Vitamin K

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While some complementary and alternative techniques have been studied scientifically, high-quality data regarding safety, effectiveness, and mechanism of action are limited or controversial for most therapies. Whenever possible, it is recommended that practitioners be licensed by a recognized professional organization that adheres to clearly published standards. In addition, before starting a new technique or engaging a practitioner, it is recommended that patients speak with their primary healthcare provider(s). Potential benefits, risks (including financial costs), and alternatives should be carefully considered. The below monograph is designed to provide historical background and an overview of clinically-oriented research, and neither advocates for or against the use of a particular therapy.

Related Terms:
- 2-methyl-1,4-naphthoquinone, AquaMEPHYTON®, Konakion®, menadiol (not available in United States), menadion diphosphate (vitamin K3), menadione, menaquinones, menatetrenone, Mephyton®, Phylloquinone®, Phytonadione®, phytomenadione.

BACKGROUND

- The name "vitamin K" refers to a group of chemically similar fat-soluble compounds called naphthoquinones. Vitamin K1 (phytonadione) is the natural form of vitamin K, which is found in plants and provides the primary source of vitamin K to humans through dietary consumption. Vitamin K2 compounds (menaquinones) are made by bacteria in the human gut and provide a smaller amount of the human vitamin K requirement. Vitamin K1 is commercially manufactured for medicinal use under several brand names (Phylloquinone®, Phytonadione®, AquaMEPHYTON®, Mephyton®, Konakion®). A water-soluble preparation is available for adults only as vitamin K3 (menadione).
- Vitamin K is necessary for normal clotting of blood in humans. Specifically, vitamin K is required for the liver to make factors that are necessary for blood to properly clot (coagulate), including factor II (prothrombin), factor VII (proconvertin), factor IX (thromboplastin component), and factor X (Stuart factor). Other clotting factors that depend on vitamin K are protein C, protein S, and protein Z. Deficiency of vitamin K or disturbances of liver function (for example, severe liver failure) may lead to deficiencies of clotting factors and excess bleeding.
- Vitamin K deficiency is rare, but can lead to defective blood clotting and increased bleeding. People at risk for developing vitamin K deficiency include those with chronic malnutrition (including those with alcohol dependency) or conditions that limit absorption of dietary vitamins such as biliary obstruction, celiac disease or sprue, ulcerative colitis, regional enteritis, cystic fibrosis, short bowel syndrome, or intestinal resection (particularly of the terminal ileum, where fat-soluble vitamins are absorbed). In addition, some drugs may reduce vitamin K levels by altering liver function or by killing intestinal flora (normal intestinal bacteria) that make vitamin K (for example, antibiotics, salicylates, anti-seizure medications, and some sulfa drugs). Vitamin K is routinely given to newborn infants to prevent bleeding problems related to birth trauma or when surgery is planned.
- Warfarin is a blood-thinning drug that functions by inhibiting vitamin K-dependent clotting factors. Warfarin is prescribed by doctors for people with various conditions such as atrial fibrillation, artificial heart valves, history of serious blood clot, clotting disorders.
(hypercoagulability), or placement of indwelling catheters/ports. Usually, blood tests must be done regularly to evaluate the extent of blood thinning, using a test for prothrombin time (PT) or International Normalized Ratio (INR). Vitamin K can decrease the blood thinning effects of warfarin and will therefore lower the PT or INR value. This may increase the risk of clotting. Therefore, people taking warfarin are usually warned to avoid foods with high vitamin K content (such as green leafy vegetables) and to avoid vitamin K supplements. Conversely, vitamin K is used to treat overdoses or excess anticoagulant effects of warfarin and to reverse the effects of warfarin prior to surgery or other procedures.

### Uses

These uses have been tested in humans or animals. Safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.

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### Hemorrhagic disease of newborn (vitamin K deficiency bleeding / VKDB)

Vitamin K deficiency in infants can lead to hemorrhagic disease of the newborn, also known as vitamin K deficiency bleeding (VKDB). Although up to half of newborns may have some degree of vitamin K deficiency, serious hemorrhagic disease with bleeding is rare.

Because vitamin K given by injection has been shown to prevent VKDB in newborns and young infants, the American Academy of Pediatrics recommends administering a single intramuscular injection of vitamin K1 to all newborns. Oral dosing is not considered adequate as prevention, particularly in breastfeeding infants. Initial concerns of cancer risk were never proven and are generally not considered clinically relevant.

### Treatment

In cases of true VKDB, bleeding may occur at injection sites, at the umbilicus, or in the gastrointestinal tract. Life-threatening bleeding into the head (intracranial) or in the area behind the lower abdomen (retroperitoneum) can also occur. Evaluation by a physician is imperative.

### Vitamin K deficiency

Vitamin K deficiency is rare in adults, but can lead to defective blood clotting and increased bleeding, as well as osteoporosis. People at risk for developing vitamin K deficiency include those with chronic malnutrition (including those with alcohol dependency) or conditions that limit absorption of dietary vitamins such as biliary obstruction, celiac disease or sprue, ulcerative colitis, regional enteritis, cystic fibrosis, short bowel syndrome or intestinal resection (particularly of the terminal ileum, where fat-soluble vitamins are absorbed). In addition, some drugs may reduce vitamin K levels by altering liver function or by killing intestinal flora (normal intestinal bacteria) that make vitamin K (for example, antibiotics, salicylates, anti-seizure medications, and some sulfa drugs). Evaluation by a physician should be sought.

### Warfarin reversal (elevated INR / pre-procedure)

Warfarin is a blood-thinning drug that inhibits vitamin K-dependent clotting factors. Warfarin is prescribed by doctors for people with various conditions such as atrial fibrillation, artificial heart valves, history of serious blood clot, clotting disorders (hypercoagulability), or placement of indwelling catheters/ports. Usually, blood tests must be done regularly to evaluate the extent of blood thinning, using a test for prothrombin time (PT) or International Normalized Ratio (INR). The range for the PT/INR depends on the condition being treated. The PT/INR can become elevated for many reasons and sometimes can get dangerously high and increase the risk of serious bleeding. Patients taking warfarin should be aware of these potential causes, which include many drugs that interact with warfarin, liver disorders, or accidental warfarin overdose. Because the effects of warfarin on anticoagulation are usually delayed by several days, the PT/INR may not increase immediately at the time of overdose. If a person’s blood becomes too “thin,” management should be under strict medical supervision and may include oral or injected vitamin K to help reverse the effects of warfarin.
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If a person's blood becomes too "thin," management should be under strict medical supervision and may include oral or injected vitamin K to help reverse the effects of warfarin.

Bleeding disorders (prevention of bleeding or thrombotic events in anticoagulant therapy)

Agents that block vitamin K, such as warfarin and phenprocoumon, are often used in anticoagulant therapy. Because dietary intake of vitamin K can affect anticoagulant function, inconsistent levels of vitamin K in the diet may make it difficult to control anticoagulant stability. Some studies suggest that daily, low-dose vitamin K supplementation may help stabilize anticoagulant therapy.

Osteoporosis prevention

Vitamin K appears to prevent bone resorption and adequate dietary intake is likely necessary to prevent excess bone loss. Elderly or institutionalized patients may be at particular risk and adequate intake of vitamin K-rich foods should be maintained. Unless patients have demonstrated vitamin K deficiency, there is no evidence that additional vitamin K supplementation is helpful. Some studies show that vitamin K supplements may increase bone mineral density and bone strength, while others show that vitamin K has no effect on bone turnover. However, vitamin K may play a role in the prevention and treatment of glucocorticoid-induced bone loss. Furthermore, vitamin D and calcium supplementation may enhance the beneficial effects of vitamin K. Further research is needed to confirm these results.

Hepatocellular carcinoma (recurrent hepatocellular carcinoma prevention)

Infection with the hepatitis C virus (HCV) may lead to hepatocellular carcinoma (HCC), a form of liver cancer. So far, the results from clinical studies are unclear and do not indicate any beneficial effects of vitamin K in preventing HCC recurrence.
Key to grades: A: Strong scientific evidence for this use; B: Good scientific evidence for this use; C: Unclear scientific evidence for this use; D: Fair scientific evidence against this use (it may not work); F: Strong scientific evidence against this use (it likely does not work).

TRADITION/THEORY

The below uses are based on tradition, scientific theories, or limited research. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider. There may be other proposed uses that are not listed below.

- Cancer, celiac disease, cystic fibrosis, liver function testing, osteoporosis treatment.

DOsing

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

Dietary intake

- Foods rich in vitamin K include green, leafy vegetables such as spinach, broccoli, asparagus, watercress, cabbage, cauliflower, green peas, beans, olives, canola, soybeans, meat, cereals, and dairy products. Cooking does not remove significant amounts of vitamin K from these foods.

Adults (over 18 years old)

- Vitamin K deficiency management should be under medical supervision. If the PT is only slightly elevated and poor dietary intake is thought to be the cause, increasing the ingestion of vitamin K-rich foods can be tried. In non-emergency situations, oral vitamin K1 (Phytonadione®, AquaMEPHYTON®, Mephyton®, Konakion®) can be given in a daily dose of 5-10 milligrams (single doses up to 25 milligrams are given in some cases). If there is a concern of bile salt deficiency or malabsorption in the ileum, a water-soluble oral form of vitamin K can be considered. If necessary, vitamin K1 can be injected at a dose of 10 milligrams, repeated after 8-12 hours, or administered daily until the deficiency is corrected.

- Elevated PT/INR (warfarin reversal) or acute liver dysfunction management should be under medical supervision.

Children (under 18 years old)

- Vitamin K1 given by injection has been shown in newborns and young infants to prevent "hemorrhagic disease of newborn," also known as vitamin K deficiency bleeding (VKDB). The American Academy of Pediatrics therefore recommends administering a single intramuscular injection of 0.5 to 1 milligram of vitamin K1 to all newborns. Oral dosing is generally not regarded as adequate for prevention, particularly in breastfeeding infants.

- Warfarin toxicity/reversal should be under strict medical supervision.

- Menadiol (not available in the United States) should not be given to infants or children due to
rare reports of liver damage and blood cell toxicity (hemolytic anemia).

The U.S. Food and Drug Administration does not strictly regulate herbs and supplements. There is no guarantee of strength, purity or safety of products, and effects may vary. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy. Consult a healthcare provider immediately if you experience side effects.

Allergies

- Intravenous or intramuscular vitamin K has been associated rarely with anaphylactoid reactions, including shock, heart attack, respiratory arrest, and death. Therefore, these routes of administration should be avoided if possible. If given intravenously, preparations should be dilute and administration should be slow under strict medical supervision.
- Skin hypersensitivity reactions are rare and may occur in particular with injections of vitamin K1 (Phytonadione®, AquaMEPHYTON®). A raised, itchy plaque may arise at the injection site that may take 1-2 months to resolve and can cause a scar.

Side Effects and Warnings

- An unusual taste in the mouth has been rarely reported with vitamin K injections. Liver damage has been reported rarely in infants and children with use of the vitamin K preparation Menadiol (not available in the United States). Conditions that interfere with absorption of ingested vitamin K may lead to deficiency, including short gut, cystic fibrosis, malabsorption (various causes), pancreas or gall bladder disease, persistent diarrhea, sprue, or ulcerative colitis.
- Red, painful swelling at vitamin K injection sites has been reported. A raised, itchy plaque can arise at the injection site that may take 1-2 months to resolve and can cause a scar. Transient flushing has been reported.
- Dizziness has rarely been reported with vitamin K injections.
- Damage to red blood cells causing anemia (hemolysis) has been reported rarely in infants and children with the use of the vitamin K preparation Menadiol (not available in the United States). This type of vitamin K should be avoided in people with glucose-6-phosphate dehydrogenase (G6PD) deficiency because vitamin K may cause hemolytic episodes. Vitamin K deficiency decreases blood factors needed for clotting and increases the risk of bleeding.
- Although initial concerns were voiced about the possible cancer risk of universally administering vitamin K by injection to newborns, there is no scientific evidence to support this risk. This is generally considered not to be a concern in the medical community.

Pregnancy and Breastfeeding

- The U.S. Food and Drug Administration (FDA) has categorized vitamin K as Pregnancy Category C. There is not sufficient scientific evidence in animals or humans to clearly conclude the effects on the fetus. Vitamin K given to mothers soon before birth is generally not recommended. Regular supplementation with vitamin K during pregnancy (beyond normal dietary intake) may increase the risk of jaundice in the newborn.
- The American Academy of Pediatrics recommends administering a single intramuscular injection of vitamin K1 to all newborns to prevent vitamin K deficiency bleeding (VKDB), a potentially life-threatening condition. Excessive amounts of vitamin K supplementation in
newborns may lead to serious complications, including hemolytic anemia, hemoglobinuria, kernicterus, brain damage, or death. Reactions may be particularly severe in premature infants.

- Vitamin K ingested by mothers is generally considered to be safe during breastfeeding. There is very little vitamin K transmitted to infants through breast milk (as opposed to many infant formulas, which do include vitamin K). It is not known if the amount of vitamin K in breast milk is increased if mothers take vitamin K supplements, but the scientific evidence suggests that this likely would make little if any difference. If an infant formula is used that is not fortified with vitamin K, a physician should be consulted to find another way for the infant to receive vitamin K.

**INTERACTIONS**

Most herbs and supplements have not been thoroughly tested for interactions with other herbs, supplements, drugs, or foods. The interactions listed below are based on reports in scientific publications, laboratory experiments, or traditional use. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy.

**Interactions with Drugs**

- Warfarin is a blood-thinning drug that functions by inhibiting vitamin K-dependent clotting factors. Warfarin is prescribed by doctors for people with various conditions such as atrial fibrillation, artificial heart valves, history of serious blood clot, clotting disorders (hypercoagulability), or placement of indwelling catheters/ports. Usually, blood tests must be done regularly to evaluate the extent of blood thinning using a test for prothrombin time (PT) or International Normalized Ratio (INR). Vitamin K can decrease the blood thinning effects of warfarin and will therefore lower the PT or INR value. This may increase the risk of clotting. Therefore, people taking warfarin are usually warned to avoid foods with high vitamin K content (such as green leafy vegetables) and to avoid vitamin K supplements. Conversely, vitamin K is used to treat overdoses or excess anticoagulant effects of warfarin and to reverse the effects of warfarin prior to surgery or other procedures. Over-the-counter vitamin K1-containing multivitamin supplements disrupt warfarin anticoagulation in vitamin K1-depleted patients. Vitamin K-depleted patients are sensitive to even small changes in vitamin K1 intake.

- Some antibiotics may decrease the bacteria in the human gut (which synthesize a small amount of the human vitamin K requirement). Broad-spectrum antibiotics, particularly sulfonamides such as Bactrim®, may lower vitamin K levels and increase the risk of deficiency in people not ingesting adequate amounts.

- High doses of salicylates (aspirin) may increase vitamin K requirements.

- Sucralfate or high doses of aluminum hydroxide antacids may decrease absorption of fat-soluble vitamins such as vitamin K.

- Cholestyramine (Questran®) mineral oil may decrease the absorption of oral vitamin K and increase vitamin K requirements.

- Quinine, or quinidine, may increase vitamin K requirements.

- Dactinomycin, a cancer chemotherapy drug, may decrease the effects of vitamin K and increase vitamin K requirements.

- Menadiol sodium diphosphase is a form of vitamin K that is not used in the United States. Multiple drugs may cause complications when taken with menadiol.

**Interactions with Herbs/Supplements**
Vitamin K may decrease the blood thinning effects of herbs that act like warfarin (Coumadin®) in the body by decreasing clotting factors made in the liver. In particular, this may apply to herbs with coumarin constituents, such as alfalfa (*Medicago sativa*), American ginseng (*Panax quinquefolius*), and angelica (*Angelica archangelica*).

While the effects of vitamin K on bone density are still unclear, beneficial effects may be enhanced with vitamin D and calcium supplementation.

**AUTHOR INFORMATION**

This information is based on a systematic review of scientific literature edited and peer-reviewed by contributors to the Natural Standard Research Collaboration (www.naturalstandard.com).

**REFERENCES**

Natural Standard developed the above evidence-based information based on a thorough systematic review of the available scientific articles. For comprehensive information about alternative and complementary therapies on the professional level, go to www.naturalstandard.com. Selected references are listed below.
