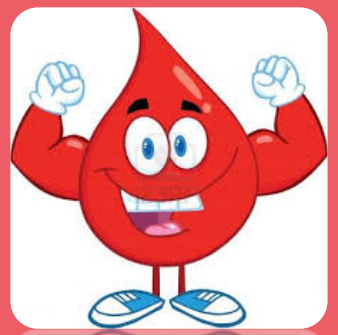
Lecture 4

Biochemistry of Vitamin K



The Objectives

- Types and chemistry of vitamin K
- Sources and daily requirements
- Functions
- Synthesis of γ-carboxyglutamate in:
  - Prothrombin and blood clotting factors
  - Osteocalcin
  - Interaction of prothrombin with platelets
- Deficiency and disorders

Red = Import-ant

Blue = explain

Green = addition notes

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Mind Map

- *Vitamin K*
  - *Types and Chemistry*
    - Vitamin K_1 (Phylloquinone)
    - Vitamin K_2 (Menaquinone)
    - Vitamin K_3 (Menadione)
  - *Sources of Vitamin K*
    - Phylloquinone: Green leafy vegetables (in plant)
    - Menaquinone: Intestinal bacteria
    - Menadione: synthetic form
  - *Functions of Vitamin K*
    - Coenzyme for the synthesis of prothrombin and blood clotting factors in the liver
  - *Analogs of Vitamin K*
  - Synthesis of g-carboxyglutamate in osteocalcin
  - *Deficiency of Vitamin K- Causes*
  - *Clinical manifestations of the deficiency*

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Types and source of Vitamin K	*RDA for Vitamin K* (mg/day)
Vitamin K1 (Phylloquinone) : Green leafy vegetables **Vitamin K2 (Menaquinone):** Intestinal bacteria (Intestinal bacterial synthesis meets the daily requirement of Vitamin K even without dietary supplement) Vitamin K3 (Menadione): synthetic form	**Infant (0-1 year):** 2-2.5 **Children (1-8):** 30-55 **Men (19+): 120** **Women (19+): 90** **Pregnancy / lactation:** 90 / 90 **UL:** Not established **because there is no enough studies to establish UL** New edition of Lippincott's they Write AI (Adequate intake)

NO NEED TO MEMORIZE IT

Functions of Vitamin K

- Coenzyme for the synthesis of prothrombin and blood clotting factors in the liver
  - Prothrombin (clotting factor II) and clotting factors are protein in nature
  - Synthesis of **prothrombin and clotting factors VII, IX, X** require **carboxylation** of their glutamic acid (Glu)
  - **Mature prothrombin** and clotting factors contain γ-carboxyglutamate (Gla) after carboxylation reaction
  - **Vitamin K is essential for the carboxylase enzyme involved**
  - Dihydroquinone **(= Hydroquinone)** form of vitamin K is essential for this reaction

1) Glutamate is converted to γ-carboxyglutamate by Carboxylase enzyme .

2) Carboxylase enzyme takes (OH) group from Vit.K hydrquinone(and will convert point (1))

3)Vit.k hydrqunone after Decarboxylation will become Vit.k epoxide .

4) we need the reductase enzyme to make vit.k hydrquinone (the reduced or active form).

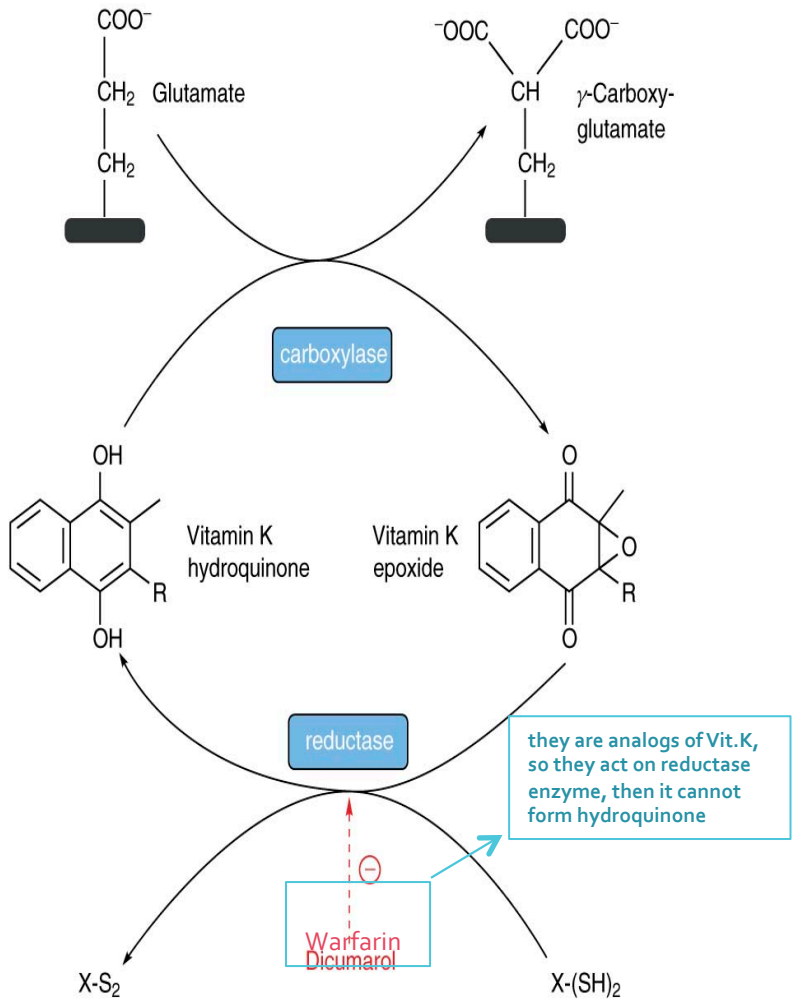

Figure 28.7. Function of Vitamin K.

Analogs of Vitamin K

- Anticoagulant drugs (warfarin and dicoumarol) are structural analogs of vitamin K
- They inhibit the activation of vitamin K to hydroquinone form
- Hence prothrombin and clotting factors are not carboxylated
- Blood coagulation time increases upon injury

{ structural analogs: is a compound having a structure similar to that of another one, but differing from it in respect of a certain component } that's mean Warfarin & dicoumarol are similar to Vit.K

Functions of Vitamin K –Prothrombin – platelets interaction

- Carboxylated prothrombin contains two carboxylate groups (COO^-)
- These groups bind to Ca^{2+} forming prothrombin-calcium complex
- The complex then binds to phosholipids on the surface of platelets (important for blood clotting)
- Converting prothrombin to thrombin and clot formation

Next slide :")

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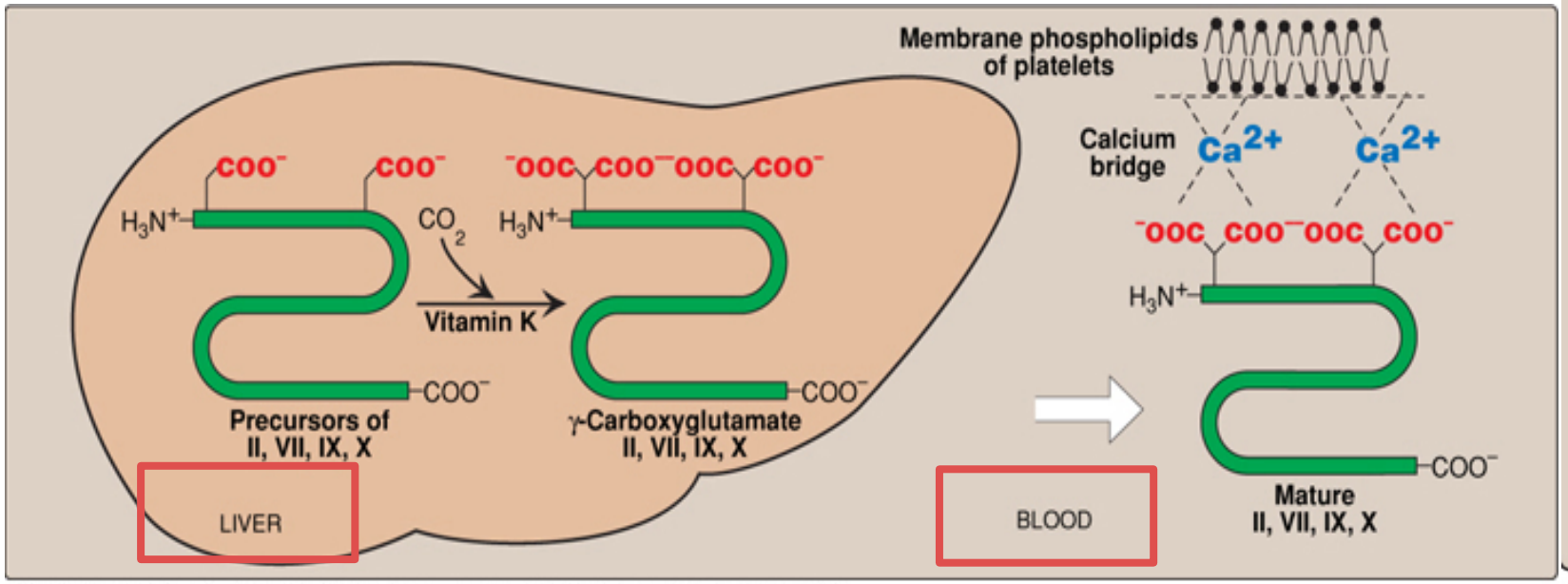
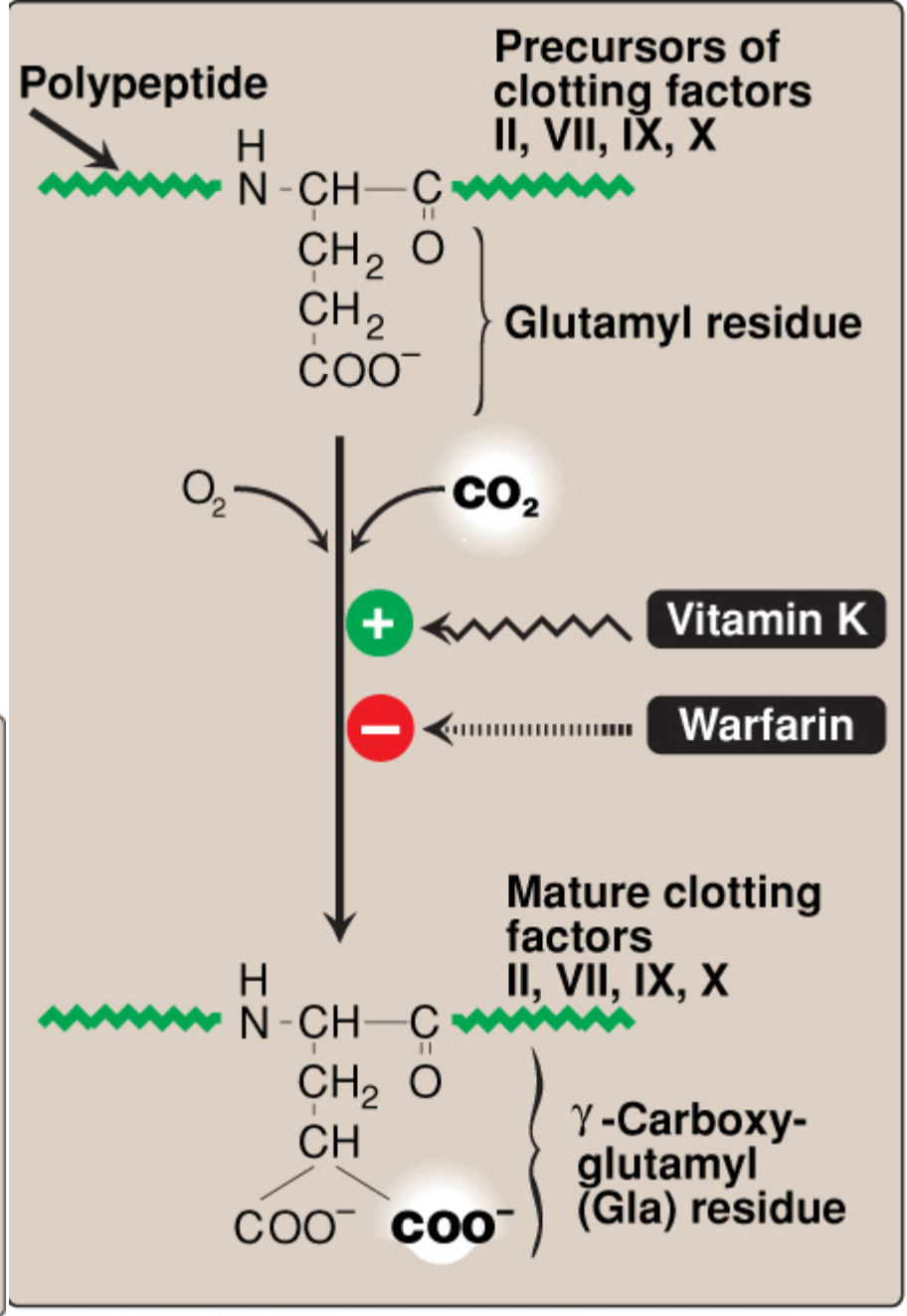
Prothrombin – platelet interaction

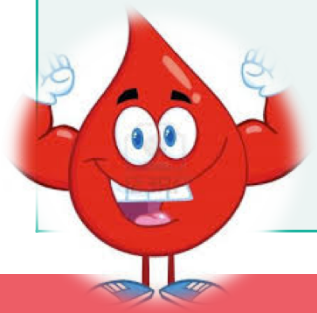




Functions of Vitamin K in other proteins

- Synthesis of γ-carboxyglutamate in osteocalcin
  - Osteocalcin is a bone protein
  - May have a role in bone formation and mineralization
  - γ-carboxyglutamate is required for its binding to hydroxyapatite (a mineral) in the bone
  - The function of bone osteocalcin is unclear

osteocalcin synthesized by osteoblasts (bone forming cells), In patients with osteoporosis circulating osteocalcin is undercarboxylated.



Deficiency of Vitamin K- Causes

- Deficiencies are rare: it is synthesized by the intestinal bacteria
- Malabsorption of lipids due to obstructive jaundice leads to vitamin K deficiency (Vit.K lipid soluble)
- Deficiency most common in newborn infants
  - Newborns lack intestinal flora
  - Human milk cannot provide enough vitamin K
  - Supplements are given by injection
- Prolonged antibiotic therapy
- Gastrointestinal infections with diarrhea
  - Both of the above destroy the bacterial flora and can also lead to vitamin K deficiency

Deficiency of Vitamin K- Effects

- Hypoprothrombinemia: increased blood coagulation time
- May affect bone growth and mineralization

Clinical manifestations of the deficiency

- Hemorrhagic disease of the newborn
- Bruising** tendency, ecchymotic* patches, mucus membrane hemorrhage, post-traumatic bleeding and internal bleeding
- Prolongation of the prothrombin time

*Ecchymotic:
medical term for a bleeding underneath the skin

**Bruising كدمة :
To injure the underlying soft tissue or bone of (part of the body) without breaking the skin

Summary

1) Vitamin K has 3 types (Phylloquinone , Menaquinone , Menadione)
2)Vitamin K is a Coenzyme for the synthesis of prothrombin and blood clotting factors in the liver.
3) Vitamin K is essential for the carboxylase enzyme involved
4) Anticoagulant drugs (warfarin and dicoumarol) , inhibit the activation of vitamin K
5) Malabsorption of lipids due to obstructive jaundice leads to vitamin K deficiency (Vit.K lipid soluble)
6)its Deficiency is most common in newborn infants
7) Gastrointestinal infections with diarrhea cause vitamin K deficiency .
8) Vit.k is essential for clot formation ,decreases coagulation time, and is present in low concentration in milk. It is one of Four fat-soluble Vitamins.
9) High levels of undercarboxylated osteocalcin and low serum vit K are associated with lower bone mineral density and higer risk of fractures (osteoporosis)

Test your knowledge ..!

1) What factors of Vit K are procoagulants?
A. II , II & X
B. II (prothrombin), VII, IX, & X
C. IX,V&X

2) All factors and proteins in blood clotting are synthesized in :
A. Pancreas
B. Kidney
C. Liver by carboxylation

3) Vitamin K is synthesized in the body by :
A. intestinal bacteria
B. liver
C. non

4) deficiency in vitamin K results in a decreased level of
A. Prothrombin
B. Thrombin
C. Fibrin
D. Fibrinogen

5) What groups of people need additional Vitamin K?
A. Premature newborns
B. People who do not have enough bile to absorb fat
C. Both A and B

6) Anticoagulant drugs (warfarin and dicoumarol) are :
A. increase capability of vitamin k
B. inhibit the activation of vitamin K
C. both

For your knowledge :

1) In liver diseases, an increase in prothrombin time is noted. Is this connected to a deficiency in vitamin K?

No, in liver diseases there is an increased prothrombin time due to deficient synthesis of coagulation factors. Further, vitamin K fails to restore Prothrombin Time when administered.

2) How are vitamin K and antibiotics connected?

Increased use of amoxicillin will decrease the synthesis of vitamin K since there will be a reduction in the bacteria in the intestine.

1) B 2)C 3)A 4)A 5)C 6)B

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If you find any mistake, please contact us:)
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Thank you