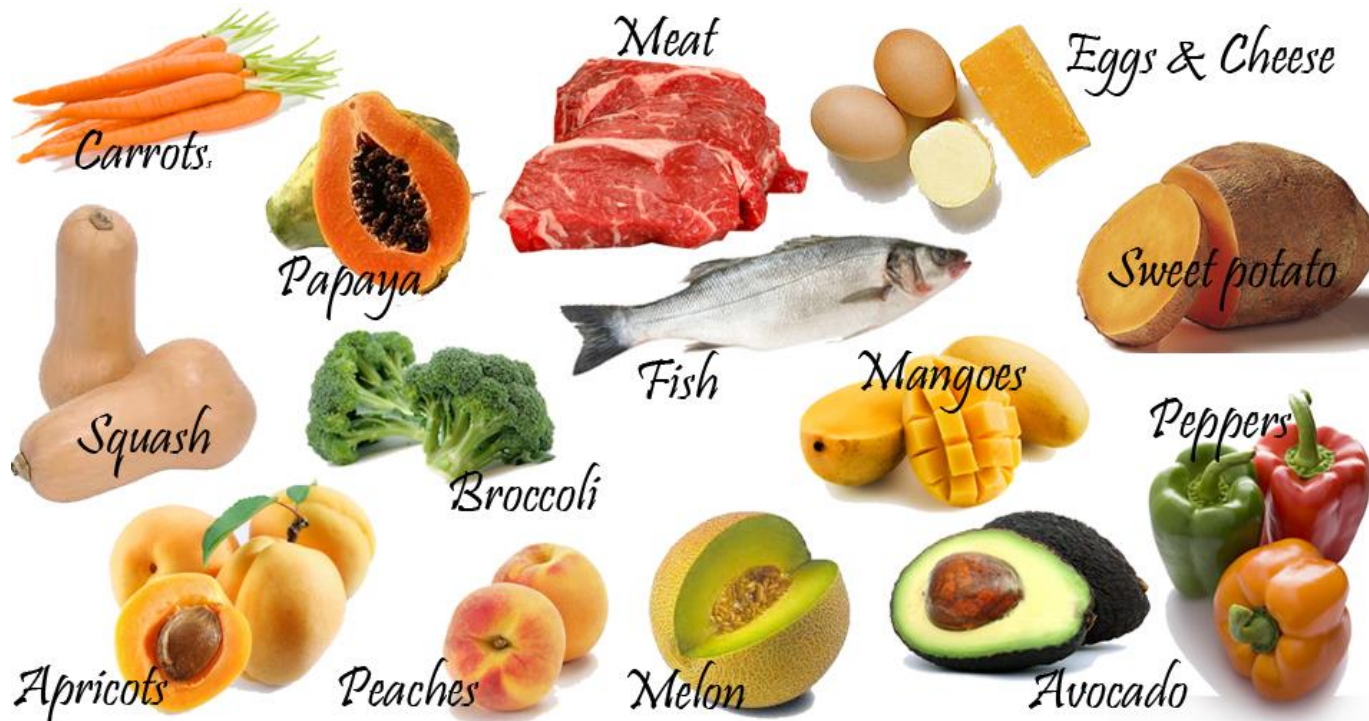


Functions of vitamin A

- Visual cycle: 11-cis retinal specifically binds the protein opsin (rhodopsin)
- Growth (retinoic acid): Vitamin A deficiency results in a decreased (growth rate & bone development) in children
- Reproduction: Retinol and retinal (not retinoic acid) are essential for spermatogenesis in the male and preventing fetal resorption in the female
- Maintenance of epithelial cells (retinoic acid): Vitamin A is essential for normal differentiation of epithelial tissues & mucus secretion
- Animals given vitamin A only as retinoic acid from birth are blind and sterile

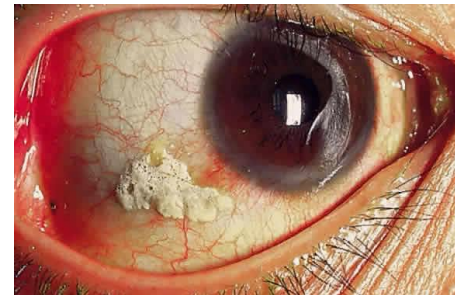
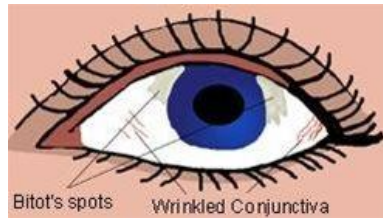
Sources of vitamin A

- Liver, kidney, cream, butter, and egg yolk are good sources of preformed vitamin A.
- Yellow and dark green vegetables and fruits are good dietary sources of the carotenes.



Clinical indications

- Dietary deficiency: mild (night blindness); prolonged (irreversible loss for some visual cells); severe (xerophthalmia)
 - Xerophthalmia: ulceration & dryness of conjunctiva & cornea, followed by scar & blindness



- Acne and psoriasis: effectively treated with retinoic acid



Toxicity of retinoids

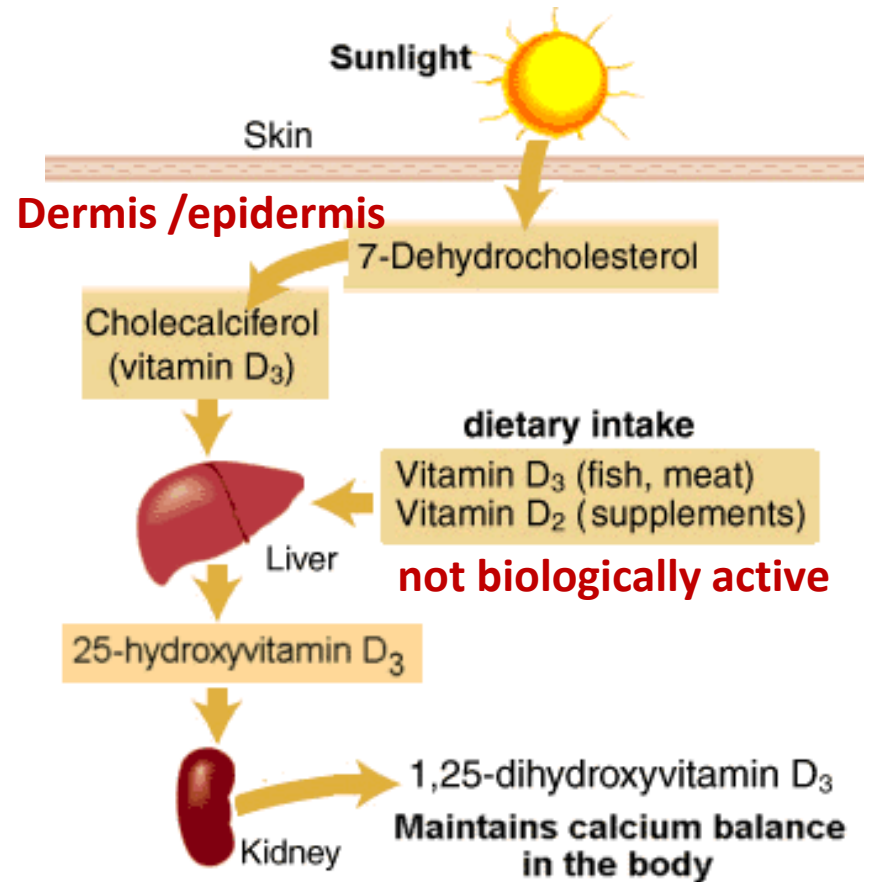
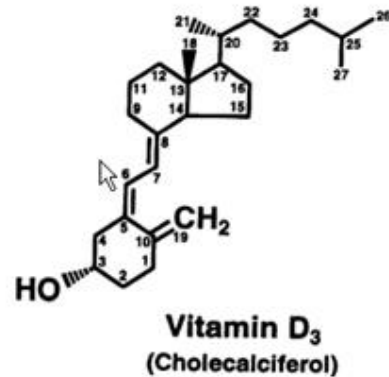
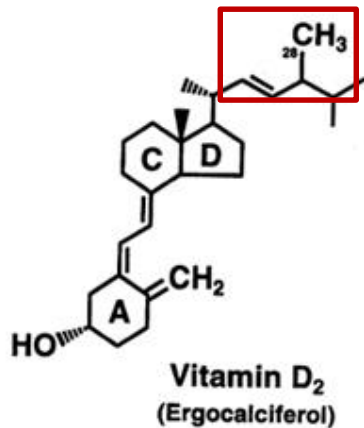


- Excessive intake → hypervitaminosis A (toxic)
- Early signs of chronic hypervitaminosis A
 - Skin: becomes dry (due to a decrease in keratin synthesis)
 - Liver: becomes enlarged and can become cirrhotic
 - Nervous system: a rise in intracranial pressure
- Pregnant women should not ingest excessive quantities of vitamin A (teratogenic).

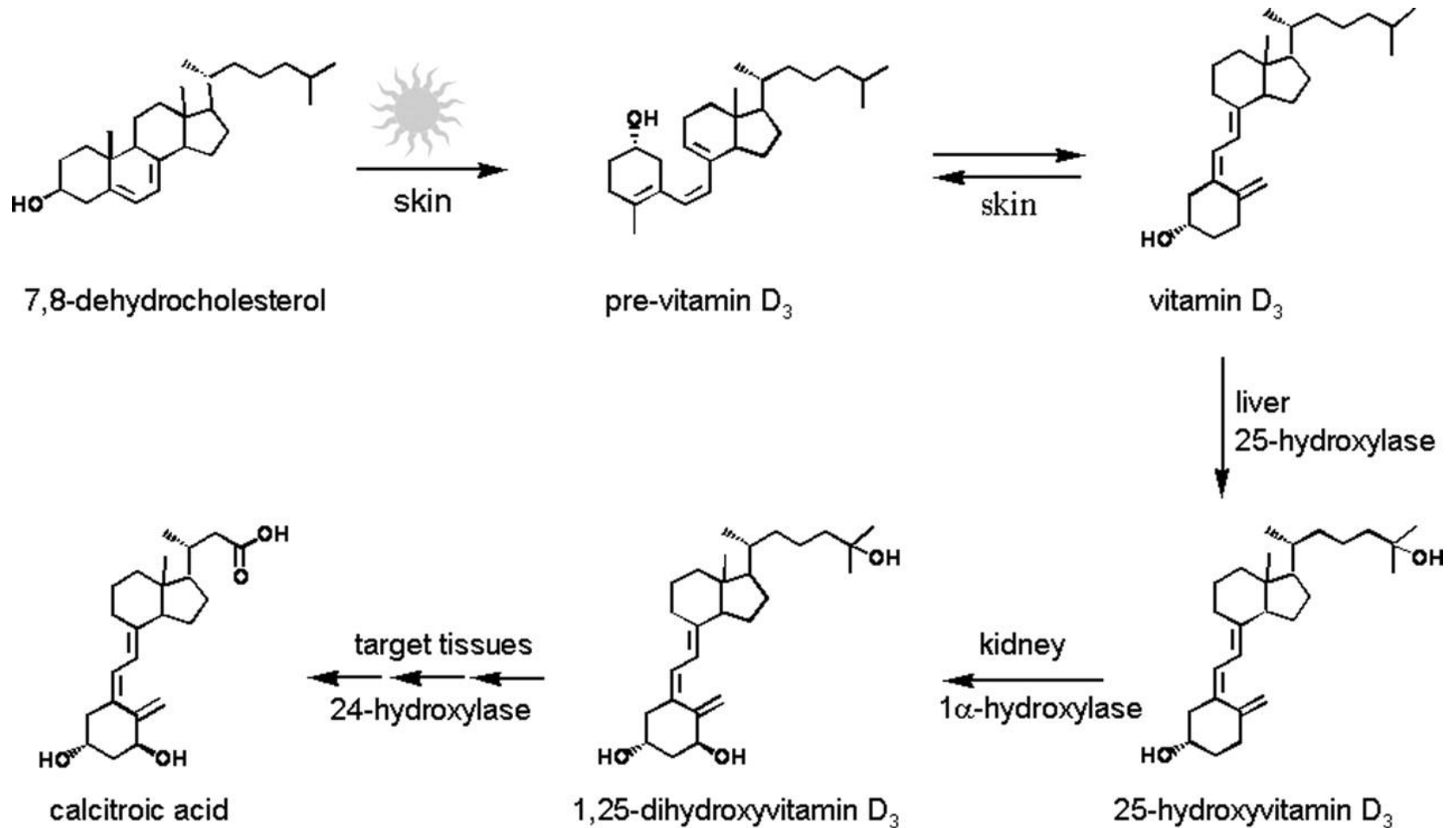
Vitamin D

- The D vitamins are a group of sterols that have a hormone-like function.
- The active molecule, 1,25-dihydroxycholecalciferol (1,25-diOH-D3), binds to intracellular nuclear receptors.
- The most prominent actions of 1,25-diOH-D3 are to regulate the plasma levels of calcium and phosphorus.

Sources of vitamin D



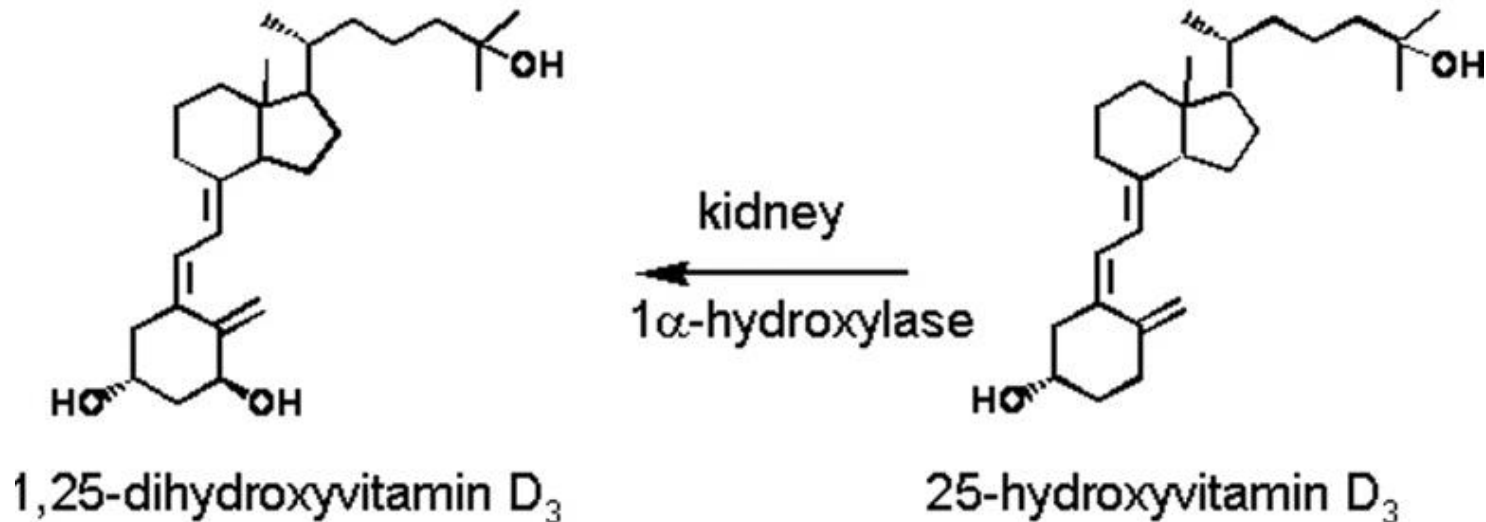
Metabolism of vitamin D



The predominant form of VD in plasma
The major storage form

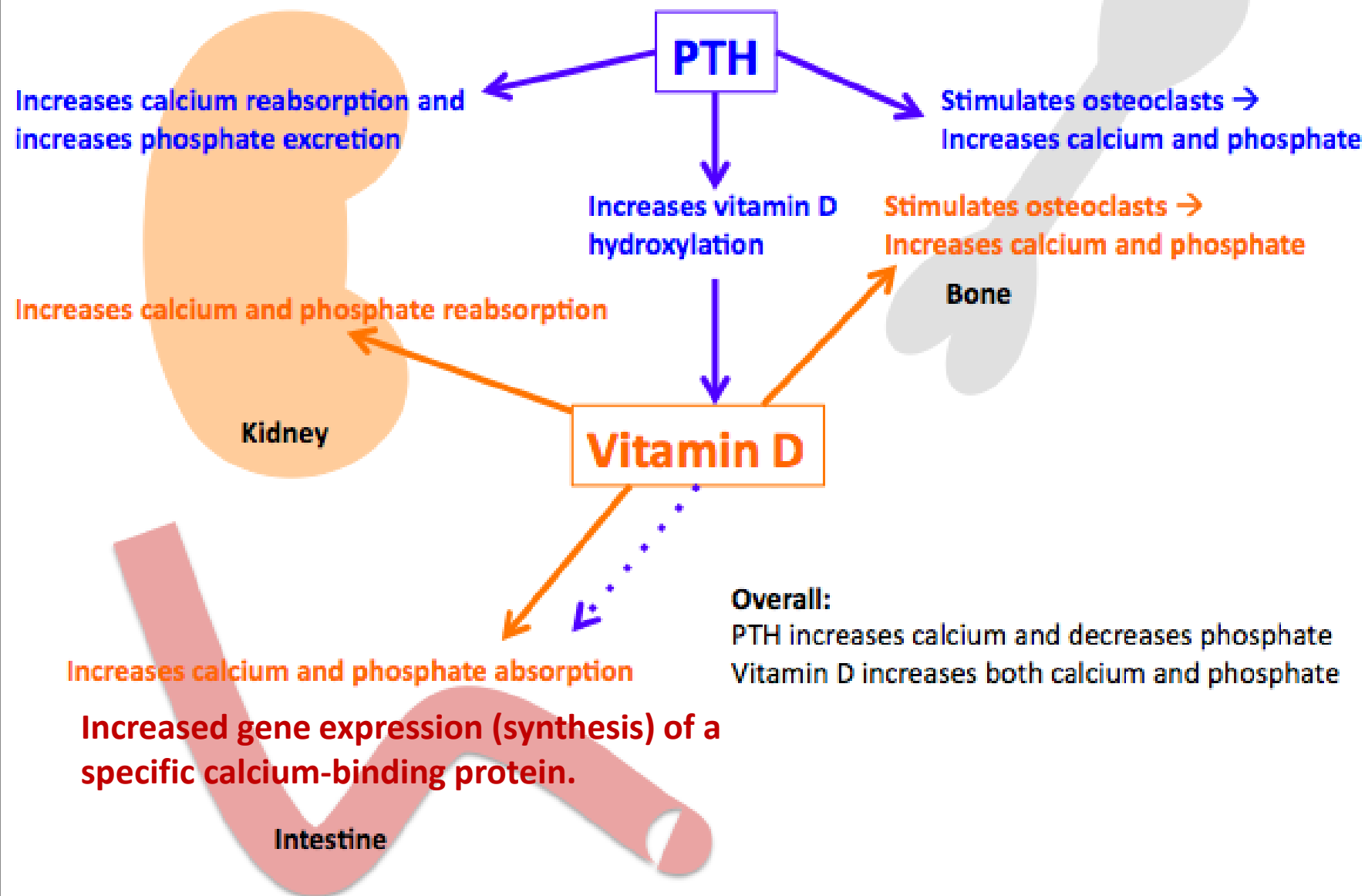
Regulation of 1-hydroxylase

- Increased directly by low plasma phosphate
- Increased indirectly by low plasma calcium (PTH)
- Decreased by excess 1,25-diOH-D₃, the product of the reaction

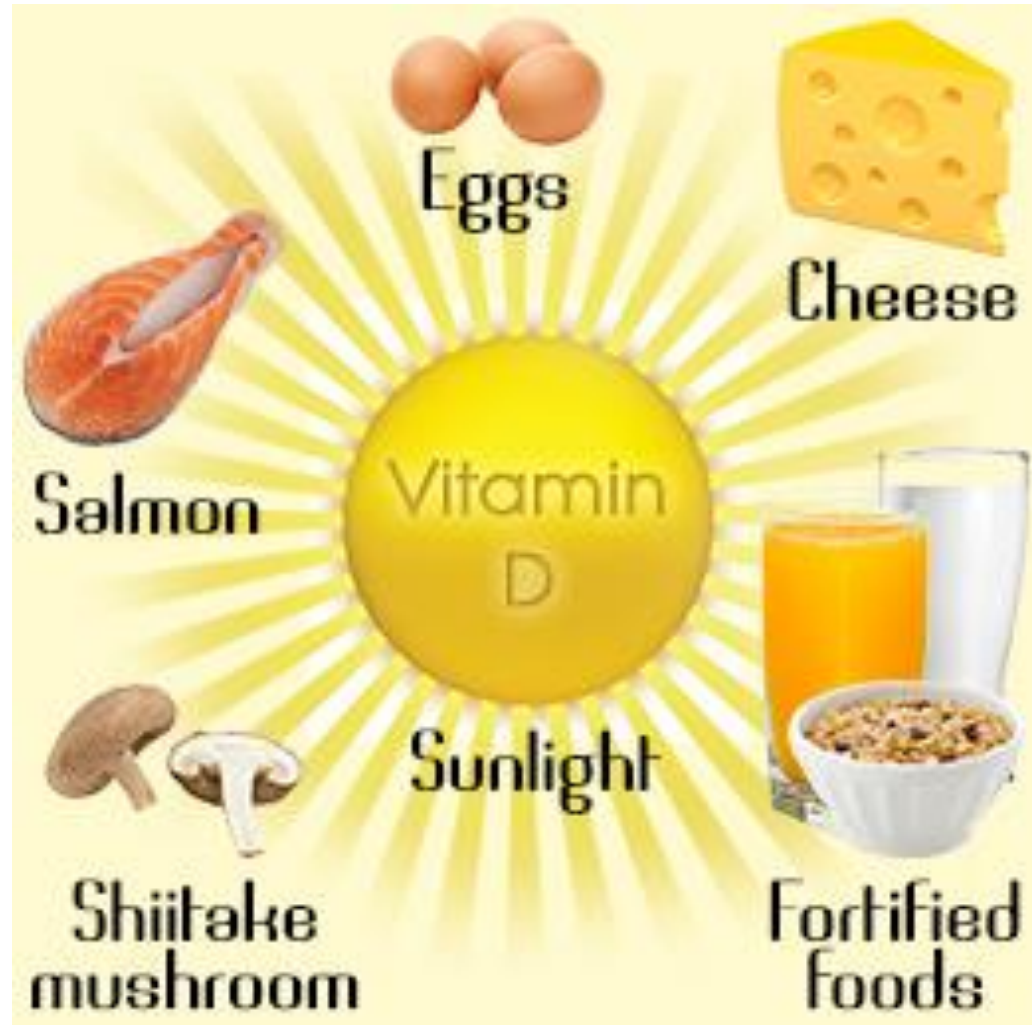


Functions of vitamin D

- The overall function of 1,25-diOH-D3 is to maintain adequate plasma levels of calcium by:
 - increasing uptake of calcium by the intestine
 - minimizing loss of calcium by the kidney
 - stimulating resorption of bone when necessary



Sources of vitamin D



Clinical indications

- Nutritional rickets: rickets in children & osteomalacia in adults (a result of net demineralization of bone)
- Renal rickets (renal osteodystrophy): chronic renal failure
- Hypoparathyroidism

Normal anatomy



Rickets

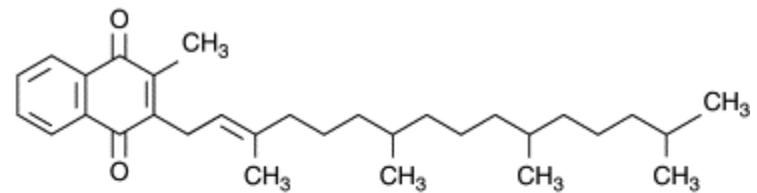


Toxicity of vitamin D

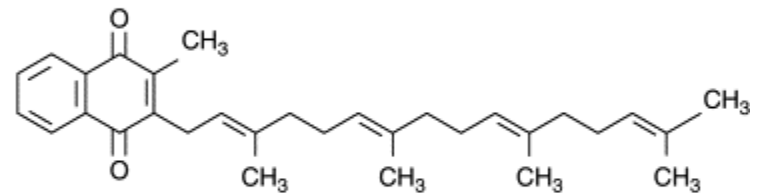
- High doses (100,000 IU for weeks or months) can cause loss of appetite, nausea, thirst, and stupor.
- Enhanced calcium absorption and bone resorption results in hypercalcemia, which can lead to deposition of calcium in many organs, particularly the arteries and kidneys.

Vitamin K

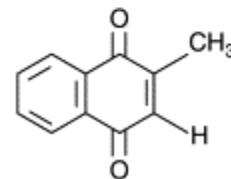
- Phylloquinone or vitamin K₁ (plants)
- Menaquinone or vitamin K₂ (intestinal bacterial flora)
- Menadione (synthetic)



Phylloquinone (vitamin K₁)



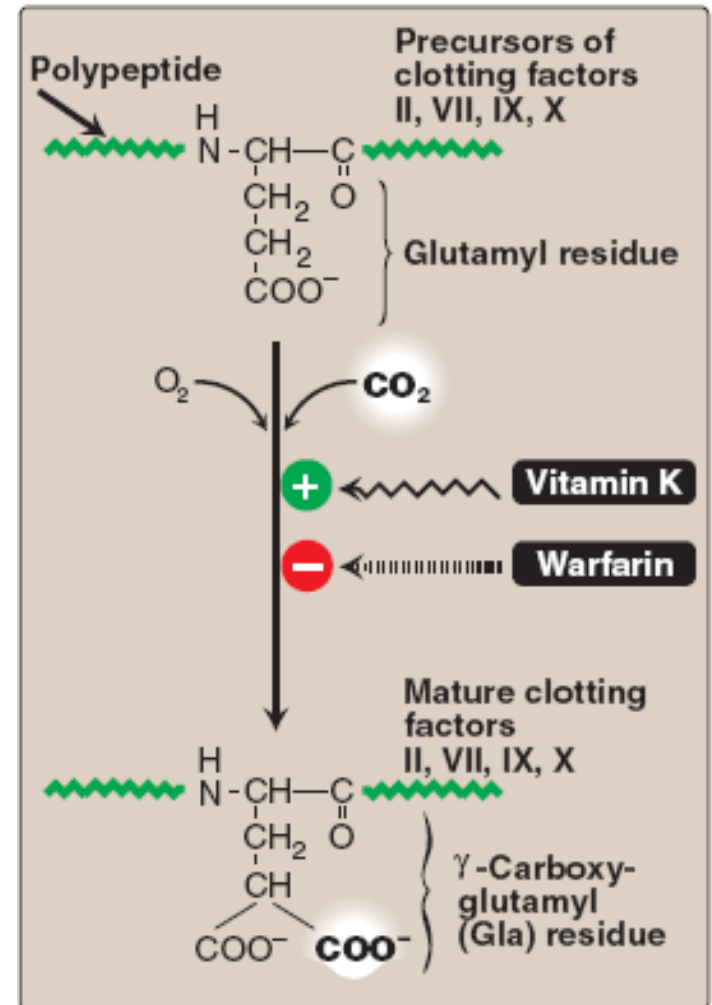
Menaquinone-4 (vitamin K₂)



Menadione (vitamin K₃)

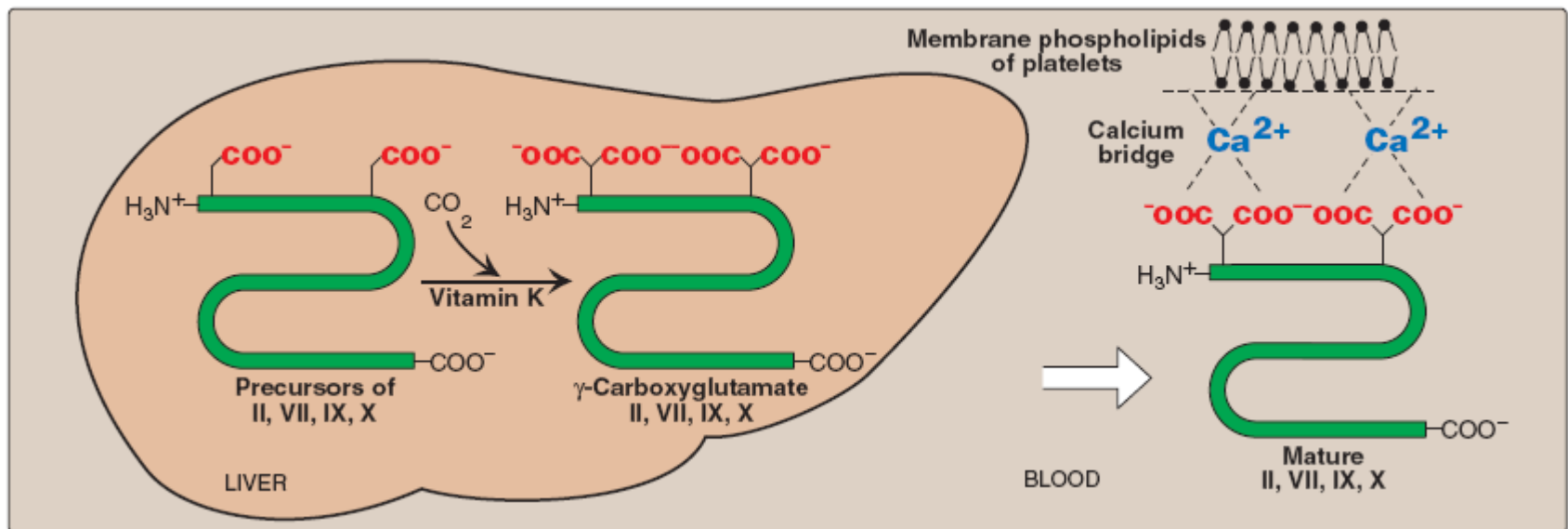
Functions of vitamin K

- The principal role of vitamin K is in the posttranslational modification of blood clotting factors (prothrombin and blood clotting factors II, VII, IX, and X)
- How? It serves as a coenzyme in the carboxylation of certain glutamic acid residues present in these proteins.



So what?!!

- The carboxylated glutamate can chelate Ca^{2+}
- The prothrombin–calcium complex can then bind to phospholipids essential for blood clotting on the surface of platelets.
- Attachment to the platelet increases the rate of proteolytic conversion of prothrombin to thrombin.



Dietary sources of vitamin K

*Vitamin **K** Rich Foods*



Avocado



Green Apples



Green Grapes



Honeydew Melon



Kiwi



Limes



Green Pears



Artichokes



Arugula



Asparagus



Broccoli



Broccoli Rabe



Brussels Sprouts



Napa Cabbage



Green Beans



Cabbage



Celery



Cucumber



Belgian Endive



Kale

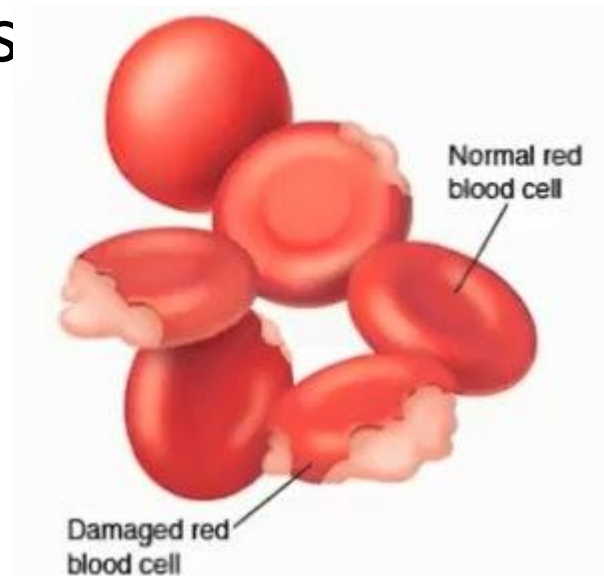
Deficiency of vitamin K

- Rare due to intestinal bacterial (antibiotics!!)
- Newborns have sterile intestines and human milk can provides only about one fifth of the daily requirement for vitamin K.
- It is recommended that newborns receive a single intramuscular dose of vitamin K as prophylaxis against hemorrhagic disease.



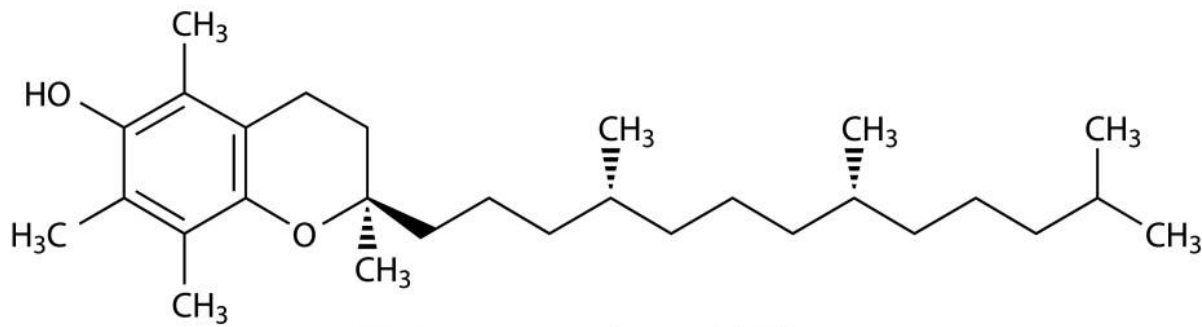
Toxicity of vitamin K

- Prolonged administration of large doses of synthetic vitamin K (menadione) can produce hemolytic anemia and jaundice in the infant, due to toxic effects on the membrane of red blood cells



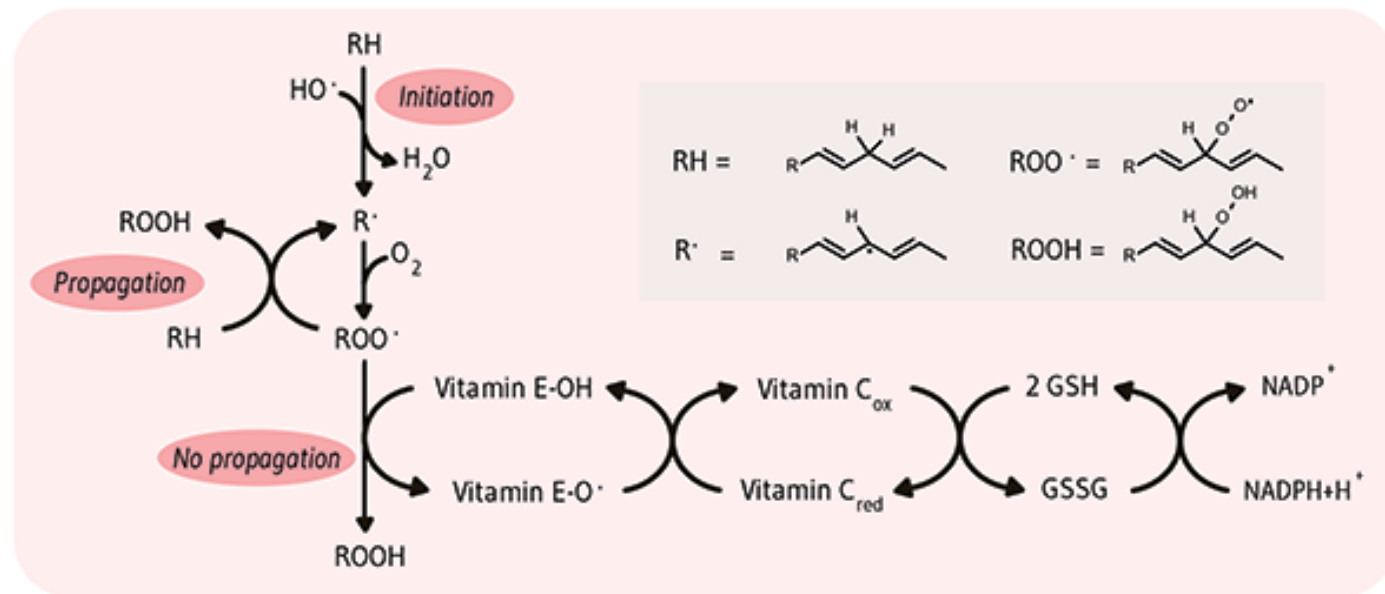
Vitamin E

- The E vitamins consist of eight naturally occurring tocopherols, of which α -tocopherol is the most active.
- The primary function of vitamin E is as an antioxidant in prevention of the nonenzymic oxidation of cell components.
 - Oxidation of polyunsaturated fatty acids by molecular oxygen and free radicals.



Alpha-tocopherol (E)

Mechanism of action of vitamin E



The peroxidation of unsaturated lipids leads to the formation of lipid peroxy radicals (ROO^\bullet), which easily diffuse in biological systems. Peroxyl radicals react 1,000 times faster with α -tocopherol than with unsaturated lipids (RH). The hydroxyl group in the chromanol head of α -tocopherol can donate hydrogen to scavenge lipid peroxy radicals, which halts their propagation in membranes and circulating lipoproteins. The presence of other antioxidants, such as vitamin C (ascorbate), is required to regenerate the antioxidant capacity of α -tocopherol. *GSH*, oxidized glutathione; *GSSH*, reduced glutathione; *NADP*, nicotinamide adenine diphosphate; *NADPH*, reduced *NADP*; *RH*, unsaturated lipid; *R[•]*, lipid (carbon-centered) radical; *ROO[•]*, lipid peroxy radical; *ROOH*, hydroperoxide; *Vitamin E-OH*, α -tocopherol (reduced form); *Vitamin E-O[•]*, tocopheroxyl radical (oxidized form); *Vitamin C_{ox}*, dehydroascorbate (oxidized vitamin C); *Vitamin C_{red}*, ascorbate (reduced vitamin C).

Deficiency of vitamin E

- Almost entirely restricted to premature infants.
- In adults, it is usually associated with defective lipid absorption or transport.
- Signs: sensitivity of erythrocytes to peroxide, and the appearance of abnormal cellular membranes.