

# **The Benefits of Vitamin K1 and K2:**

## **A Special Interview with Dr. Leon Schurgers**

By Dr. Joseph Mercola

**DM: Dr. Joseph Mercola**

**LS: Dr. Leon Schurgers**

**DM:** We all know the importance of vitamin D as do many physicians at this time. However, the underappreciated and virtually equivalent in benefit vitamin is vitamin K2. Very little is known about it. The media doesn't talk about it too much. We're going to find out more about that today. This is Dr. Mercola, helping you take control of your health. Today I'm joined by Dr. Schurgers, who is a senior scientist and who comes to us from the Netherlands. He's doing his PhD work in vitamin K. He's one of the leading researchers in the world on this.

We're just delighted to have you with us today. I'm wondering if you could help us in our effort to understand more about vitamin K2 and its benefits on human health. If you can give us a little history of how you first started your research on this, so our viewers will have a better understanding of what your technical expertise is.

**LS:** Thank you for inviting me to give some background on vitamin K. I started my research some 20 years ago at Maastricht University, which is located in the Netherlands, at the very south of the Netherlands. Like every young PhD student, I was appointed to do a certain subject. Our group was located in the biochemistry department, which is thrombosis and hemostasis. Actually vitamin K is well known for its function in thrombosis, because it activates certain proteins, which are involved...

**DM:** Well, that's vitamin K1, right?

**LS:** Well, also vitamin K2.

**DM:** Is that right?

**LS:** Yes. Both K1 and K2.

**DM:** Interesting. I thought it was pretty much exclusively connected to K1.

**LS:** All K vitamins have more or less the same function, which is related to the first part of the vitamin, which is called the naphthoquinone ring structure. That is similar...

**DM:** What is it again?

**LS:** Naphthoquinone ring structure. That is actually the same for K1 and K2. They're both vitamins, different in side chain.

When I started this research, I was appointed to investigate vitamin K. I thought it's interesting to look also at vitamin K2, because at that time, we were in collaboration with a university in the western part of the Netherlands, which is Rotterdam University. They were looking on the so-called Rotterdam Study. For that, they wanted to investigate vitamin K intake with cardiovascular outcome. Actually my task in

my PhD thesis was to measure vitamin K1 and also K2 in a whole list of food items, which are very frequently eaten in the Netherlands. Actually that was the first time that I became interested in vitamin K.

**DM:** I'm wondering if you could help us understand the benefits or the functions of vitamin K1 and K2 and then ideally the food sources that we get them from, so that people can have a fuller appreciation of the benefits. In my perspective, I mean, certainly vitamin K1 is crucial. We have to have it otherwise... People who don't, they have very serious bleeding issues. But K2 is just the stealth master supplement – not vitamin – that has such profound influence on our health, but it really isn't appreciated. In my mind, it almost seems to almost have as many similar benefits as vitamin D. Why don't we start hearing from the expert who's looking at this full-time?

**LS:** I have to go back one step and maybe explain that vitamin K is extremely important in general for certain areas in your body.

**DM:** Okay.

**LS:** For example, it is known that vitamin K is important for good blood clotting. I don't want you to get bleeding. We know all of that because all newborns in the world, they receive at birth a shot of vitamin K. Even before they do anything else with your babies, they give them vitamin K to prevent the hemorrhagic disease of the newborn or as we call it today vitamin K deficiency in newborn. Vitamin K is extremely important for blood clotting, for good blood clotting.

In the '80s, there was this other protein, osteocalcin, which is also vitamin K-dependent. We know that it needs vitamin K to be activated. Later on, it was in the mid90s, matrix Gla protein (MGP), another vitamin K-dependent protein, has a function outside of the blood clotting.

**DM:** Osteocalcin and MGP...

**LS:** MGP.

**DM:** They're mostly vitamin K2 or vitamin K1 also?

**LS:** Both.

**DM:** Oh, interesting.

**LS:** I want to explain it and then come back to the benefit of vitamin K2.

**DM:** Okay.

**LS:** At least what it showed is that MGP also needs to be activated. Actually at this moment, we do not know any of the vitamin K-dependent proteins would function when it is not carboxylated, when it is not activated by vitamin K. All of the vitamin K-dependent proteins are really in need of vitamin K to fulfill a kind of biological function. Where does the difference between K1 and K2 come about? Actually we established that for the first time in the Rotterdam Study. What we did is...

**DM:** Were you a part of this study?

**LS:** Yes. We published this in 2004. Actually the study started, as I explained, when I started my PhD in '98. I measured a bunch of food items on vitamin K content. Everybody is always forcing on vitamin K1. That is because vitamin K1 is really highly available in green, leafy vegetables – spinach, kale, and...

**DM:** Cabbage.

**LS:** Cabbage, yes. There is a high amount. However – and that is something which was already shown before I started my PhD – the absorption of vitamin K1 from food is extremely low. Only 10 percent of the vitamin K, which is found in green leafy vegetables, is absorbed in our body. Even if you have a high amount in food item, only 10 percent of that is absorbed by the body.

That was when we started to measure also vitamin K2 in food items. We discovered that it was only present in fermented foods. Vitamin K2 is produced by bacteria in the fermentation product. For example, cheese is a fermented milk product. There, we find high amounts of vitamin K2. Still, the total amount of vitamin K2 in cheese is lower than K1 in green leafy vegetables. However, all the vitamin K2 is absorbed by the body. There's no difference between our synthetic K2 and K2 in the food item. Vitamin K2 in the food item is nearly completely absorbed. That makes a huge difference. There is a better absorption in K2 compared to K1.

In the Rotterdam Study, we looked at K1 and K2 intake. People had to fill in a preconceived questionnaire, and then you'll have an idea of how much food occurred and consumed and how much vitamin K is remitted to them – K1 or K2, or K1 and K2.

What we found out is that there was a huge difference. K2 in the highest tertile of intakes, where people consuming K2 the most compared to the other two tertiles, had the lowest risk of cardiovascular disease, had the lowest risk of cardiovascular calcification, and also had the lowest chance of dying from cardiovascular disease. That was really a great discovery, because for K1 such a correlation was not there. Vitamin K2 has certain benefits above K1 that protects the vasculature from being calcified; protects people from, let's say, dying from cardiovascular disease, at least this epidemiological study showed that.

Later on, there were more studies also from the Netherlands. They showed that actually it was safe. K2 has benefits; K1 has none. That is when we started to investigate what the difference between K1 and K2 is. If you absorb vitamin K1 and K2, we showed that K1 is mainly going to the liver and also stays there. It has a relatively short half-life. After three to four hours that you ingest a dose of vitamin K or one from the food, it is gone. It is taken up by the liver. However for K2, it is going to the liver, but the liver also redistributes it by the low density lipoprotein (LDL) cholesterol fraction. Now, we all know that the LDL cholesterol is also going to peripheral tissues such as bone and vasculature.

**DM:** Are they equally fat-soluble?

**LS:** Both are fat-soluble, but K2 is more fat-soluble, at least in long-chain menaquinones such as MK7.

**DM:** Okay.

**LS:** MK7 is transported, when you take it from the food, more to the vasculature as compared to the vitamin K1. We reasoned and we hypothesized that that is one of the main functions – that K2 has such benefit in cardiovascular system and that K1 is more present in the liver.

**DM:** I was surprised to learn that there's only 10 percent of the K1 that's absorbed from the vegetables.

**LS:** Yes.

**DM:** I'm wondering, does your research show any way to increase that absorption? Would juicing increase the absorption or are there any other food sources you could take with it that could enhance the absorption?

**LS:** Yes. That's a good question. We did several studies. Let's say, increasing the amount of fat in the diet together with the green leafy vegetables and to cook it more [roughly 09:14]. But actually only 10 percent or 50 percent...

**DM:** [Inaudible 09:18], too?

**LS:** You couldn't.

**DM:** There's no variable or modification of the consumption that will increase the absorption?

**LS:** None. And the difference is a little bit. Spinach is only 10 percent absorption and some other... Broccoli, for example, has slightly higher vitamin K1.

**DM:** Okay. You also mentioned the two primary benefits of K2 would be the calcification. It essentially transfers the calcium from where it's not supposed to be (in the lining of the blood vessels) to where it's supposed to be (in the bone). It does it much better in the adolescent years when you're still forming your bone.

But I'm wondering if there are any neurological benefits when you think of the discussion of Alzheimer's, which we really don't know what causes or at least precisely. I mean, we have some good theories about it. But it seems that the vascular flow to the brain has to be an important component. Many of the people who have a form of diagnosis of Alzheimer's, once they're autopsied, they find out that there really wasn't this cellular degeneration; it was more of a vascular degeneration. I'm wondering what the research shows in the neurological...

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**LS:** Actually, it's a very good question and it's a very intriguing question. Nobody actually knows. Nobody ever really studied vitamin K2, researching Alzheimer's disease. It's funny that you mentioned this disease, because Alzheimer's disease is characterized by amyloid deposition, plaque deposition. The same is what happens in our arteries if you get atherosclerosis.

**DM:** Interesting.

**LS:** We recently showed that vitamin K deficiency induced by vitamin K antagonists (VKA) makes unstable plaques. Maybe this has also an effect on Alzheimer's. However, we don't know yet.

**DM:** So, it has not been studied. But there's good experimental evidence that suggest that it plays a major role there.

**LS:** In plaque deposition, yeah. There is another function of vitamin K2. It's not from our group. It is from a study, which was published two years ago in *Science*, a very high-ranking journal. They showed that vitamin K2 has a major function in delivering energy for Parkinson's disease patients.

**DM:** Interesting. In the prevention or treatment – or both?

**LS:** That would be in the treatment. Because Parkinson's disease patients, they lack energy production in the brain and certainly in the cells. Vitamin K2 could help in providing the energy by being an electron transporter and thereby delivering adenosine triphosphate (ATP) and more energy in these cells. Just to stress out and to mention this, my group is really working on vitamin K2 and cardiovascular calcification, but there are more functions of vitamin K, which we do not know of.

**DM:** It's in the early stages.

**LS:** Yes.

**DM:** Does it work similar to coenzyme Q10 or ubiquinol, where it works on the mitochondrial function?

**LS:** Yes. That is the idea: the bacteria in fermented food that produced the menaquinones, the long-chain menaquinones like MK7, to transport the electrons.

**DM:** Okay.

**LS:** And to generate ATP in the cells.

**DM:** That's really how you get your energy.

**LS:** That's the fuel.

**DM:** Absolutely. That's your engine that gives you energy. You got to bring it something.

**LS:** Yes.

**DM:** The food that we consume really drives the transfer of electrons at a cellular level.

**LS:** Yes. It's great interplay between bacteria and the human body.

**DM:** Interesting. Do you have a research group out there in vitamin K2?

**LS:** At this moment, I have. Yes.

**DM:** How many people are under your department?

**LS:** At this moment, my chemistry department is somewhere around 70 persons. Our group, working on vitamin K and cardiovascular calcification, is me... We have one post-doc and we have four PhD students.

**DM:** Great. Can you tell us some of the exciting... Well, right before some of the research you have done now. Maybe a nice summary of the differences between K1 and K2, because many people are not familiar about the clotting component. Actually that is a common question. People want to get the benefits of vitamin K, yet they're concerned because they get some type of clinical condition where their clinician needs to have them on an anti-clotting agent like Coumadin or Warfarin. They're told not to take vitamin K. But my understanding previously was that was vitamin K1. Maybe we can talk about that and the process. Differentiate the two components.

**LS:** It's a very good question and very relevant also, clinically relevant. Vitamin K1 and K2 interferes or actually activates certain coagulation factors. There are four – 2, 7, 9 & 10 – in the coagulation cascade, which are activated by vitamin K. Our group, my group, did a lot of research on that, investigating the effects of vitamin K, both K1 and K2, on activity. One thing we have to make clear and which we can state is that if you take a lot of vitamin K, it does not overcoagulate. In other words, your coagulation factors, your coagulation system will not be more active if you take more vitamin K, either K1 or K2. People can very safely consume vitamin K in the absence of oral anticoagulants.

Your second question relates to some people... And actually there quite a number of elderly people who has atrial fibrillation (AF) or for example, venous or deep-vein thrombosis, they are put by their clinicians on oral anticoagulants. And as the name says, they're vitamin K antagonists; they're antagonizing the function of vitamin K. They do that for both K1 and K2. There is no differential...

**DM:** These drugs block both vitamin?

**LS:** Yes.

**DM:** Okay.

**LS:** What the drug does is it blocks the recycling of vitamin K, not only K1 but also K2.

**DM:** Interesting.

**LS:** If you take oral anticoagulants – Coumadins and Warfarins (I think those are the most common, Coumadin is taken in the United States) – you have to be careful with K1 and K2. However, the advice in the United States is to skip everything that contains vitamin K, and that is something I argue against. Because if you take away all the K1 and K2 from the diet, every little interference if you take a little bit of vitamin K, it has already a dramatic effect on the anticoagulant level. However, if you have a steady state or intake level of vitamin K1 or K2 or both, a little bit of interference is not that bad anymore.

**DM:** Yes. They're relative.

**LS:** Yes. I advocate, please take every day vitamin K from the diet and, like your clinician, put the anticoagulant level on top of that.

**DM:** That seems to be a very pragmatic approach. But I'm wondering if there's any benefit to doing that. Does the time it takes for the drug to inactivate the vitamin K, are they able to support the body in some way? Or is it just simply, if you're taking this drug, you're not going to get any vitamin K1 or K2?

**LS:** Well, you anticoagulate, do lower. You got to be observant of vitamin K-dependent proteins. You do that in the liver, the coagulation effect. But you also do that in the bone, whether it's osteocalcin, a vitamin K-dependent protein, or in the vasculature where you have matrix Gla protein, also a vitamin K-dependent protein. Unfortunately, there is no real benefit, at least it is not proven yet, to take extra vitamin K on top of this Coumadin and I would not advocate that. I would always listen to my...

**DM:** No, I understand that. You're suggesting getting vitamin Ks from natural sources – in the case of K1 these green leafy vegetables and in the case of K2, it's some type of fermented foods.

**LS:** Yes.

**DM:** But if you have that stable level and the clinician adjusted the anticoagulant dose, so that you're properly anticoagulated to prevent some type of catastrophe, is the underlying level of the vitamins before they activate going to provide some benefits in promoting the osteocalcin and the matrix Gla protein to improve bone density and cardiovascular health?

**LS:** It's a good question. Actually, there is no true science on that, so we cannot... We don't know. The only thing we know – and that is a major part of my research – is how do you convince people in the medical community that vitamin K metabolism is important for cardiovascular health? How do you do that? You can advocate taking more vitamin K, but then they will say, "Okay, we have commissions. We are not busy with these kinds of things."

I approached it from a different side. We, my group, approached it as how is your cardiovascular health if you take vitamin K antagonists long-term? We have now several studies showing – and they're all published in high-ranking journals – that if you take vitamin K antagonists long-term, you are more susceptible to vascular calcification. And of course...

**DM:** And I assume osteoporosis, too.

**LS:** There is less evidence on osteoporosis.

**DM:** Interesting. So, mostly just vascular calcification?

**LS:** Yes, mainly vascular calcification. I think it is because of the osteoporosis, because adult bone is not [inaudible 18:57] anymore.

**DM:** Okay.

**LS:** There are a lot of pre-clinical studies in experimental animals showing that in growing bone, Warfarin and Coumadin, which are vitamin K antagonists, do have an effect. On mature bone, it's less.

**DM:** Interesting. That really is an interesting observation. It's just fascinating all this new science that's coming up. But I'm wondering if you can comment on some of the research as it relates to some of the cardiovascular complications of vitamin K2.

**LS:** Yes. Actually that started that this protein, matrix Gla protein, is present in the vasculature. It's one of the strongest inhibitors in the theory of calcification. That was found out by researchers here in New York, in the United States, where they made a mouse, which lacks this protein, so that they can study the function of this protein. Because the protein was purified from bone, people were thinking, "Okay, this protein has something to do with bone remodeling."

However, all that mice were born to term and all died within eight weeks after birth. When they gave the mice a closer examination, they saw that all the vasculature, all the big arteries were completely calcified, and all the mice died due to rupture of these calcified arteries. From that time on, everybody knew that this MGP, matrix Gla protein, a vitamin K-dependent protein, is a strong inhibitor of the theory of calcification, which is modified.

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There was another group in San Diego State University that investigated the use of Coumadin and Warfarin, and also showed that if you inactivate this protein, this MGP, rats develop serious medial arterial calcifications. That is a model which my group also adapted, and we are working on that. Actually if you give mice or rats this vitamin K antagonist, which is actually a rat poison (it's common as a rat poison or used as a rat poison), you'll induce arterial calcification both in the media but also in the internal atherosclerotic plaques. We can use this model to interfere with vitamin K later on.

What we showed – and this is a recent study which we did together with the University Clinic Aachen with their nephrologists, medical doctors working with kidney disease. We did a collaboration in mice, which we treated with Warfarin in combination with vitamin K1 to prevent bleeding. But if we gave this mice additional K2, we found out that these mice didn't calcify in the vessel wall. There is a benefit of giving extra vitamin K to prevent vitamin K deficiency in the vessel wall and thereby prevent arterial calcification. This is actually a study that is complementary with a study we performed in 2007, which we published.

Vitamin K can prevent and even regress a little bit arterial calcification induced by vitamin K deficiency. The beauty of this is that you can use these quick clinical models, but of course, it's difficult to translate that into human physiology or human pathology. But at this moment, we are facing three or four clinical trials in which vitamin K is given as a treatment option in patients to ward off the progression of arterial calcification.

I can elaborate a little bit on that. There is one study in our institute that is funded by the Dutch Heart Foundation, which is a grant from the government. What we investigated in this grant are 200 patients with already some arterial calcification in their coronary arteries. Placebo-controlled, double-blind study – 100 patients on placebo and 100 patients on MK7. For two years, we screened computed tomographic (CT) measurements – one at baseline, one at one year, and one at two years of treatment. What we hoped

to find out as a primary outcome is “Can vitamin K2 hold progression or even induce regression of coronary artery calcification?”

**DM:** When do you expect to get the results?

**LS:** Well, we are actually including now the last patients. Beginning 2015, we hope that we have included all the 200 patients. There are another two years before the end of the study. Hopefully, in two years, we can come back and tell that we have a major breakthrough.

**DM:** It’s very interesting, because when I was in medical school in the late ‘70s, matrix Gla protein was not known by any human on the planet, which underlines the importance of physicians... Because many physicians will go to school and they just stop reading. The only information they get on advancements in health they is the drug model.

The reason I mentioned this is it was discovered in the ‘90s, matrix Gla protein, so 20 years ago. Prior to that, it was not known. This has virtually no exposure in the traditional media and certainly not from public health officials, yet it may be, from what you’re saying, one of the most important contributing variables to cardiovascular health.

I’m wondering, from your review of the literature and understanding of this protein, how do you frame in it in the whole scheme of things. Obviously information is an issue and your dietary components – I mean, limiting trans fats, sugar, and insulin resistance. How do you rate that in the whole scheme of things? Because it’s easy to design a study. You could put these people with extra vitamin K2 on a diet that’s full of trans fat and sugar.

**LS:** Yes.

**DM:** And you may not see a result – or you may. I don’t know if you’re looking at that in your study. But it would seem to me, if you have optimized all the variables, you cleaned them up, and you ran a matrix, how do you think will it play out? What are the most important variables?

**LS:** It’s a very good question because I think that the deficiency of vitamin K is a risk factor. It’s not curing a complete disease because more factors are involved in developing certain diseases, especially diseases like atherosclerosis, cardiovascular disease, oxidized lipids, inflammation, everything counts. Actually it’s funny to mention that when I started my post-doctoral, I wanted to investigate calcification in our health. I went to the department of pathology in our institute and I said I want to have specimens that are calcified.

**DM:** Specimen from humans?

**LS:** From humans. They started laughing and they said, “How many do you want? Because all of them are calcified. Why look into something that is always there, which is a passive process and is not clinically relevant?” Still, it had my attention. I wanted to investigate calcification. Today calcification is one of the most-studied areas in cardiovascular disease and atherosclerosis. Actually, sometimes it needs time to realize that something which is always there has a meaningful impact.

This calcification, especially the microcalcification, small microcalcification, they are the bad things in our vessels. You have to envision that as a kind of rubber tire with a small stone in it. Every time this rubber tire, which has a smooth surface, hits the road, the small stone in this tire, makes a kind of rupture, a small rupture. Every time the blood flow hits the atherosclerotic plaque, where the small crystal is, it makes small ruptures. That is why we think that this microcalcification make the plaque vulnerable to rupture. If you can’t inhibit this microcalcification, that would really be a [inaudible 26:54].



What we did is we used very sensitive techniques to analyze elements in atherosclerotic plaques, in very early stages of atherosclerotic plaque.

**DM:** These are early stages that couldn't be seen without a microscope?

**LS:** Yes. You have already some intimal thickening. However, calcification is regarded in the literature only to be present for stage IV. That means a very advanced atherosclerotic plaque. However we showed already in the first lesion that type I lesion of microcalcifications are already present.

We also showed that that always colocalizes, nearly always colocalizes, with the inactive form of matrix Gla protein, indicative that vitamin K deficiency results in microcalcification or that these microcalcifications exhaust vitamin K stores locally and then you have the growth of the crystal. There is a very strong correlation between inactive MGP and these microcalcifications. It's very interesting to speculate that vitamin K deficiency is causative of microcalcification, which then sets on a whole cascade of processes leading to atherosclerosis.

**DM:** Thank you for sharing that. But some of the people viewing this might become a little sort of... Well, not fearful or I guess fearful. What does it matter? Because it sounded like if you go to the morgue and the pathologist says, "Well, everyone's got calcifications." But I think the good part of the story that could come out of this is, as you mentioned earlier, that this matrix Gla protein, in the right circumstances, likely reverses the process.

Even though you may have had it because of the typical individual swallowing the standard American diet and you've got this pathologic process pretty well down the road, if you changed your lifestyle and you mitigated some of the other factors – cleaned up the fats and improved the quality, eliminated the trans fats, cut the sugar down, got your insulin resistance resolved, and upregulated the intake of vitamin K2 to improve the function matrix Gla protein. Because I'm assuming that everyone has this.

**LS:** Yes.

**DM:** You're born with this. It's just a matter of it's not working, because you need K2 to activate it. If you get that K2 up, do you think you can get the typical person to regress? And it's very limited. Obviously, if you're dead, you're dead. But I mean, if you have a 90 or 95 percent occlusion in the vessel due to calcification, is it possible to reverse that?

**LS:** That's a good question. I want to say that calcification is an elderly disease. Everybody who grows older gets calcification at a certain stage. My intention, my focus would be to stop the process of calcification and extend the age that calcification starts. We know already that everybody grows older these days. Let's say, 50 years ago, you are older you are 50. Nowadays you're old... Well, you are still young when you are 50 or you are still young when you are 70. People grow older and older. The question is how can you prevent these elderly diseases?

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What I say is you have a risk factor which is vitamin K deficiency. If you have vitamin K deficiency, you are more likely to end up with calcifications. We are designing studies to prove that. It's now still a hypothesis and not proven. But we have some preliminary data and pre-clinical models that indeed vitamin K deficiency leads to accelerated calcification.

**DM:** Interesting. I've got a personal question for you because it affects me and it affects a lot of people. I have to go to a dental hygienist on a far more regular basis than I would like to. There are some individuals who are years in their prime and who now tends to develop plaque, which then calcifies and progresses to tartar, which become impossible to remove without some mechanical appliance. I'm

wondering if it would seem that vitamin K2 would play a role in plaque. Have you looked at that or aware of any studies that do – dental plaque?

**LS:** No. We have never looked at dental plaque.

**DM:** Interesting. What is your guess? Because I mean, you are one of the top experts in the world. What do you think?

**LS:** Yeah. Well, we first have to prove our vitamin K-dependent proteins and MK4. That would be the first step. Secondly, we know already that in salivary food there is a lot of MK4, vitamin K2. That could be something where vitamin K2 is important,

**DM:** And no one has looked there?

**LS:** Nobody ever looked at that.

**DM:** Interesting. But you could I guess theoretically either have an [inaudible 31:40] or something that K2 would just wind up where the typical proteins are and kind of inhibit the process.

**LS:** Interesting idea.

**DM:** Yeah, I think so.

**LS:** I got a new research idea.

**DM:** Well, the reason I mentioned it is it's a bit of a pretty lifelong challenge for me. When I started increasing fermented foods, which obviously are high in vitamin K2, I noticed that it started to reduce. I suspect there's an issue there and that probably would be a good point for someone to study, because obviously oral health has a phenomenal influence on our biological health.

Okay, now that everyone's really interested in the new information about vitamin K2, what are the biomarkers that we can use to assess this? Because the last time I talked to Dr. Vermeer, unlike vitamin D, which we've only really had for about 18 years, there's a clinical assay. You can go to your doctor, you can measure vitamin D level and you know whether it's adequate or not, your vitamin D levels. But it doesn't exist for vitamin K2. What are the substitutes? How readily available are these biomarker tests?

**LS:** It's again a very good question. How do you measure vitamin K deficiency? Actually if you want look at vitamin D, you just measure vitamin D3. Then you have level and, you know if you are sufficient or deficient. You can do that for vitamin K – K1 or K2 – as well. The problem is that vitamin K2 has very low presence in food items. The levels you can measure in your blood after, let's say, taking food items rich in vitamin K is very low. It's very difficult to judge.

**DM:** It's the deactivated form. It's kind of like vitamin D2, the 1,25-dihydroxy., it's very low. It's measured, but most clinicians and experts don't believe it has much value unless you're a chemist.

**LS:** K1 and K2 are both directly active. They don't need to be metabolized. But because vitamin K1 is more present in green leafy vegetables and we eat more green leafy vegetables, sometimes you can measure them. However, it is really depending on what you consume the day before. For example, if I measure now vitamin K in your blood and yesterday you consumed a lot of spinach, your vitamin K1 will be high. If you consumed yesterday a hamburger, for example, with low amount of vitamin K, your vitamin K will probably be very low. It's not a very good marker for vitamin K status.

That is when researchers started to design other tests to measure vitamin K deficiency or vitamin K sufficiency. What we used is we made antibodies, which can detect the active form of matrix Gla protein

or the inactive form of matrix Gla protein. We developed enzyme-linked immunosorbent assays (ELISA), which are blood tests in which you can measure the active form of MGP and you can measure the inactive form of MGP. By that, you can say that you are sufficient in vitamin K or you are insufficient in vitamin K.

The funny thing is that what we found in our research – and we published this – is that actually everybody is some kind of clinically vitamin K-deficient if you do tell that from matrix Gla protein. There is always a certain amount of matrix Gla protein, which is circulating in the inactive form, meaning in biochemistry, you need extra vitamin K to activate this form. Because while we can make...

**DM:** Can you overactivate? Is there a downside?

**LS:** No.

**DM:** As far as you know, there are no downsides to overdosing?

**LS:** None. The World Health Organization (WHO) even set no bowel tolerance level for vitamin K.

**DM:** Okay.

**LS:** It's relatively safe.

**DM:** What would you suggest, from your understanding of the benefits, as the minimum threshold that we should not go below on a daily basis, and perhaps an optimum goal to establish or seek to consume on a regular or at least the ideal level?

**LS:** In the Netherlands, we say at least 200 grams of vegetables per day.

**DM:** Okay. For vitamin K1?

**LS:** For vitamin K1. I always say you should also consume vitamin K2, because we see that that is even more active in activating this MGP. The problem is that vitamin K2 is only present in, let's say, fermented foods such as cheese, and cheese also contains a lot of saturated fat. There is always...

**DM:** Interesting though.

**LS:** Yes.

**DM:** We're coming to appreciate that. Some of the newer research, some of the meta-analyses now show that actually saturated fat is beneficial.

**LS:** Oh.

**DM:** It is. Yeah. The reason there is confusion is from the previous studies is that it never differentiated between the trans fats and the saturated fats. The damage was being done by the trans, but the saturated is actually beneficial biologically and necessary. I think that's okay if it's from a healthy source.

**LS:** Okay. Interesting.

**DM:** Yeah, it really is. Vermeer had the same confusion. He gave this caution that you can't have... That you have to worry about that. But that really is not the case. It actually is beneficial. The recent meta-analyses that looked at this, they are very clear that it's not dangerous. There have been books written on this and major front cover stories on *Time* magazine. Butter is back.

**LS:** Which is good.

**DM:** Yeah.

**DM:** I like butter.

**DM:** Yeah. Who doesn't? That's great, as long as you don't have dairy intolerance. Some people do and are unfortunate that they have that. They're avoiding that.

**LS:** But I can elaborate more about this.

**DM:** Sure. Yeah, go.

**LS:** This MGP assay, which we are using to tell if somebody takes sufficient vitamin K, we used that in patient populations (and also this is what we published recently). What we showed is that those patients with the highest inactive form of MGP had the highest chance of dying.

**DM:** Interesting.

**LS:** If you have local vascular vitamin K status as induced by this uncarboxylated form of MGP, that is really a risk factor for cardiovascular mortality. What we did, together with some nephrologists in Aachen, is we designed a pilot study in which we gave dialysis patients, because they are really vitamin K-deficient, MK7 on daily doses for six weeks. We looked at the activation...

**DM:** What was the dose?

**LS:** 360 micrograms, 135 micrograms, or 45 micrograms. We used three different doses. It was kind of a dose-establishing pilot study. We found that the highest dose had a really true effect on activated matrix Gla protein over six weeks of time. It activated osteocalcin, which is this other vitamin K-dependent protein in bone. It also activated inactive prothrombin, which was also to a certain amount increased in dialysis patients, meaning they are really vitamin K-deficient. MK7 had a true effect on activating these proteins. Actually that was the reason why now several clinical studies were started to supplement the patients with vitamin K to see if there is an effect on holding off progression of arterial calcification by activating these byproducts.

**DM:** For insurance, is there a minimum threshold that we shouldn't go below on a daily basis in vitamin K2? And sort of a follow-up to that question would be, is there really a difference between some of the... Because we didn't really talk about the different families of vitamin K2. There are quite a few and a dozen more of them. Maybe you can talk about that

**LS:** Yes. We have K1 and K2. K1 is phylloquinone. It's in green leafy vegetables. And then you have vitamin K2, which is a whole family of menaquinones. You have MK4, MK5, MK6, MK7, and it goes on to MK14. The most important ones I would consider are MK4 and MK7, and maybe MK8 and MK9 because those are in fermented foods as well. But most of the data in the literature are based on MK4 or MK7. The preference I would say...

**DM:** The lower the number, the smaller it is, right?

[----- 40:00 -----]

**LS:** The smaller the molecule is and the more hydrophilic it is. Actually they are all lipophilic; they love fat. But the longer the side chain, the longer the numbers (7 means 7 parts on the side chain), the more lipophilic it is. Also the longer the side chain, the longer the half-life is. Your classmates will love this. MK7 has some benefits over MK4 because it has longer presence in your blood, so it has a better chance to activate or to reach...

**DM:** The compliance is better because...

**LS:** The compliance is better.

**DM:** Once a day, right?

**LS:** Yes.

**DM:** Whereas MK4 is three to four times a day.

**LS:** Well, if you want to have the studies...

**DM:** Who wouldn't?

**LS:** Well, yes. At least it's easy to follow up.

**DM:** Compliance is always a challenge. Is there still a minimum threshold that you can find? You mentioned 360 micrograms in the study. Do you think 500 micrograms would be better? A gram or a milligram a day?

**LS:** It's a question I often get. Actually we do not have the dose evidence yet. The only thing...

**DM:** But there is no downside to overdose?

**LS:** There is no downside. I would say if you look at the Rotterdam Study where you have these tertiles, the highest tertile was to prevent... That is where we said, okay, the medium or the highest tertile was 45 micrograms of vitamin K2. That is always what I say. If you want to have a healthy diet, at least consume 45 micrograms of vitamin K2.

**DM:** You've mentioned it frequently that they're actually in fermented foods. I just like to mention it's important to understand that there are bacteria in fermented foods. But there's a whole variety of different bacteria and many bacteria don't really make much vitamin K. That's what we've done. You can do a lot of fermentation using a starter culture. With a starter culture, you reduce the fermentation from three weeks down to about a week and it's more consistent.

But the most important thing is that we found that we could get 400 to 500 micrograms of vitamin K2 using a starter culture in vegetables in a two-ounce serving. Vitamin K2 can be expensive. I mean, that's another issue here. Because of the process of the bacteria, isolating them, and putting them in capsule. But if you get it from foods that are high in K2, you just can't blindly eat fermented foods, thinking you'll get a lot of K2 unless it's like natto, because that's the highest strain. It's *Bacillus subtilis*.

**LS:** Right.

**DM:** But normally, you'll get some but it could be 10 micrograms or it could 500. You really want the more the better with this. Maybe you can comment on that.

**LS:** It's a very intriguing idea because some people always say, "Why is vitamin K2 more important, whereas there's K1 in the diet? Where does this benefit come from?" The only explanation I can come up with, which is just purely hypothetical, is that 100 years ago, we didn't have refrigerators. Most of the food were in our house for more days and were most likely fermented.

**DM:** For centuries.

**LS:** Absolutely. What you now mentioned is that if you could ferment green leafy vegetables with certain bacterial strains producing vitamin K2, there may be some benefits.

**DM:** Yeah. It's not so much the green leafy, because it has to be a...

**LS:** A vegetable.

**DM:** Yeah, like cabbages or carrots that have really tough fibers. Because if it's a fermented lettuce, it could be mushy. You want some texture. It has to be palatable, which is key.

**LS:** You have to want the vegetable which is fermented, like sauerkraut.

**DM:** Oh, yeah.

**LS:** That is rich in vitamin K2.

**DM:** But it has a starter culture.

**LS:** Absolutely.

**DM:** What are the ranges that you're seeing in sauerkrauts that you've measured?

**LS:** That's a good question. It's still not that very high. I think up to 20 micrograms of K2.

**DM:** The starters were at 500. That is a clinically therapeutic dose, which is very good. These biomarkers, you have mentioned they exist. What I'm curious about is, are they widely available clinically? In other words, can a person go to their physician and order an uncarboxylated matrix Gla protein or is it... And I wasn't sure. Do you measure the uncarboxylated versus the carboxylated? Or is it the ratio of the two?

**LS:** At this moment, we can measure both. The most common one we use is the uncarboxylated, which is proving that there is vitamin K deficiency in the vasculature.

**DM:** Is it widely available?

**LS:** It is not widely available, but it will be commercialized. It is coming in Europe with old patents.

**DM:** Commercialized. When do you think it will be available?

**LS:** I think it will be early 2015.

**DM:** Interesting. That's soon.

**LS:** It will not be in the hospitals yet. We have to convince the medical doctors that measure it.

**DM:** Is that just in Europe or the US, too?

**LS:** I think it will be in the US as well.

**DM:** Okay good.

**LS:** I think it will be both.

**DM:** Because if the test is available commercially, then a giant lab like Quest or LabCorp... It may be a specialty test, but at least they could get it done. You're not going to get that the next day. It might be back in a week or two, but at least you'll get it. That's good to know. Is the same true for osteocalcin?

**LS:** Osteocalcin is present. You can buy the assay. Everybody can...

**DM:** Okay, so those are available?

**LS:** Yes.

**DM:** Ideally, you could do one or just the matrix Gla protein?

**LS:** Our group is located in the Cardiovascular Research Institute Maastricht (CARIM).

**DM:** [Inaudible 45:31]

**LS:** Well, yeah, we are focusing on cardiovascular research. I'm more focused on the MGP.

**DM:** Yeah. And as an adult, as you mentioned earlier, I was somewhat surprised to find out that there really isn't a significant impact on the bone of a mature adult, whose bone is already formed. I mean, there's not a lot of dynamic function going out there. But I suspect it may have some role as part of a healthy strategy to reverse osteoporosis or at least certainly stop it. I know a lot of people personally who actually increased their bone density, and vitamin K2 is an important part of that.

**LS:** Absolutely.

**DM:** A lot of the important minerals in the knees.

**LS:** Well, there is a lot of confusion in the vitamin K component for bone strength. There was a recent publication by the group of Dr. Cees Vermeer. They showed that if you take three years of vitamin K2 (MK7) – and it was in this case compared to placebo – bone strength increased, and in the placebo forcibly declined. It seems to be a true major effect of MK7 on bone health.

**DM:** I've got another question for you, too. It's actually one that Dr. Vermeer commented on and actually created quite a controversy at least on the people in our site. That is what you mentioned earlier, the use of vitamin K2 to prevent vitamin K deficiency in newborn, which is actually K1. Typically in the US and I suspect in Europe as well, it's given as a intramuscular (IM) injection at very high doses, thousands of times higher than is required.

He was opposed to that practice and felt that it would be acceptable to give oral dose, which requires more frequent administration. I guess the only justification for the use for the IM is really the compliance issue. I took his side. I thought it made perfect sense, because it really is a traumatic event to give a newborn an injection. It just seems more natural even though there's no toxicity that we know of... although I think the... I don't think that using natural K1 was a vital point. Is there a synthetic version they're using?

**LS:** It is synthetic.

**DM:** That was another concern. If it's a natural one by nature, we know there's virtually no toxicity that we know of. But when you start going synthetic and you start using injections, it makes a lot more sense to swallow this thing rather than to inject it. What are your thoughts?

**LS:** Well, I think that it's very difficult to change the K1 for the K2 at this moment because K1 is completely... [inaudible 48:05-07]. I think it's quite proven. What I would stress is that those women who are breastfeeding, it's known that the baby has to get drops of vitamin K every day, because in your breast milk, there's too little vitamin K or good vitamin K.

**DM:** And mostly vitamin D unless you're really getting a lot of good sunlight.

**LS:** Absolutely. You get drops. In these drops, they now use K1. I would say that would be a very, very good reason to swap that to K2 for the long-haul flight.

**DM:** Oh, and put K2 in there, too.

**LS:** Absolutely.

**DM:** Okay, so, K1 and K2. That's interesting.

**LS:** Or only K2. Because it does all the functions.

**DM:** Okay. Well, that's just terrific. I love picking the brains of smart people. I think it has so... This has so much potential for improving our health. It's such a simple intervention, especially if you could integrate it into your lifestyle with these fermented foods. For me, it's what the take-home message is. You provide the science to support the benefits of this. I think that you are health-wise irresponsible if you're not making a conscious and deliberate effort to integrate more vitamin K2 fermented-type foods in your diet. You can buy them pre-packaged. You can swallow the supplements. But it's far easier to get vitamin K2 from fermented vegetables or some of the cheeses. What are some of the highest amount in cheeses?

**LS:** I think up to 50 micrograms or 100 grams.

**DM:** Yes. Three ounce of cheese, you only get 50 micrograms. Some of these cheeses also are very expensive. You'd be far better off from a health perspective at least and maybe from taste appreciation, eating the fermented vegetables. Unless I'm travelling, I always have them every day in one of my meals. It's a phenomenal thing.

[----- 50:00 -----]

I think it really is a crucial element of a nutritional strategy to optimize your health. I think you're really irresponsible if you don't understand that and integrate that to your health, because you're going to pay the consequences, which is going to be, most likely as your research is showing, cardiovascular disease and probably neurological diseases like Alzheimer's or Parkinson's, where it has an influence.

**LS:** There actually still has a lot of research to be done.

**DM:** There's no downside.

**LS:** Actually cardiovascular disease there is a known indication for sure.

**DM:** Thank you so much for coming all the way from the Netherlands to Chicago [despite] the cold weather.

**LS:** It's my pleasure.

**DM:** Well, it's probably cold in the Netherlands, too.

**LS:** Well, a little bit warmer than here.

**DM:** Okay. All right. Well, thank you for coming and sharing your wisdom with us and helping us understand the importance of this vitamin.

**LS:** You're welcome.

[END]