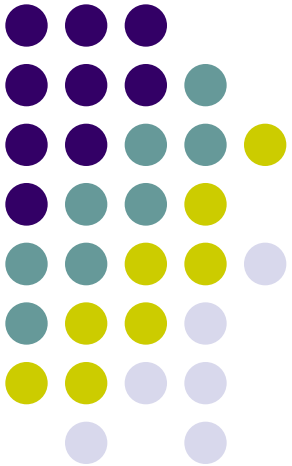
بسم الله الرحمن الرحيم

VITAMIN K

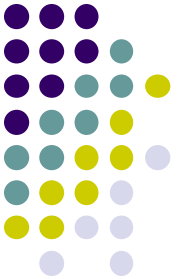


LECTURE OBJECTIVES

- At the end of the lecture students should be able to :

- Define & classify vitamins.
- List of fat soluble vitamins.
- Study different forms of vitamin K.
- List the dietary source and daily requirement.
- Study various functions of vitamin K specially in co-agulation process and its deficiencies.

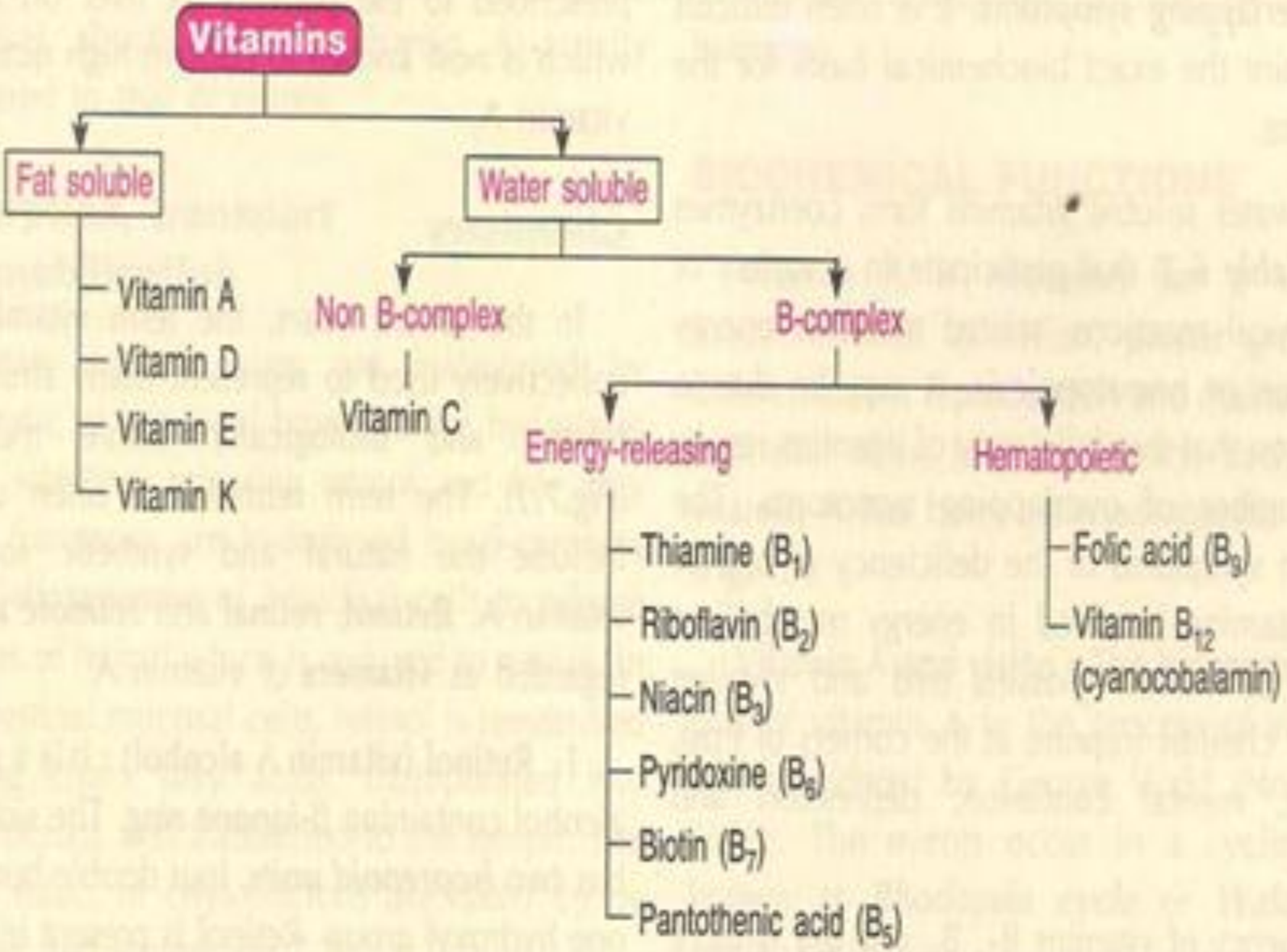
Vitamins



Essential organic substances

- **Yield no energy, but facilitate energy-yielding chemical reactions**
- **If absent from a diet, it will produce deficiency signs and symptoms**

Table 7.1 Classification of vitamins



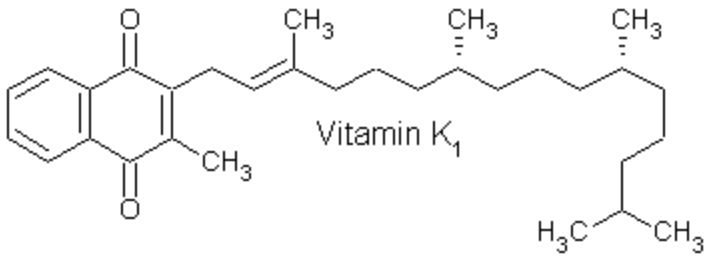
The Fat-Soluble Vitamins

	Water-Soluble Vitamins: B Vitamins and Vitamin C	Fat-Soluble Vitamins: Vitamins A, D, E, and K
Absorption	Directly into the blood.	First into the lymph, then the blood.
Transport	Travel freely.	Many require protein carriers.
Storage	Circulate freely in water-filled parts of the body.	Stored in the cells associated with fat.
Excretion	Kidneys detect and remove excess in urine.	Less readily excreted; tend to remain in fat-storage sites.
Toxicity	Possible to reach toxic levels when consumed from supplements.	Likely to reach toxic levels when consumed from supplements.
Requirements	Needed in frequent doses (perhaps 1 to 3 days).	Needed in periodic doses (perhaps weeks or even months).

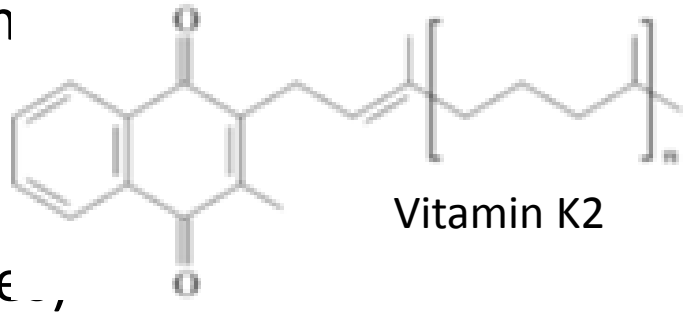
NOTE: Exceptions occur, but these differences between the water-soluble and fat-soluble vitamins are valid generalizations.

What is Vitamin K?

- Fat soluble compound
- Necessary for the synthesis of several proteins required for blood clotting



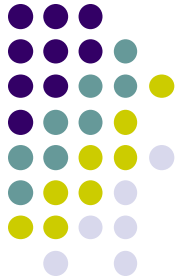
1) Vit K 1 (Phylloquinone)
   - natural form
   - found in plants
   - provides the primary source of vitamin K to humans through dietary consumption



Vitamin K2

2) Vitamin K2 compounds (Menaquinone),
   - made by bacteria in the human gut
   - provide a smaller amount of the human vitamin K requirement

VITAMIN K



- Fat soluble vitamins
  - Found in the fats and oils of food.
  - Absorbed into the lymph and carried in blood with protein transporters = **chylomicrons.**
  - Stored in liver and body fat and can become toxic if large amounts are consumed.

Vitamin K

- Role = Post translational carboxylation of blood clotting factors

- Sources: Cabbage, cauliflower, spinach, egg yolk, liver, synthesis from intestinal bacteria

- RDA: No RDA but recommendation is 70-140 μg/day

- Exists in several forms:

  Phylloquinone = vitamin K_1 (plants)

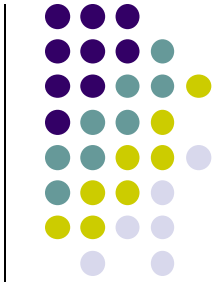
  Menaquinone = vitamin K_2 (intestinal bacteria)

  Menadione = synthetic derivative of vitamin K_1

Vitamin K

- **Vitamin K** is a group of lipophilic, hydrophobic vitamins.
- They are needed for the postranslation modification of proteins required for blood coagulation.
- They are involved in metabolism pathways, in bone mineralisation and cell growth.

Absorption , transport and storage



- Vitamin k is taken in the diet or synthesized by the intestinal bacteria.

Its absorption takes place along with fat (chylomicrons) and is dependent on bile salt. Vitamin K is transported along with LDL and is stored mainly in liver and , to a lesser extent, in other tissues.

Biochemical functions

The functions of vitamin K are concerned with blood clotting process.

Post-translational (after protein biosynthesis in the cell) modification of certain blood clotting factors.

The clotting factors II (prothrombin) VII ,IX and X are synthesized as inactive precursors (zymogens) in the liver.

Vitamin K act as a Coenzyme for the carboxylation of glutamic acid residues and this reaction is catalysed by a carboxylase.

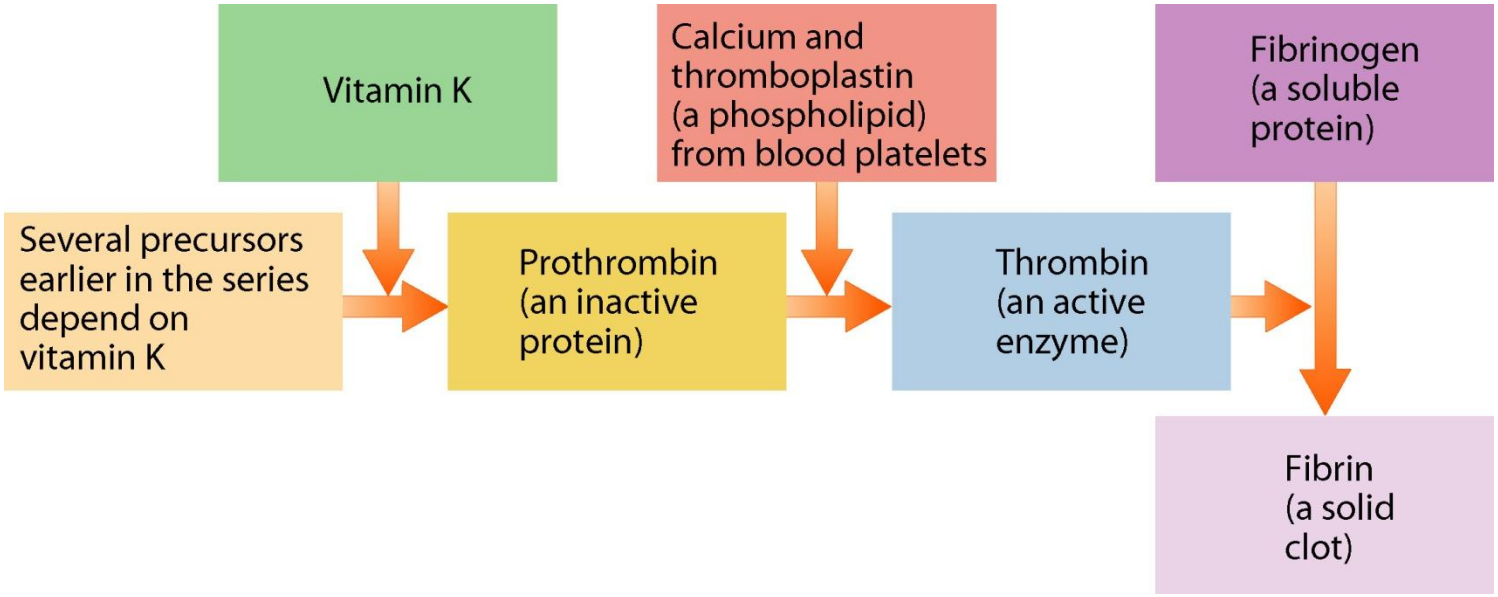
It involves the conversion of glutamate (Glu) to carboxyglutamate (Gla).

It is inhibited by dicumarol, an anticoagulant found in spoilt sweet clover.

Warfarin is a synthetic analogue that can inhibit vitamin K action.

Vitamin K

- Chief functions in the body
  - Synthesis of blood-clotting proteins and bone proteins that regulate blood calcium



Dietary Sources

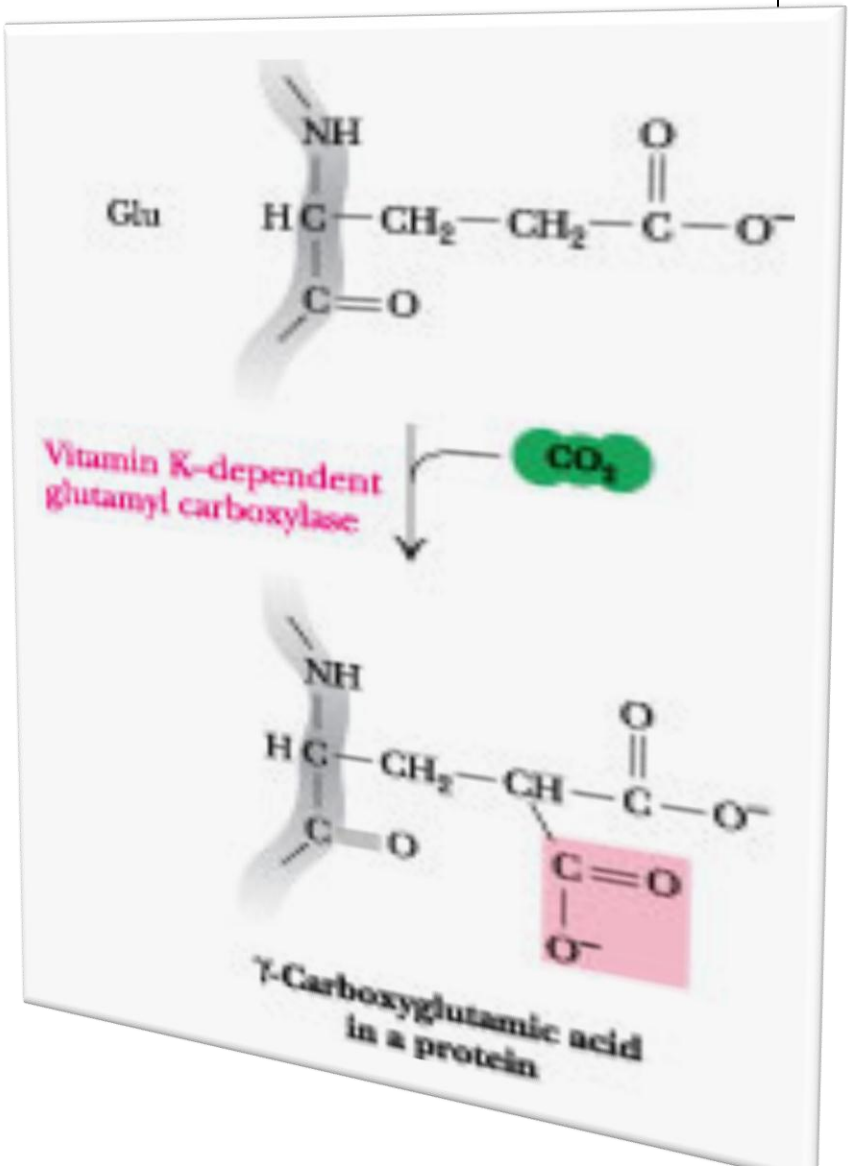
Vitamin K is consumed primarily from green leafy vegetables and some fruits. It may also be found in dairy products, meats and eggs.

Vitamin K Rich Foods	
Vitamin K Rich Foods	**FOOD Vitamin K (mcg)**
Brussel sprouts, _ cup cooked	460
Broccoli, _ cup cooked	248
Cauliflower, _ cup cooked	150
Swiss chard, _ cup cooked	123
Spinach, raw, 1 cup	120
Beef, 3.5 oz	104
Pork, 3.5 oz	88
Eggs, whole, 11g	25

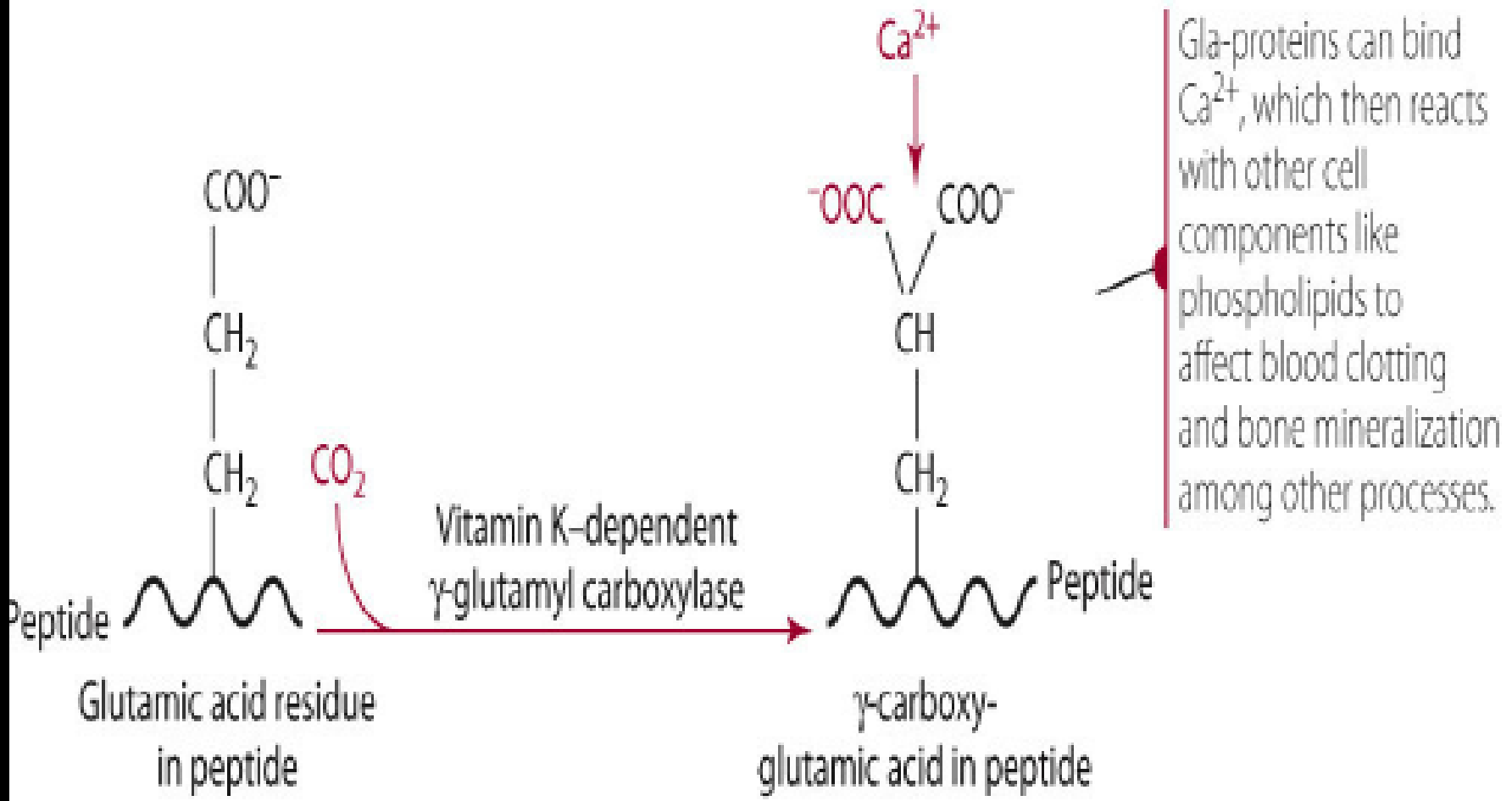
Physiological Effects of Vitamin K

- Vitamin K serves as an essential cofactor for a carboxylase that catalyzes carboxylation of glutamic acid residues on vitamin K-dependent proteins. These proteins are involved in:

1) Coagulation
2) Bone Mineralization
3) Cell growth

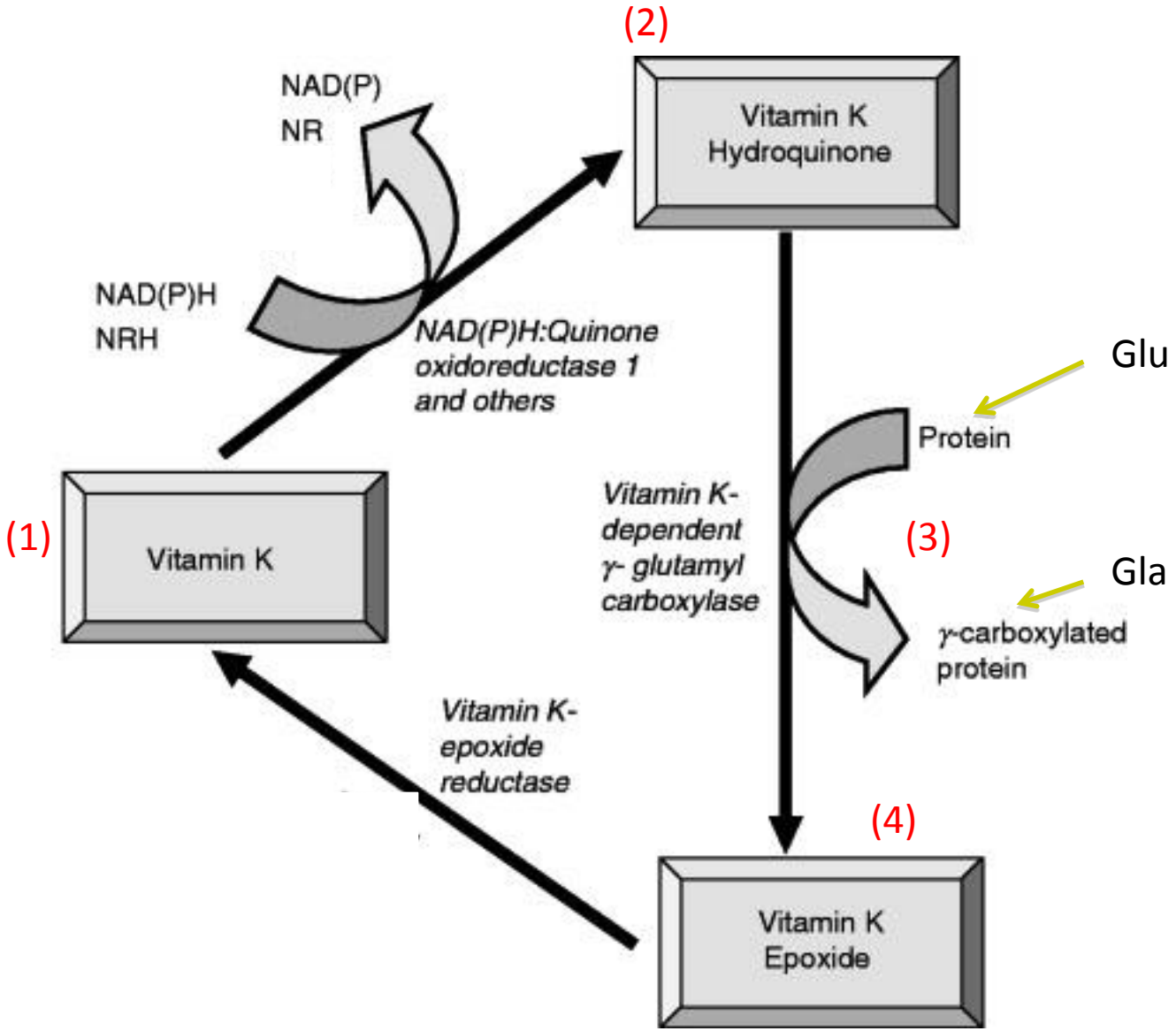


Production of Gamma carboxy glutamic acid (Gla) via Vitamin K-dependent Carboxylation



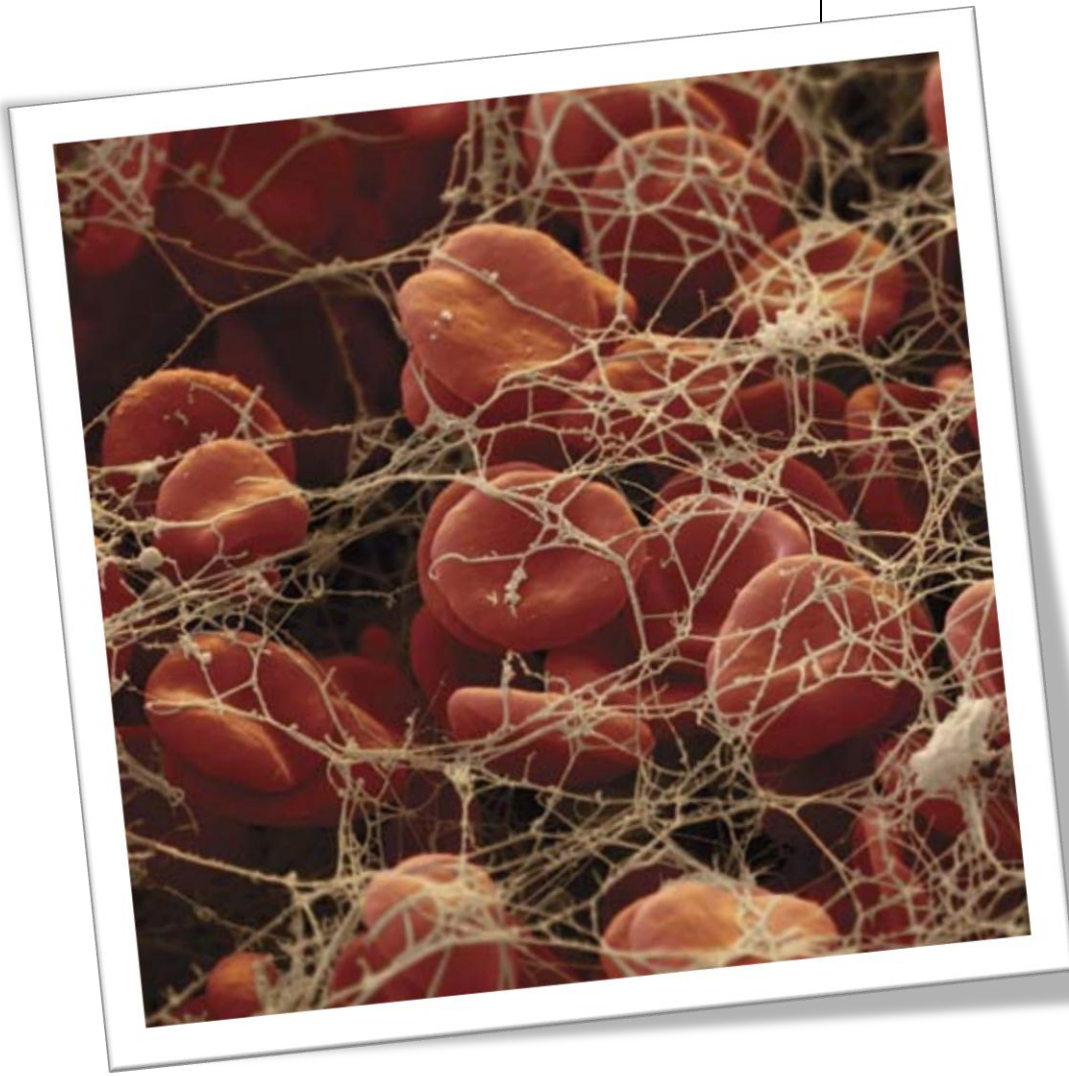
© Wadsworth, Cengage Learning

Biosynthesis of Glu→Gla

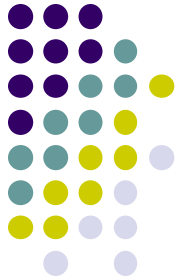


Coagulation

- The transformation of liquid blood into a solid gel
- Stops blood flow in the damaged area
- Involves a cascade of activation of plasma proteins
- These proteins are produced in the liver
- Fibrin is the final protein which produces a meshwork to trap RBC and other cells

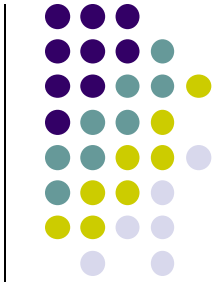


Vitamin K Dependent Coagulation



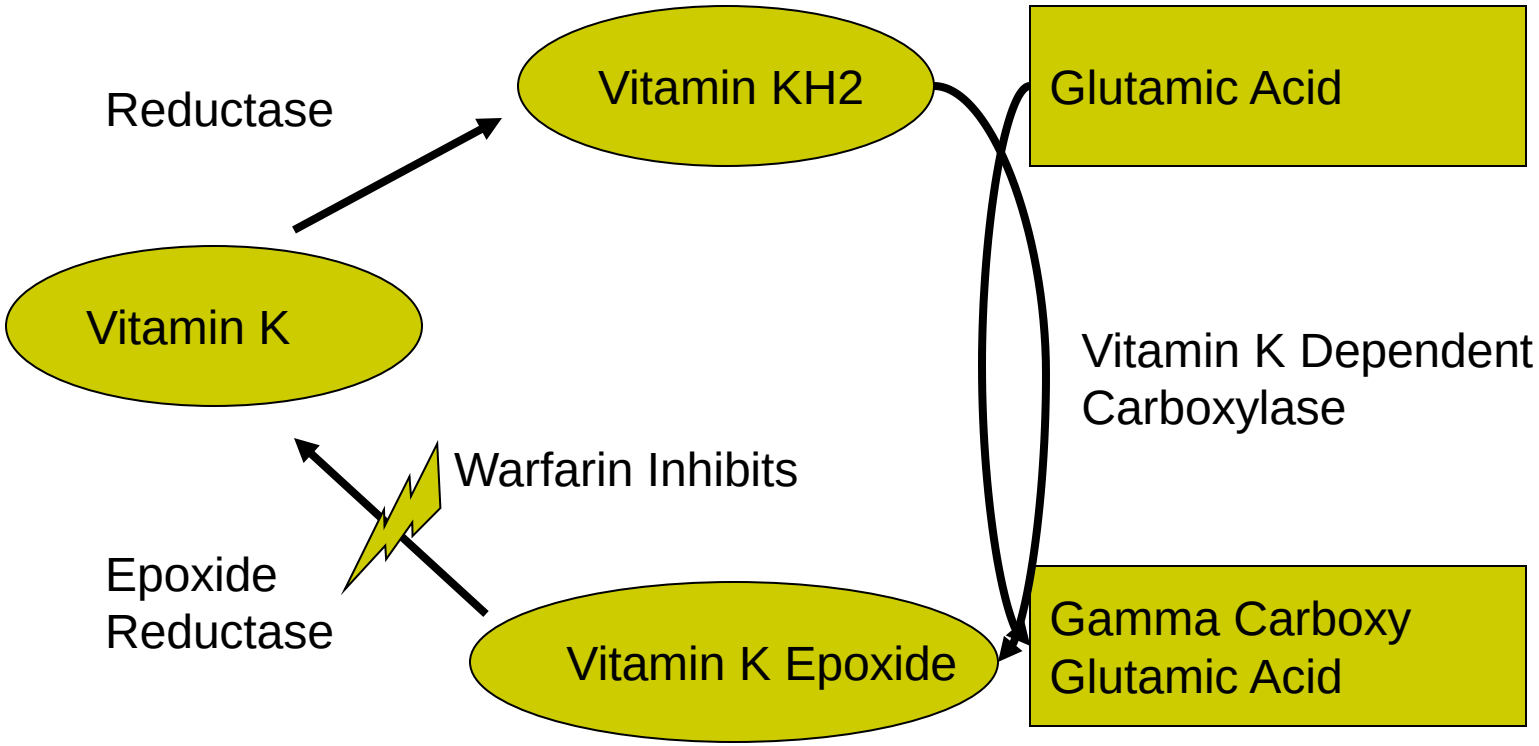
- Certain clotting factors/proteins require calcium to bind for activation
- Calcium can only bind after gamma carboxylation of specific glutamic acid (Glu) residues in these proteins
- Glu --> Gla modification needed for Ca2+ binding, clot formation
- Vitamin K acts as a cofactor for this carboxylation reaction
- The role of vitamin K in the carboxylation of specific proteins is a cyclic process called “Vitamin K Cycle”
- These proteins are known as “Vitamin K dependent” proteins

Vitamin K Dependent Proteins

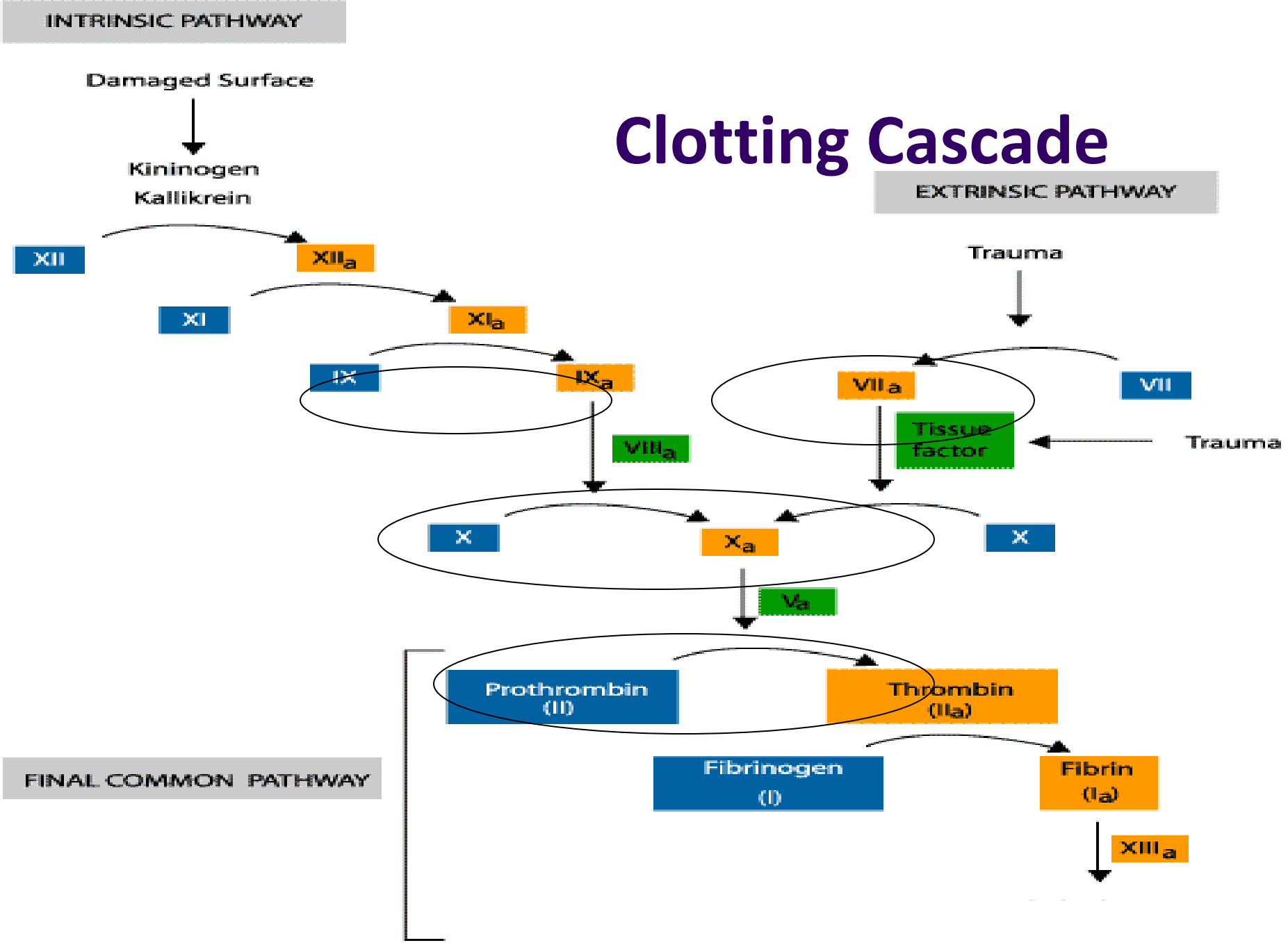


- factor II (prothrombin)
- factor VII (proconvertin)
- factor IX (thromboplastin component)
- factor X (Stuart factor)
- protein C & protein S
- Protein Z

Vitamin K Cycle

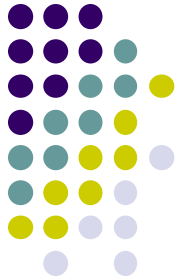


Clotting Cascade



AnaesthesiaUK

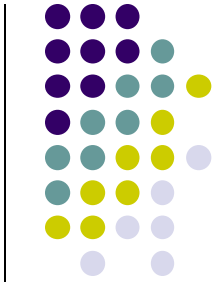
PIVKA



- Deficiency of vitamin K is associated with a decrease of the functional activity of these factors.

- These non-functional proteins are released into the circulation in normal levels & are called Protein Induced by Vitamin K Absence or Antagonism (PIVKA).

WHY TO MONITOR WARFARIN THERAPY?



- Narrow therapeutic range
- Can increase risk of bleeding

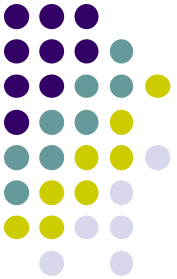
Vitamin K Deficiency

Results in impaired blood clotting and, potentially, bleeding.

Vitamin K deficiency can result from:

- a lack of vitamin k in the diet
- disorders that reduce fat absorption
- Taking certain drugs, including anticonvulsants and some antibiotics
- Use of coumarin anticoagulants

Vitamin K Deficiency in Adults



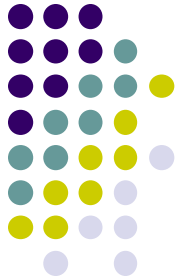
Uncommon in adults because normal bacteria found in the gut synthesize Vitamin K2

and the vitamin may be consumed from several food sources.

Contributing Factors:

- Biliary obstruction
- Maladsorption
- Cystic fibrosis
- Resection of small intestine

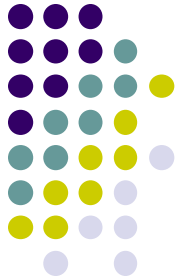
Vitamin K Deficiency in Adults



Increases risk of bleeding in individuals who suffer from Vitamin K deficiency:

- Coumarin anticoagulants
- Certain antibiotics
- Salicylates
- Large doses of vitamin E
- Hepatic insufficiency

Vitamin K Deficiency in Infants



Newborns are prone to vitamin K deficiency because…

1. Vitamin K and lipids are not easily transported across the placental barrier
2. Prothrombin synthesis in the liver is an immature process in newborns, especially when premature.
3. The neonatal gut is sterile, lacking the bacteria that is necessary in menaquinone synthesis.
4. Breast milk is not a good source of vitamin K

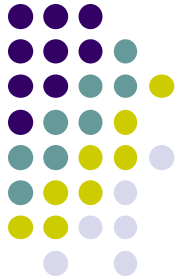
Results in a hemorrhagic disease called vitamin K deficiency bleeding (VKDB)

This disease is associated with breastfeeding, maladsorption of lipids, or liver disorders.

Vitamin K - Toxicity

- Not common except with over-supplementation
  - Phylloquinone and menaquinone are relatively nontoxic
    - Jaundice; brain damage
- Menadione toxic to skin and respiratory tract in high doses

Vitamin K Deficiency



Results in impaired blood clotting and, potentially, bleeding.
Vitamin K deficiency can result from:

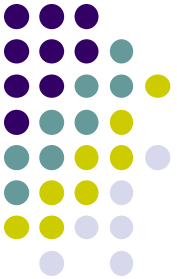
- a lack of vitamin k in the diet
- disorders that reduce fat absorption
- Taking certain drugs, including anticonvulsants and some antibiotics
- Use of coumarin anticoagulants
- Salicylates
- Large doses of vitamin E
- Hepatic insufficiency

Adequate Intake for Vitamin K

Life Stage	Age	Males (mcg/day)	Females (mcg/day)
Infants	0-6 months	2.0	2.0
Infants	7-12 months	2.5	2.5
Children	1-3 years	30	30
Children	4-8 years	55	55
Children	9-13 years	60	60
Adolescents	14-18 years	75	75
Adults	19 years and older	120	90
Pregnancy	18 years and younger	-	75
Pregnancy	19 years and older	-	90
Breast-feeding	18 years and younger	-	75
Breast-feeding	19 years and older	-	90

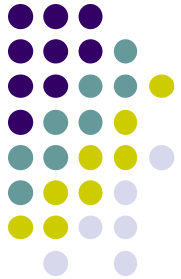
As outlined by the Food and Nutrition Board (FNB) of the Institute of Medicine in the US (January 2001)

Vitamin K: Indications



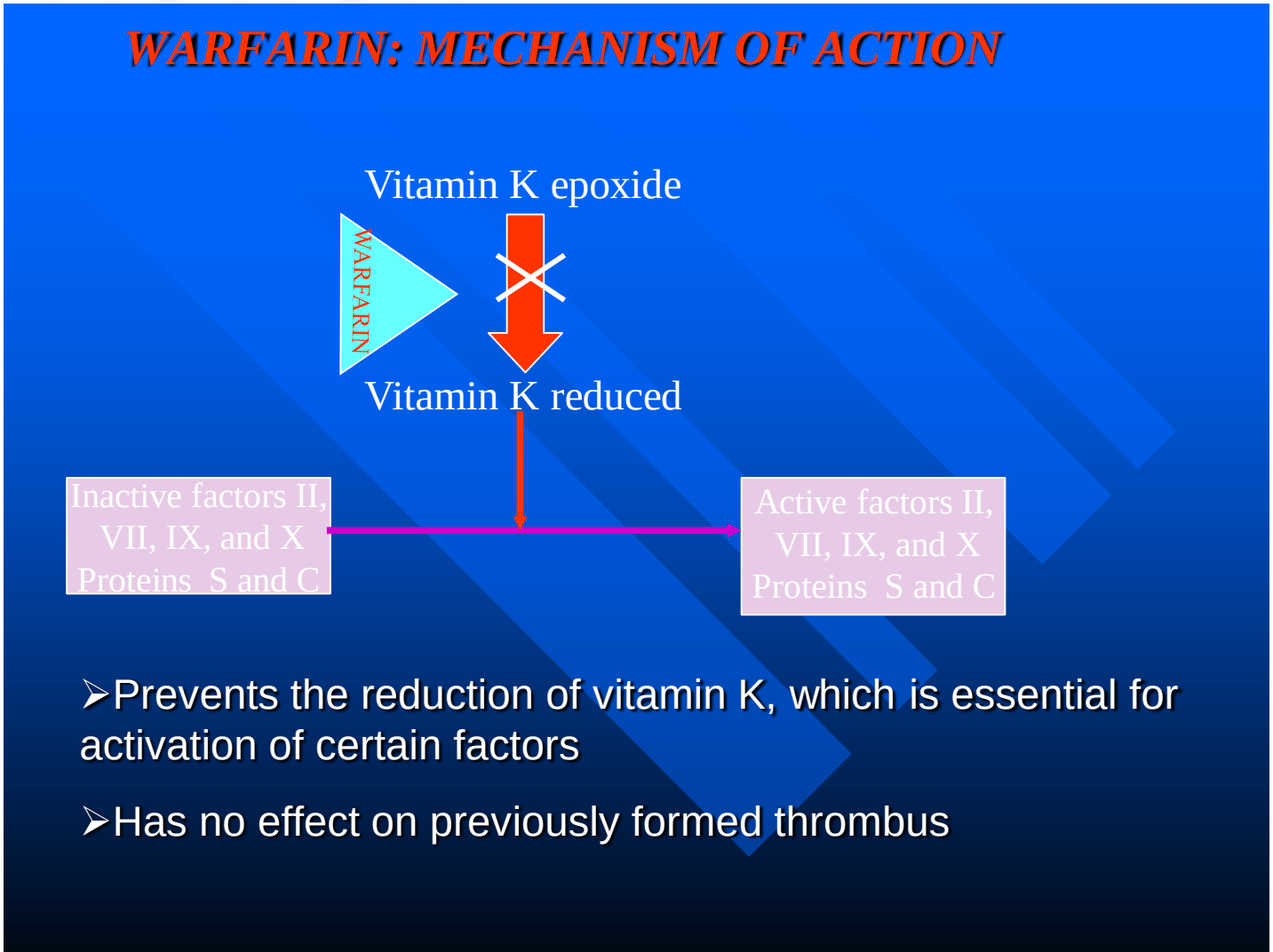
- Dietary supplementation
- Treatment of deficiency states (rare)
  - Antibiotic therapy
  - Newborn infants
  - Malabsorption
- Reverse the effects of certain anticoagulants (warfarin)

Why does the body recycle Vitamin K?

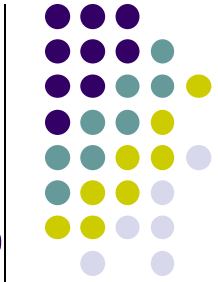


- Very minimal body stores
- Must have regular dietary intake
- Recycles so that the same vitamin K can be cycled and re-used many times (decreasing need in dietary intake)

WARFARIN: MECHANISM OF ACTION

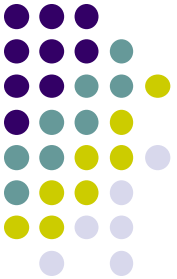


Prevention/Treatment



- Vitamin K can be given orally
- In the case of someone who improperly absorbs fat or is at high risk of bleeding, Vitamin K can be injected under the skin
- If a drug is causing Vitamin K deficiency, the dose is altered or extra Vitamin K is given
- In people who suffer from both severe liver disorders and Vitamin K deficiency, Vitamin K injections may be insufficient so blood transfusions may be necessary to replenish clotting factors
- It is recommended that all newborns are given an injection of phylloquinone (Vitamin K_1) into the muscle to prevent intracranial bleeding after delivery
- Formulas for infants contain Vitamin K

Quiz Time!



Where are two ways we get Vitamin K?

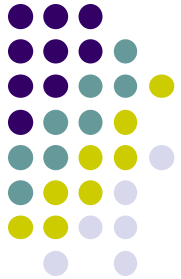
Name a good source of dietary Vitamin K

What type of chemical reaction does Vitamin K assist in?

Which anticoagulant inhibits Vitamin K?

Name a sign of Vitamin K deficiency.

Summary



- Vitamin K is a fat soluble compound necessary for the synthesis of several proteins involved in blood clotting
- It acts as a cofactor for a carboxylation reaction
- A deficiency in Vitamin K results in impaired blood clotting and possibly bleeding
- The anticoagulant Warfarin inhibits Vitamin K
- Vitamin K can be given orally or through injection for prevention/treatment of deficiency