

Menadione (Vitamin K3) Dangerous?
By Cheri Pursell of It's Kibblesense!

What are the facts in question?

- 1. Is this substance toxic in the application of pet food supplement?**
- 2. What facts or evidence are present in scientific literature to support the argument that this substance is a dangerous ingredient in a pet food formulation?**
- 3. What is the common amount of menadione used in pet food formulations and how does this amount relate to possibly toxicity?**

To offer another side of this argument here is a link to an article on the topic by a pet food industry expert (<http://www.petfoodindustry.com/ViewArticle.aspx?id=16414>) as well as an interesting article about a study in pet birds and Vitamin k3 (<http://www.ingentaconnect.com/content/b...rmat=print>)

My view? After tons of searching I have yet to be able to find an article that discusses an actual case of Vitamin k3 poisoning. It appears, according to the NRC (National Research Council) that it takes 1,000 times the normal dosage to cause toxicity in animals. We know there is not that amount in pet food. The synthetic version of vitamin k that we are talking about is also water soluble rather than fat soluble like vitamin k1 (the natural form found in green leafy veggies etc). Water soluble vitamins do not build up in the system; fat soluble vitamins do.

This was also stated in the Wysong article; (see <http://www.wysong.net/vitamink.shtml>)

Quote: Menadione (150-200 mg/day IV), as a radiosensitizing agent, was discovered to increase survival time (5.42 months with Menadione and radiation versus 3.77 months with radiation alone) in inoperable bronchial carcinoma patients. (36) Pretreatment of mice with transplanted mouse liver tumors by oral or intraperitoneal injection of vitamins K3 and C greatly potentiated the action of radiation (20-40 Gy dosages) compared to controls. (37) In rats, Menadione was active against Adriamycin-resistant leukemia cells. (3) Hepatoma-bearing rats receiving intraperitoneal injections of Menadione (10 mg/2mL weekly for four weeks) demonstrated an increased survival rate of 60 days compared to 17 days for controls (five of 16 lived longer than controls). (15) The anticancer activity of Menadione has also been demonstrated in a number of in vitro studies using both rodent (10,39-42) and human cancer cell lines. (11,12,43-45) Menadione was effective against multidrug-resistant leukemia cell lines and parental leukemia cell lines. (43)

This is apparently the study that produced the above quote;

Potential therapeutic application of the association of vitamins C and K3 in cancer treatment. Calderon PB, Cadrobbi J, Marques C, Hong-Ngoc N, Jamison JM, Gilloteaux J, Summers JL, Taper HS. Unite de Pharmacocinetique, Metabolisme, Nutrition et Toxicologie, Faculte de Medecine, Universite Catholique de Louvain, Bruxelles, Belgium. calderon@pmnt.ucl.ac.be

The decision of stressed cells to die or to survive is made by integrating signals at different levels through multiple check points. However, initiation and continued progression toward cell death by apoptosis in cancer cells may be blocked by mutation of the tumor suppressor p53 or overexpression of members of the bcl-2 family of proteins. The existence of such mechanisms indicates that cancer cells lose the controls regulating their cell cycle. Therefore, the activation of their programmed cell death appears as a major therapeutic target. Oxidative stress can stimulate growth, trigger apoptosis, or cause necrosis

*depending upon the dose and the exposure time of the oxidizing agent. A large body of evidence supports the idea that oxidative stress induced by redox cycling of vitamins C and K(3) in association surpasses cancer cellular defense systems and results in cell death. The molecular mechanisms underlying such a process are, however, still unknown. Indeed, several types of cell death may be produced, namely autoschizis, apoptosis and necrosis. Combined vitamin C and K(3) administration in vitro and in vivo produced tumor growth inhibition and increased the life-span of tumor-bearing mice. CK(3)-treatment selectively potentiated tumor chemotherapy, produced sensitization of tumors resistant to some drugs, potentiated cancer radiotherapy and caused inhibition of the development of cancer metastases without inducing toxicity in the host. We propose the association of vitamins C and K(3) as an adjuvant cancer therapy which may be introduced into human cancer therapy without any change in the classical anticancer protocols, and without any supplementary risk for patients.
PMID: 12470246 [PubMed - indexed for MEDLINE]*

Basically, I personally am not seeing this ingredient as a problem. I have seen no real facts that show that this chemical is toxic or causes ill health when used as directed.
My conclusions as far as the questions I posed above?

1. Is this substance toxic in the application of pet food supplement?

No, this ingredient has been used in pet and animal foods for over 50 years with no documented toxicity issues.

2. What facts or evidence are present in scientific literature to support the argument that this substance is a dangerous ingredient in a pet food formulation?

None. To this date, I have found no such peer reviewed scientific or acceptable articles or case studies that give such information.

3. What is the common amount of Menadione used in pet food formulations and how does this amount relate to possibly toxicity?

Nutrient Requirements of Dogs 1985," the 6-member panel of experts on dog nutrition makes the following statement (page 27): "Although it is doubtful that supplemental vitamin K is necessary for the normal dog, it may be prudent to provide 22 micrograms of Menadione (or vitamin K equivalent) per kilogram of body weight daily for adult maintenance and 44 micrograms per kilogram of body weight during growth. This would be more than supplied by a dry diet concentration of 1.0 mg of Menadione per kilograms."

Hypervitaminosis K

Vitamin K1 is apparently safer in large quantities than the water-soluble analogs and derivatives of Menadione (vitamin K3). The latter are widely employed, but they may produce toxic side effects in the newborn when administered parenterally. **Doses up to 10 to 25 mg of vitamin K have been administered to pregnant women prior to and during delivery, or to the newborn infant, to prevent hypoprothrombinemia and hemorrhagic disease in the child. When vitamin K1 was used, this practice was apparently not harmful; however, 5 to 10 mg of menadiol sodium diphosphate administered daily to infants produced hemolytic anemia, and 10 mg given 3 times a day for 3 days to premature infants resulted in kernicterus and death. (note this previous section is about HUMANS and Vitk3 effects on HUMAN newborns.)**The mechanism of toxicity involves erythrocyte hemolysis and subsequent overloading of an immature liver with bilirubin, which cannot be sufficiently conjugated and which in turn proves toxic to the neonatal brain (kernicterus) (Miller and Hayes, 1982). The only reported case of toxicity in the dog occurred in a 1-year-old female Great Dane that ingested a packet of Warfarin and was treated intravenously with 30 mg of vitamin K1 in 5 percent dextrose and lactated Ringer's solution. An acute urticaria was observed with wheals first appearing on the face before

progressing caudally over the entire trunk. Flatulence, lacrimation, and salivation were also noted (Jordan, 1979).

So, it appears the recommended dosage of Menadione in dog food would be 1.0mg per kg of food. The only reported toxicity issue/reaction to vitamin k in a dog was to the natural form Vitamin K1.

Now, I did go to The Dog Food Project article and again read through it. I searched the references provided and found they are all references to German books on nutrition or vitamins, none are studies. It appears the author of this article has assumed that because VitK3 is so very dangerous to human newborns it must also be dangerous to dogs (and cats.) This is a false assumption IMO as one reads all the literature they would understand that the negative reaction to vitk3 is severe in human beings (specifically infants) but not in animals. There is not one fact present within that article to show the possible toxicity in dogs, not one. It all revolves around the problem in human beings. This does not make vitamin k3 toxic to dogs anymore than dogs being sensitive to chocolate makes chocolate toxic to human beings.

I believe this is simply a case of over-reaction and oversimplification. The industry, the chemists, the veterinarians and pet food companies know this ingredient is not harmful to dogs as it is their job to know such things. They have a wealth of information to draw upon to reach their conclusions whereas we, the general public do not. References in a few nutritional books for human beings do not support the premise that Menadione in any form is toxic when used to supplement vitk in pet foods.

Here is some additional veterinary information on Vitamin K and Menadione:

http://books.nap.edu/openbook.php?record_id=949&page=31