Vitamin K

Types	**Occurs in several forms:** ■ Vitamin K_1 (Phylloquinone) ■ Vitamin K_2 (Menaquinone) ■ Vitamin K_3 (Menadione) – synthetic form
Sources	**Dietary sources:** - Cabbage, kale, spinach, egg yolk, liver
Sources of Vitamin K	- **Phylloquinone**: Green leafy vegetables - **Menaquinone**: Intestinal bacteria Intestinal bacterial synthesis meets the daily requirement of vitamin K even without dietary supplement - **Menadione**: synthetic form A precursor of menaquinone
RDA for Vitamin K (mg/day) (you don't have to memorize it)***	- 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

Functions of Vitamin K

- Coenzyme for the synthesis of prothrombin and blood clotting factors in the liver
  1- Prothrombin and clotting factors are protein in nature
  2- Synthesis of prothrombin, clotting factors II, VII, IX, X require carboxylation of their glutamic acid (Glu) residue
  3- Mature prothrombin and clotting factors contain g-carboxyglutamate (Gla) after carboxylation reaction
  4- Vitamin K is essential for the carboxylase enzyme involved
  5- Dihydroquinone form of vitamin K is essential for this reaction
- Prothrombin – platelet interaction
  1- Carboxylated prothrombin contains two carboxylate groups (COO^-)
  2- These groups bind to Ca^{2+} forming prothrombin-calcium complex
  3- The complex then binds to phosholipids on the surface of platelets (important for blood clotting)
  4- Converting prothrombin to thrombin and initiating clot formation
- Synthesis of g-carboxyglutamate in osteocalcin
  1- Osteocalcin is a bone turnover protein
  2- Also called Bone Gla Protein (BGP)
  3- Involved in bone formation, mineralization and resorption
  4- g-Carboxyglutamate is required for osteocalcin binding to hydroxyapatite (a calcium mineral) in the bone
  5- The binding mechanism is similar to that of prothrombin-platelet binding

Analogs of Vitamin K

- **- Anticoagulant drugs: warfarin and dicoumarol**
  - **Structural analogs of vitamin K**
- **- They inhibit the activation of vitamin K to hydorquinone form (inhibiting the reductase enzyme)**
- **- Prothrombin and clotting factors are not carboxylated**
- **- Hence blood coagulation time increases upon injury**

- **Carboxylation of glutamate requires vitamin K**
- **The process is inhibited by warfarin**

Deficiency of Vitamin K

- **Deficiencies are rare: it is synthesized by intestinal bacteria**
- **Hypoprothrombinemia: increased blood coagulation time**
- **Some second-generation cephalosporin drugs cause this condition due to warfarin-like effects (antibiotics given with vit. K)**
- **May affect bone growth and mineralization**
- **Lipid malabsorption can lead to vitamin K deficiency**
- **Prolonged antibiotic therapy**
  - **Especially in marginally malnourished individuals (e.g. debilitated geriatric patients)**
- **Gastrointestinal infections with diarrhea**
- **Both of the above destroy the bacterial flora leading to vitamin K deficiency**
- **Deficiency most common in newborn infants**
  - **Newborns lack intestinal flora**
  - **Human milk can provide only 1/5th vitamin K**
  - **Supplements are given intramuscularly at birth**

Clinical Manifestations of the Deficiency

- **Hemorrhagic disease of the newborn**
- **Bruising tendency, ecchymotic patches (bleeding underneath the skin)**
- **Mucus membrane hemorrhage**
- **Post-traumatic bleeding / internal bleeding**
- **Prolonged prothrombin time**

Toxicity of Vitamin K	- **Prolonged supplementation of large doses of menadione can cause:**
	  - **Hemolytic anemia**
	  - **Jaundice**
	- Due to toxic effects on RBC membrane