
Cathy Breedon, PhD, RD, CSP, FADA
Clinical/Metabolic Nutrition Specialist and Perinatal/Pediatric Nutrition Specialist
Sanford Medical Center, and UND School of Medicine, Fargo, ND

1. Overview/Summary: Vitamin K Facts and Figures
   (All the important useful information is on pp. 1-12)

2. Just References from the Scientific Literature:

Inadequacy of Vitamin K and Contribution to:
I. Cardiovascular Disease and Arterial and Renal Calcinosis
II. Unsafe Variability of Anticoagulation Therapy
III. Osteoporosis and Osteoarthritis and Rheumatoid Arthritis
IV. Liver Cancer and Colorectal Cancer
V. Miscellaneous Health Issues: Non-warfarin-related hemorrhage
   Cholestasis  Diarrhea  Celiac disease
   Cystic fibrosis  Short bowel syndrome  Pregnancy

This is the short form of this paper with just the references at the end. Another version is available that includes the abstracts of the referenced articles. As always, this paper is a review of new issues in the scientific literature and not intended to take the place of your personal health care provider.

In particular, individuals using anticoagulant medications like Coumadin/warfarin must not make changes in their vitamin K intake without consulting their physician/PA/NP. A separate paper for health professionals is available that discusses this issue in more detail.
Overview/Summary: Vitamin K Issues

1 Vitamin K has been found to be involved in carboxylation reactions in various tissues. It is now recognized as playing a critical role in bone health, growth, diabetes, pregnancy, cardiovascular health, renal health, and certain cancers, in addition to its well-known role in blood coagulation. Allowing (or inducing) vitamin K deficiency for any reason is clearly not benign.

2 Foods that are generous in vitamin K1 are also excellent sources of beneficial antioxidant phytochemicals. This includes lutein, a pigment in leafy greens that appears to have an additional unique potential benefit in the prevention or the slowing of the progression of blindness due to macular degeneration. These foods are also very low in calories and rich in other vitamins and minerals as well.

However, many Americans eat very few of these foods and as a result, relative vitamin K inadequacy is not at all uncommon when it is actually checked. (It is currently only very rarely checked.) The most generous dietary vitamin K2 sources include bacterially fermented foods. One of the richest is natto … a strong flavored soy bean product popular in Japan but considerably less so in the US.

3 Elderly people appear to require a regular intake of vitamin K above the 2001 “Adequate Intake” (AI) level in order to assure adequacy. Note that the recommended amounts for everyone (AIs, RDI, RDA, etc.) were set at a time when it was assumed that intestinal bacteria provided about half of one’s requirements. As this source has been found to be more unreliable than was thought, it is very reasonable to aim toward an intake that is generous.

People using the drug Coumadin need to discuss this issue with their physician as described below in #6 and #8 because of a drug/nutrient interaction. However, except for this well-known drug/nutrient interaction, there is no upper level of safety for vitamin K and foods rich in vitamin K are rich in many other nutrients as well.

4 Vitamin K as phylloquinone (K1) and menaquinone (K2) are not toxic, and for that reason there is no “Upper Limit of Safety” established for this vitamin. In contrast, menadione (K3) is potentially harmful and it is generally no longer used as a vitamin K supplement.
It was previously assumed that about half of a person’s vitamin K requirements were met via production by intestinal bacteria. It is now clear that **healthy people are in fact MUCH more dependent on vitamin K from foods and/or supplements to assure adequacy than we thought.**

**Misunderstanding about recommendations for vitamin K intake for people on anticoagulant therapy has resulted in many people avoiding all sources of vitamin K** (instead of taking in a CONSISTENT but ADEQUATE amount of vitamin K as recommended by the drug manufacturers.) One result, for example, is the association seen between anticoagulant use and increased risk of osteoporosis and cardiac and renal calcification. Initially it was thought to be due to the drug itself, but it turned out to be related to the far too common inappropriate excessive restriction of vitamin K.

**It appears that dangerous VARIABILITY of blood clotting among some patients taking anticoagulants can be controlled significantly by assuring a consistent daily intake of an adequate amount of vitamin K.** Coagulation variability is a much greater problem among patients whose usual vitamin K status is low. Those are the people most greatly affected by fluctuations in vitamin K content of diet or supplements. Persons with a reliable adequate intake level are far less affected by additional intake in vitamin K.

**Vascular calcification, a known cardiovascular risk factor, is another side effect related to the problem of inducing low vitamin K status in patients on anticoagulants and among the population at large.** Failure to activate the hormone osteocalcin because of inadequate vitamin K results in failure to move calcium from the bloodstream into bone. Instead, calcium is deposited inappropriately in other tissues, such as blood vessel walls and the kidneys. This results in arteriocalcinosis (an independent risk factor for cardiovascular disease.) It also results in renal calcinosis because increased calcium needs to be excreted.

**Vitamin K inadequacy is now being identified even among healthy children** when vitamin K status is evaluated …however, at present it is only very rarely evaluated. People with **conditions that result in malabsorption** are at very high risk of deficiency. This includes conditions like cystic fibrosis, poorly controlled celiac disease, Crohn’s disease (inflammatory bowel disease or IBD,) biliary atresia, short bowel syndrome and intractable diarrhea.
10. **Others at particular risk of inadequacy of vitamin K include people using**
drugs that interfere with vitamin K such as *salicylates* (e.g. aspirin) and many
**seizure-control medications.** Similarly, some renal medications used to bind
phosphate in the intestine (e.g. *sevelamer-HCl*) can greatly impair vitamin K
absorption. [Metal ion and vitamin adsorption profiles of phosphate binder

11. **Assuring vitamin K adequacy in pregnant and breast-feeding women is an**
important new focus. Vitamin K inadequacy in pregnancy has recently been
identified as a risk factor for **pregnancy complications** like hyperemesis
gravidarum, pre-eclampsia, intracranial bleeding in the infant, and excessive
blood loss at delivery. Although vitamin K transfer across the placenta is noted
to be poor, relative inadequacy in pregnancy can also contribute to poor nutrient
stores in infants.

Whether more generous maternal stores of vitamin K might enhance the
transfer to the fetus has not been evaluated. The recommendation of the
American Academy of Pediatrics is to provide vitamin K to newborns.
Additionally, breast-fed babies are noted to be at higher risk of inadequacy
apparently for the same reason … low vitamin K content of mother’s milk.
Again, whether relative maternal vitamin K inadequacy is a factor in the
breastmilk vitamin K content has not been evaluated yet. [American
Academy of Pediatrics Policy Statement: Controversies Concerning
Vitamin K and the Newborn. Committee on Fetus and Newborn.
Pediatrics Vol. 112 No. 1 July 2003, pp. 191-192]

12. **New roles of vitamin K are being recognized.** For example, failure to
activate osteocalcin because of inadequate vitamin K appears to have a negative
effect on **energy metabolism, including insulin metabolism.** A possible role
of vitamin K inadequacy in **diabetes and obesity** is just beginning to be
examined. This is in addition to the cardiovascular, bone, and renal health
issues.

13. **Assuring vitamin K adequacy appears to be a factor in some aspects of the**
**prevention or treatment of cancers** of the liver, colon/rectum, prostate,
pancreas and ovaries. Other recent areas of investigation include a role of
vitamin K inadequacy in **hypertension** (high blood pressure) and
**inflammatory diseases** such as arthritis. Dietary vitamin K appears to have a
role in **sulfatide metabolism, myelin structure and behavior functions.**
14. Big Point:

All of the health concerns described above are made less severe by the same interventions:

Assure adequacy of vitamin K status for everyone from foods and/or supplements. (Do not ASSUME adequacy.)

If a person is on the anticoagulant medication Coumadin*, assure that the vitamin K is administered in a consistent manner each day and that the physician has approved any adjustments of vitamin K intake.

Remember that inducing a vitamin K deficiency is common in this context, makes the drug use more dangerous, and causes damage to the cardiovascular system, the renal system, bone health and increases risk of certain cancers. *Note that many anticoagulants do not involve vitamin K in their function as Coumadin does, so it makes even less sense to restrict vitamin K with these medications.

Adjust intake recommendations to compensate for conditions associated with malabsorption and the effects of aging.
Some Vitamin K Facts and Figures

Adequate Intake (AI) for Vitamin K

<table>
<thead>
<tr>
<th>Life Stage</th>
<th>Age</th>
<th>mcg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>0-6 months</td>
<td>2.0</td>
</tr>
<tr>
<td>Infants</td>
<td>7-12 months</td>
<td>2.5</td>
</tr>
<tr>
<td>Children</td>
<td>1-3 years</td>
<td>30</td>
</tr>
<tr>
<td>Children</td>
<td>4-13 years</td>
<td>55</td>
</tr>
<tr>
<td>Adolescents</td>
<td>14-18 years</td>
<td>75</td>
</tr>
<tr>
<td>Adults *</td>
<td>19 years and older</td>
<td>Males 120</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Females 90</td>
</tr>
<tr>
<td>Pregnancy or</td>
<td>18 years and younger</td>
<td>75</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy or</td>
<td>19 years and older</td>
<td>90</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


*Older adults [for sure] may benefit from higher regular intakes than are listed in the Advisable Intakes (AIs.) These were developed with the assumption that intestinal production of usable vitamin K provided a more significant amount. Current AIs for other age groups have not been re-evaluated since the discovery that the intestinal bacterial sources are far less available than was believed, so it is not just the elderly who may be at risk. The rest have not been checked yet.

Sources of Vitamin K

Leafy Vegetable Food Sources

Phylloquinone (vitamin K1) is a major dietary form of vitamin K, and the major food source is leafy green vegetables. Not all green vegetables are good sources . . . it’s the darker leafy ones that have the most! Additional benefits of these foods are the extremely low calories and the generous provision of other vitamins (such as vitamin C and vitamin A as beta carotene) and potent antioxidant phytochemicals such as lutein.

There are many excellent reasons to include these foods in one’s diet. This is also true for people using anticoagulation medications like Coumadin (warfarin.) As described earlier, the goal is to assure both an adequate intake of vitamin K and a consistent level of intake. No one benefits from vitamin K deficiency.

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving</th>
<th>Vitamin K1 (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seaweed, dulse dried</td>
<td>100g (3.5 oz)</td>
<td>1700</td>
</tr>
<tr>
<td>Kale, raw</td>
<td>1 cup (chopped)</td>
<td>547</td>
</tr>
<tr>
<td>Broccoli, cooked</td>
<td>1 cup (chopped)</td>
<td>420</td>
</tr>
<tr>
<td>Parsley, raw</td>
<td>1 cup (chopped)</td>
<td>324</td>
</tr>
<tr>
<td>Swiss chard, raw</td>
<td>1 cup (chopped)</td>
<td>299</td>
</tr>
<tr>
<td>Green tea, dried</td>
<td>1 oz (28 g)</td>
<td>199</td>
</tr>
<tr>
<td>Spinach, raw</td>
<td>1 cup (chopped)</td>
<td>120</td>
</tr>
<tr>
<td>Leaf lettuce, raw</td>
<td>1 cup (shredded)</td>
<td>118</td>
</tr>
<tr>
<td>Iceberg lettuce 1 leaf</td>
<td>(20 g)</td>
<td>22</td>
</tr>
<tr>
<td>Watercress, raw</td>
<td>1 cup (chopped)</td>
<td>20-85 (various refs)</td>
</tr>
</tbody>
</table>

Pennington, JA. Bowes & Church’s Food Values of Portions Commonly Used, Ed. 16 Phil: Lippincott Co., 1994
Oil Food Sources

Some is available in vegetable oils, but they contribute far less vitamin K than leafy green vegetables. And, it is fairly impractical and also unwise to suggest that people attempt to meet their vitamin K requirements by increasing fat intake substantially.

Additionally, hydrogenation of vegetable oils may decrease the absorption and biological effect of dietary vitamin K.


<table>
<thead>
<tr>
<th>Food Serving: 1 Tbsp</th>
<th>Vitamin K1 (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybean oil</td>
<td>26 – 76 (various refs)</td>
</tr>
<tr>
<td>Canola oil</td>
<td>20</td>
</tr>
<tr>
<td>Mayonnaise</td>
<td>12</td>
</tr>
<tr>
<td>Corn oil</td>
<td>0 - 7 (various refs)</td>
</tr>
<tr>
<td>Olive oil</td>
<td>8</td>
</tr>
</tbody>
</table>
Animal Food Sources:

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving</th>
<th>Vitamin K1 (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meat</td>
<td>3.5 oz</td>
<td>4</td>
</tr>
<tr>
<td>Raw Beef Liver (others less)</td>
<td>3.5 oz</td>
<td>104</td>
</tr>
<tr>
<td>Milk</td>
<td>8 oz</td>
<td>10</td>
</tr>
<tr>
<td>Egg Yolk</td>
<td>1 large</td>
<td>25</td>
</tr>
</tbody>
</table>

Fermented Food Sources:

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving</th>
<th>Vitamin K2 (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natto (fermented soybeans)</td>
<td>1 oz</td>
<td>245</td>
</tr>
<tr>
<td>Curd Cheese</td>
<td>1 oz</td>
<td>20</td>
</tr>
</tbody>
</table>

Non-Food Sources: Intestinal Bacteria

Bacteria that normally colonize the large intestine synthesize menaquinones (vitamin K2), which are active forms of vitamin K. Until recently it was thought that up to 50% of the human vitamin K requirement might be met by this bacterial synthesis. Recent research indicates that the contribution of intestinal bacterial synthesis is much less than previously thought, although the exact contribution remains unclear.

Most of our menaquinones we actually make ourselves from phylloquinone. The likelihood is that even healthy people are more dependent on food sources of vitamin K than we previously believed. Individuals taking chronic antibiotics are far more dependent on food or supplement sources, of course, because these “friendly” colonic bacteria are killed by the medication as well.

Non-Food Sources: Supplements

In the U.S. vitamin K1 is available without a prescription in multivitamin and other supplements in doses that generally range from 10-120 mcg per dose. Vitamin K2 supplements are also available now.  

(PDR for Nutritional Supplements. Montvale: Medical Economics Company, Inc; 2001.)

The amount of vitamin K associated with a decreased risk of hip fracture in the Framingham Heart Study was about 250 mcg/day. This can be obtained from a little more than 1/2 cup of chopped broccoli or a large salad of mixed greens every day. A multivitamin with minerals that provides at least the AI level of vitamin K would also be an excellent idea, and the label should be checked closely because vitamin K is notoriously variable between various products.

Many vitamin supplement products contain none because of the earlier assumptions about the GI bacterial sources providing a significant amount. Some chewable calcium supplements provide some vitamin K and vitamin D. Again, check the label. A form of vitamin K2, menatetrenone (MK-4) has been used to treat osteoporosis in Japan and is currently under study in the U.S National Institutes of Health. K2 as MK-7 is the form produced in natto.

Many earlier references state that vitamin K inadequacy is extremely unusual in adults. Testing for vitamin K inadequacy is also generally rare because inadequacy is assumed to not be a problem. Traditionally testing involves measuring prothrombin time. However, it appears that this hematological manifestation of inadequacy may not reflect adequacy of vitamin K for other functions. For example, newer studies use undercarboxylated osteocalcin or other measures as a marker of vitamin K inadequacy in bone and cardiovascular applications in particular.

Vitamin K adequacy has not been in the public health radar … or the radar of health care professionals. Consider, for example, the mypyramid.gov guidelines*, which are an effort to help people achieve an advisable intake of all nutrients over two weeks in 2000 kcals/day. Vitamin K is simply not included in the analysis. Vitamin D is missing as well. Apparently these nutrients are assumed to be adequate because “you can make your own.” In the case of vitamin D, this assumed adequacy
is now being discarded because of the overwhelming evidence that vitamin D deficiency is actually a huge but previously unrecognized public health problem. It is possible that the assumption of vitamin K adequacy may turn out to be similarly suspect. **In any case, with the clear safety of generous vitamin K in normal circumstances, it would be advisable to simply assure adequacy rather than to assume it.**


### Vitamin K Nomenclature

<table>
<thead>
<tr>
<th>Older nomenclature</th>
<th>IUPAC (abbreviation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>K1</td>
<td>Phylloquinone (K)</td>
</tr>
<tr>
<td>K 2(n)</td>
<td>Menaquinone-n (MK-n)</td>
</tr>
<tr>
<td>K2(4)</td>
<td>Menatetrenone (MK-4)</td>
</tr>
<tr>
<td>K2(35)</td>
<td>Menaquinone-7 (MK-7)</td>
</tr>
<tr>
<td>K3</td>
<td>Menadione</td>
</tr>
</tbody>
</table>


### Toxicity Issues

**There is no known toxicity associated with high doses of phylloquinone (vitamin K₁), or menaquinone (vitamin K₂) forms of vitamin K.**

**No tolerable upper level (UL) of intake of these forms of vitamin K has been established.**

The same is not true for menadione (vitamin K3) and its derivatives. Menadione can interfere with the function of glutathione, one of the body's natural antioxidants, resulting in oxidative damage to cell membranes. Menadione given by injection has induced liver toxicity, jaundice, and hemolytic anemia (due to the rupture of red blood cells) in infants, and is no longer used for treatment of vitamin K deficiency.

Contrary to popular belief, the fat-soluble status of vitamin K does NOT make it more likely to be toxic than water soluble vitamins.

The toxicity traditionally ascribed somewhat globally to the fat soluble vitamins is in fact due to the fact that two of them (vitamins A and D) have actual hormonal messenger roles in the body. For this reason, relative inadequacy or excess of the active hormonal form of these two vitamins can actually induce metabolic changes to occur. The other two fat soluble vitamins (E and K) and the water soluble vitamins (C and the B vitamins) are much less likely to be toxic because they exert no hormonal influence on tissues.

The fact that a substance dissolves in butter is not a measure of its potential toxicity, although most of us were taught that it is. This is an important big change in our understanding.

**Memory Devices:**

I always find it hard to keep these kinds of terms and numbers straight, so I usually make up a little mnemonic device to help me out.

Here’s the one I use for remembering which form of vitamin K comes from which source, and which is K1 and which is K2 (Feel free to totally disregard this section and make up your own.)

**Phylloquinone** starts with a P … as in “Plants.” (The vitamin K in leafy greens is Phylloquinone)

I think of the kind made in people’s intestines by bacteria or made in man from phylloquinone is **menaquinone** … that is, the kind made “in men.” (The kind of vitamin K made in men is menaquinone. Women too, of course.)

Because we convert phylloquinone to menaquinone for many of its uses, I think of **phylloquinone** (the spinach one) coming first (K1) and **menaquinone** (the kind made in man out of K1) as coming along **secondarily** (K2)
References by Topic:

(A version with abstracts of these references is also available.)

Inadequacy of Vitamin K:

(General and interesting:  J Nutr. 2014 May;144(5):743-50. Dietary intake of vitamin K is inversely associated with mortality risk.)

I. Contribution to Cardiovascular Disease: Arterial Calciosis, Renal Calciosis, Diabetes, Inflammation and Hypertension

2015


Thromb Res. 2015 Jan 26. Two enzymes catalyze vitamin K 2,3-epoxide reductase activity in mouse: VKORC1 is highly expressed in exocrine tissues while VKORC1L1 is highly expressed in brain.


Development. 2015 Mar 15;142(6):1095-101. Vitamin K reduces hypermineralisation in zebrafish models of PXE and GACI.

Atherosclerosis. 2015 Feb 24;240(1):10-16. Prevention of vasculopathy by vitamin K supplementation: Can we turn fiction into fact?


Nephrol Ther. 2015 Mar 17. The matrix-gla protein awakening may lead to the demise of vascular calcification.

2014


2013


Diabetologia. 2013 Sep;56(9):2100-1. The vitamin K-dependent Gla proteins and risk of type 2 diabetes.

2012


2005-2011


J Mal Vasc. 2009 Apr 2. Origin of the mediacalcosis in kidney failure


Osteoporos Int. 2009 Mar 12Prior treatment with vitamin K(2) significantly improves the efficacy of risedronate.


J Bone Miner Res. 2009 Jun;24(6):983-91. Vitamin k treatment reduces undercarboxylated osteocalcin but does not alter bone turnover, density, or geometry in healthy postmenopausal north american women.


J Vasc Res. 2008 Apr 10;45(5):427-436. The Circulating Inactive Form of Matrix Gla Protein (ucMGP) as a Biomarker for Cardiovascular Calcification.


Blood. 2006 Nov 30; Regression of warfarin-induced medial elastocalcinoses by high intake of vitamin K in rats.

Am J Health Syst Pharm. 2005 Aug 1;62(15):1574-81 Vitamin K in the treatment and prevention of osteoporosis and arterial calcification


II. Inadequacy of Vitamin K:

Contribution to Unsafe Variability of Anticoagulation Therapy

2011-2015


Am J Ther. 2014. Warfarin use and prevalence of coronary artery calcification assessed by multislice computed tomography.


2008-2010

J Manag Care Pharm. 2009 Apr;15(3):244-52. Meta-analysis to assess the quality of warfarin control in atrial fibrillation patients in the United States.
Blood Coagul Fibrinolysis. 2009 Apr 3. Erythrocyte folate and 5-methyltetrahydrofolate levels decline during 6 months of oral anticoagulation with warfarin.

2004-2007

INRJ Thromb Thrombolysis. 2007 Feb 24; Prospective study of supplemental vitamin K therapy in patients on oral anticoagulants with unstable international normalized ratios.
J Am Diet Assoc. 2007 Nov;107(11):2022. Vitamin K: what are the current dietary recommendations for patients taking coumadin?
Blood. 2006 Nov 16 Vitamin K supplementation can improve stability of anticoagulation for patients with unexplained variability in response to warfarin.

---------------------------------------------
III. Inadequacy of Vitamin K:

Contribution to Osteoporosis, Osteoarthritis, Bone Development, Rheumatoid Arthritis, and Related Conditions

2015

2014
Clin Nutr. 2014 May 28.. Vitamin K deficiency evaluated by serum levels of undercarboxylated osteocalcin in patients with anorexia nervosa with bone loss.
J Bone Miner Metab. 2014 May;32(3):290-7. Effects of risedronate alone or combined with vitamin K2 on serum undercarboxylated osteocalcin and osteocalcin levels in postmenopausal osteoporosis.

2013


Mod Rheumatol. 2013 Sep;23(5):1001-7. Vitamin K2 administration is associated with decreased disease activity in patients with rheumatoid arthritis.


2012

Osteoporos Int. 2012 Nov;23(11):2681-92. Vitamin K supplementation for the primary prevention of osteoporotic fractures: is it cost-effective and is future research warranted?

Calcif Tissue Int. 2012 Apr;90(4):251-62. Changes in parameters of bone metabolism in postmenopausal women following a 12-month intervention period using dairy products enriched with calcium, vitamin D, and phylloquinone (vitamin K(1)) or menaquinone-7 (vitamin K(2)): the Postmenopausal Health Study II.

2004-2010


J Bone Miner Metab. 2009 Dec 19. Hop rho iso-alpha acids, berberine, vitamin D(3) and vitamin K(1) favorably impact biomarkers of bone turnover in postmenopausal women in a 14-week trial.


Importance of calcium, vitamin D and vitamin K for osteoporosis prevention and treatment.

Vitamin K and D association stimulates in vitro osteoblast differentiation of fracture site derived human mesenchymal stem cells.

Recommendations for the management of bone demineralization in cystic fibrosis.

Effect of vitamin K supplementation on bone loss in elderly men and women.

Genomic approaches to bone and joint diseases. New insights into molecular mechanisms underlying protective effects of vitamin K on bone health.

Association of hip fracture incidence and intake of calcium, magnesium, vitamin D, and vitamin K.

Undercarboxylated osteocalcin and bone mass in 8-12 year old children with cystic fibrosis.

The balance of bone health: tipping the scales in favor of potassium-rich, bicarbonate-rich foods.

Low plasma phylloquinone concentration is associated with high incidence of vertebral fracture in Japanese women.

Steroid and xenobiotic receptor mediates a novel vitamin K2 signaling pathway in osteoblastic cells.

Nutrition and bone health projects funded by the UK Food Standards Agency: have they helped to inform public health policy?

Extremes in vitamin K status of bone are related to bone ultrasound properties in children with juvenile idiopathic arthritis.

Vitamin K linked to bone strength.

Pronounced elevation of undercarboxylated osteocalcin in healthy children.

Vitamin K content of foods and dietary vitamin K intake in Japanese young women.

Nutritional effects of gamma-glutamyl carboxylase gene polymorphism on the correlation between the vitamin K status and gamma-carboxylation of osteocalcin in young males.

Experience of vitamin K2 in Thailand.

Clinical application of undercarboxylated osteocalcin.

Measurement of serum undercarboxylated osteocalcin by ECLIA with the "Picolumi ucOC" kit.

Vitamin K2 supplementation improves hip bone geometry and bone strength indices in postmenopausal women.

Fracture risk in users of oral anticoagulants: a nationwide case-control study.

The coagulation vitamin that became omnipotent.

Not just calcium and vitamin D: other nutritional considerations in osteoporosis.

Vitamin K status in the elderly.

Fracture risk in users of oral anticoagulants: a nationwide case-control study.

Vitamin K deficiency inhibits mineralization & enhances deformity in vertebrae of haddock (Melanogrammus aeglefinus L.)


Clin Calcium. 2006 Sep;16(9):106-14 and Nutrition. 2006 Jul-Aug;22(7-8):845-52. (same article in both journals) Protective effects of vitamin K against osteoporosis and its pleiotropic actions.


Br J Nutr. 2006 May;95(5):982-8 Phylloquinone (vitamin K1) intakes and serum undercarboxylated osteocalcin levels in Irish postmenopausal women.


IV. Inadequacy of Vitamin K:

Cancer: Liver, Colorectal, Prostate, Ovarian, Pancreatic and Cancer Risk in General

2014-2015


2012-2013


Toxicology. 2013 Jan 7;303:139-46. Resveratrol inhibits TGF-β1-induced epithelial-to-mesenchymal transition and suppresses lung cancer invasion and metastasis.


Eur J Dermatol. 2013 Jan-Feb;23(1):77-82. Topical vitamin K1 may not be effective in preventing acneiform rash during cetuximab treatment in patients with metastatic colorectal cancer.


Black tea polyphenols reverse epithelial-to-mesenchymal transition and suppress cancer invasion and proteases in human oral cancer cells. Vitamin K3 analogs induce selective tumor cytotoxicity in neuroblastoma.

2007-2011

Br J Cancer. 2010 Apr 13;102(8):1224-34. alpha-Tocopheryl succinate promotes selective cell death induced by vitamin K3 in combination with ascorbate.


In situ modulation of oxidative stress: a novel and efficient strategy to kill cancer cells.


Vitam Horm. 2008;78:435-42 Hepatocellular carcinoma and vitamin K.


Cancer Sci. mitochondria-mediated cytotoxicity in human cancer cells.


Anticancer Res. 2008 Jan-Feb;28(1A):45-50. The utility of vitamin K3 (menadione) against pancreatic cancer.


J Cancer Res Clin Oncol. 2008 Jul;134(7):803-12. Induction of apoptosis in PA-1 ovarian cancer cells by vitamin K(2) is associated with an increase in the level of TR3/Nur77 and its accumulation in mitochondria and nuclei.


Hepatol Res. 2007 Sep;37 Suppl 2:S303-7. Potential role of vitamin K(2) as a chemopreventive agent against hepatocellular carcinoma.


Intern Med. 2007;46(11):711-5. Hepatocellular carcinoma with peritoneal dissemination which was regressed during vitamin K2 and vitamin E administration.


Clin Cancer Res. 2007 Apr 1;13(7):2236-45. Menatetrenone, a vitamin K2 analogue, inhibits hepatocellular carcinoma cell growth by suppressing cyclin D1 expression through inhibition of nuclear factor kappaB activation.


Clin Calcium. 2006 Sep;16(9):106-14 and Nutrition. 2006 Jul-Aug;22(7-8):845-52. (same article in both journals) Protective effects of vitamin K against osteoporosis and its pleiotropic actions.


## Miscellaneous

### Vitamin K Deficiency Associated with Intestinal Malabsorption Problems

#### 2014- 2015


2006-2013


Acta Clin Belg. 2011 Mar-Apr;66(2):142-3. Late vitamin K deficiency bleeding leading to a diagnosis of cystic fibrosis: a case report


J Cyst Fibros. 2008 May 27. Efficacy of high dose phyloquinone in correcting vitamin K deficiency in cystic fibrosis.


Masui. 2007 Feb;56(2):181-5. Suspicious case of epidural hematoma due to coagulopathy caused by vitamin K deficiency associated with antibiotics.


J Child Neurol. 2007 Jan;22(1):114-5. Cerebral hemorrhage as the initial manifestation of cystic fibrosis.


Vitamin K Inadequacy and Prenatal Health

2012-2015


2006-2011


Arch Dis Child. 2007 May 23; Vitamin K deficiency bleeding: the readiness is all.

Vitamin K deficiency bleeding in the Great Britain and Ireland; British Paediatric Surveillance Unit Surveys, 1993 - 94 and 2001 - 02.


Some Basic Science References: some recent study topics.

2010


Bioelectrochemistry. 2008 May 12. Direct and indirect methods for the determination of vitamin K(3) using differential pulse polarography and application to pharmaceuticals.


Vitam Horm. 2008;78:23-33. VKORC1 and the vitamin K cycle.


