



What's New With Vitamin K2: New Discoveries on a Critical Nutrient



Susan Allen RDN, CCN
Hosts Kiran Krishnan!



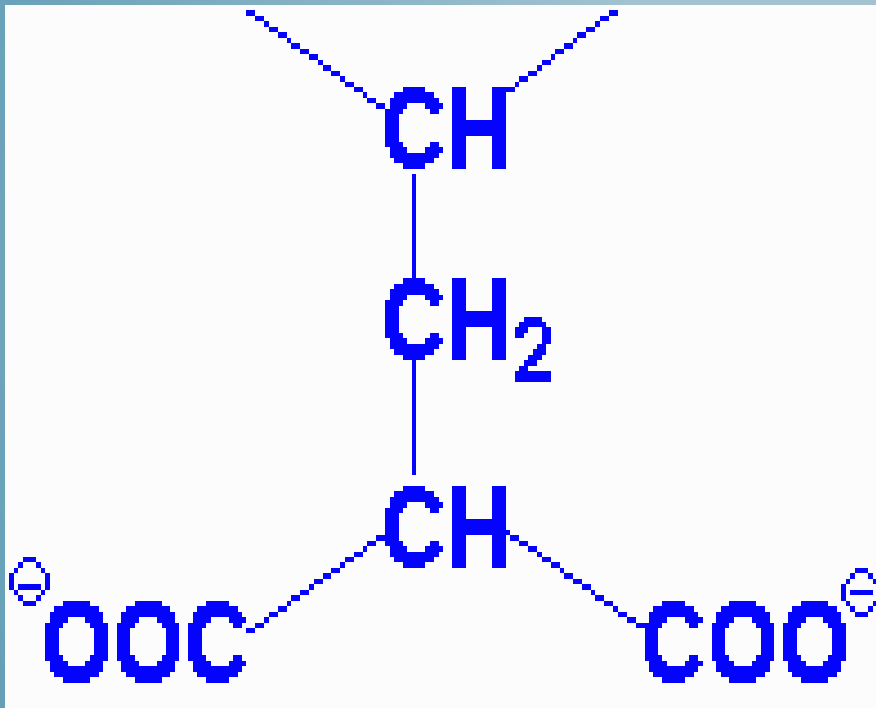
Vitamin K2-7

Defining the structural integrity and rate of aging in virtually every tissue in the body and new discoveries in the function of this critical nutrient.



Kiran Krishnan, Chief Science Officer, Physician's Exclusive, LLC.

Mechanism

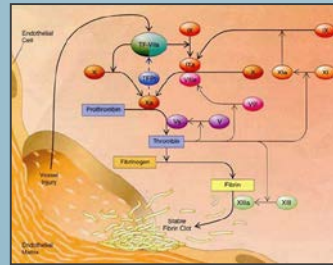


The formation of gla residues within several proteins of the blood clotting cascade is critical for their normal function. The presence of gla residues allows the protein to chelate calcium ions and thereby render an altered conformation and biological activity to the protein

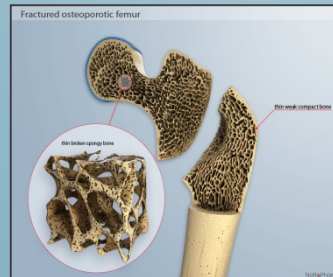
At this time more than 12 human Gla-Proteins have been discovered.

Well Known Tissues in Need of vitamin K

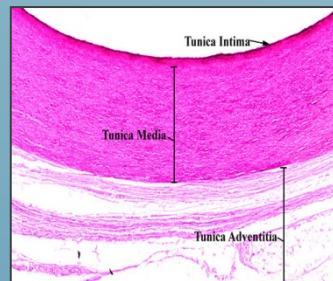
Vitamin K



clotting factors
II, VII, IX, X, C, S, Z



osteocalcin

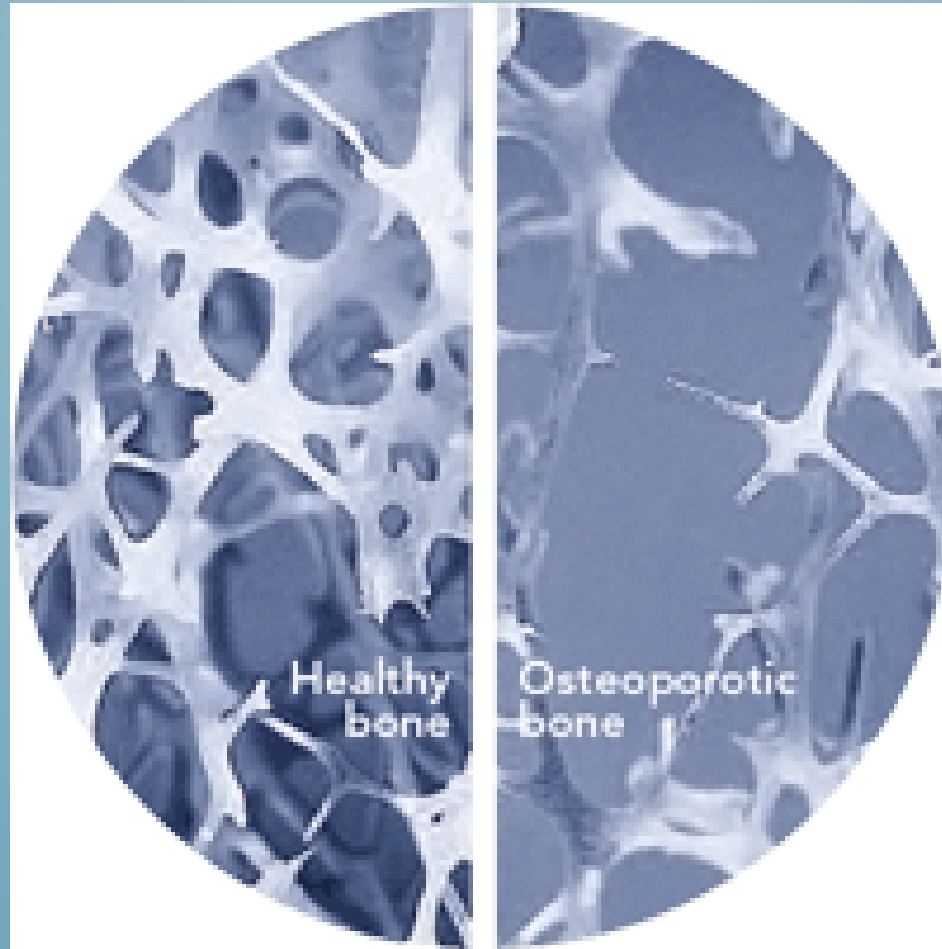


matrix Gla-protein

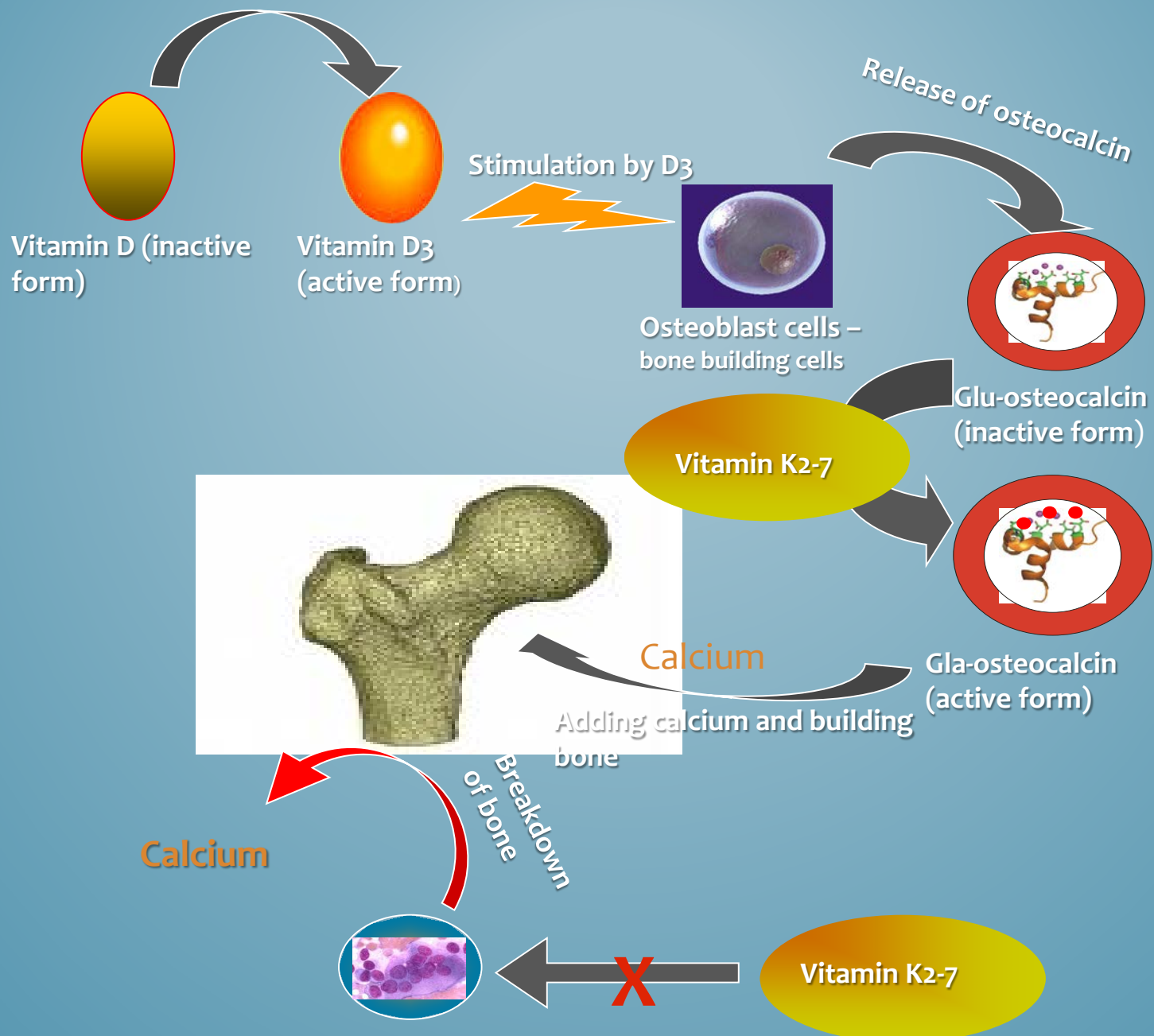
Principles for vitamin K uptake in the tissues

- **The liver takes what it needs.**
Vitamin K-dependent coagulation factors are synthesized in liver. Hence, severe liver diseases results in lower blood levels of vitamin k-dependent clotting factors and increased risk of uncontrolled bleeding.
- **The remaining K is left for other tissues.**
- **K-deficiency mainly occurs in extra-hepatic tissues.**
- **Effects of K-deficiency will be most pronounced in bone, cartilage and arteries.**

VITAMIN K AND BONE HEALTH



The Role of K2 in Building Bone and Preventing Bone Loss



VITAMIN K2 AND OSTEOCALCIN

- Osteocalcin is a vitamin K-dependent protein that creates the bone matrix upon which calcium crystallizes
- Osteocalcin - provides the “glue” that holds calcium in the bone – giving structure and order to bone tissue; without it bone would be fragile and easily broken
- Vitamin K “activates” osteocalcin through a process called “carboxylation”
- Without carboxylated osteocalcin, calcium cannot be properly utilized for bone structure

OSTEOCALCIN CARBOXYLATION, BMD AND FRACTURE RATE

- *Szulc et al:* *ucOC inversely correlates with BMD*
- *Knapen et al:* *ucOC inversely correlated with BMD*
- *Vergnaud et al:* *serum ucOC predicts hip fracture*
- *Luukinen et al:* *serum ucOC predicts hip fracture*
- *Szulc et al:* *high ucOC // 6-fold increased fracture risk*

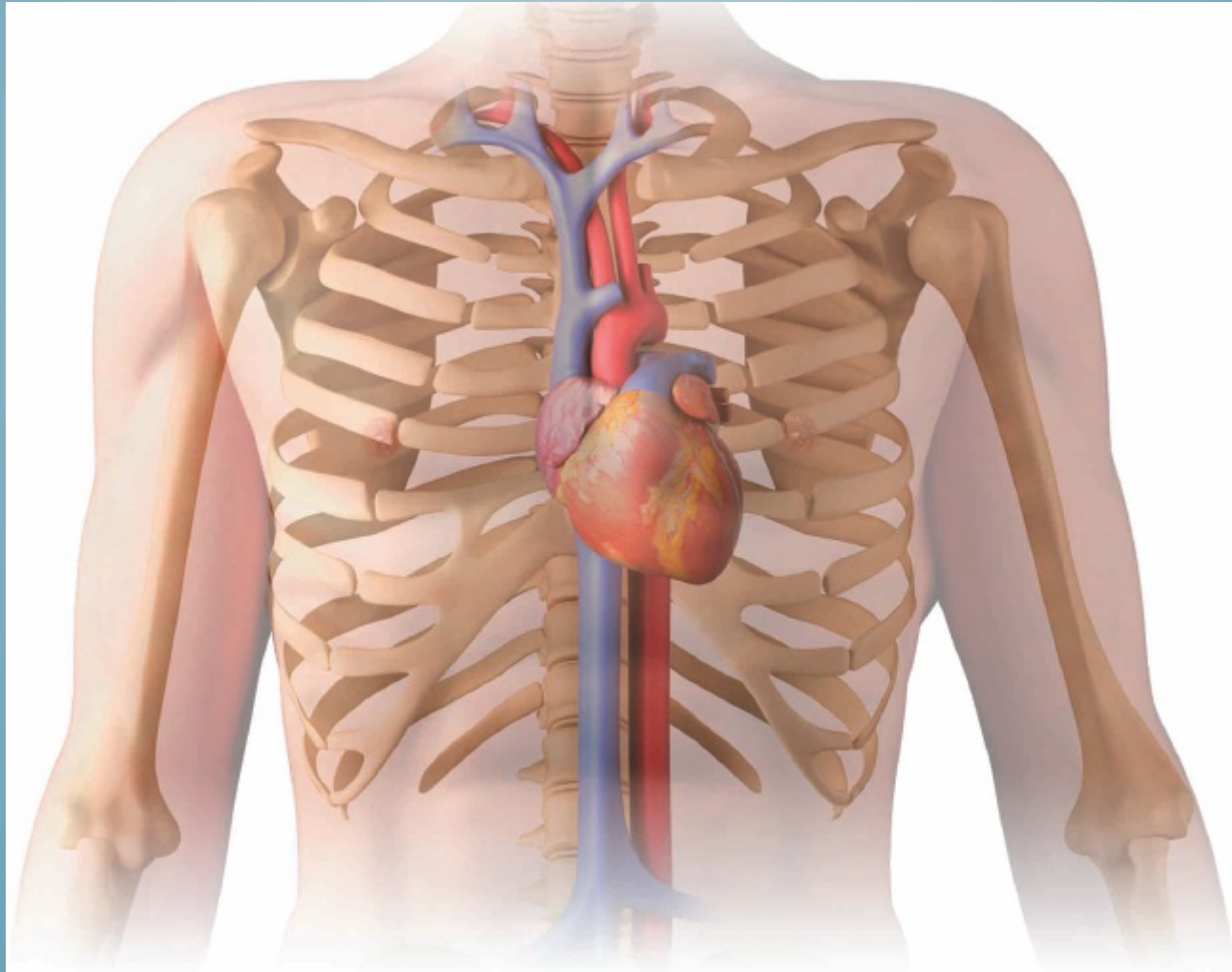
Natural Vitamin K2 as Mk-7 from Natto is Effective

- 2001 -- Kaneki – high consumption of MK-7 levels from natto resulted in better levels of activated osteocalcin and a reduced risk fracture
- 2006 -- Ikeda - natto consumption helps prevent the development of osteoporosis
- 2008 – Yaegashi showed that better vitamin K status attributed to Natto resulted in the reduction of hip fracture risk.

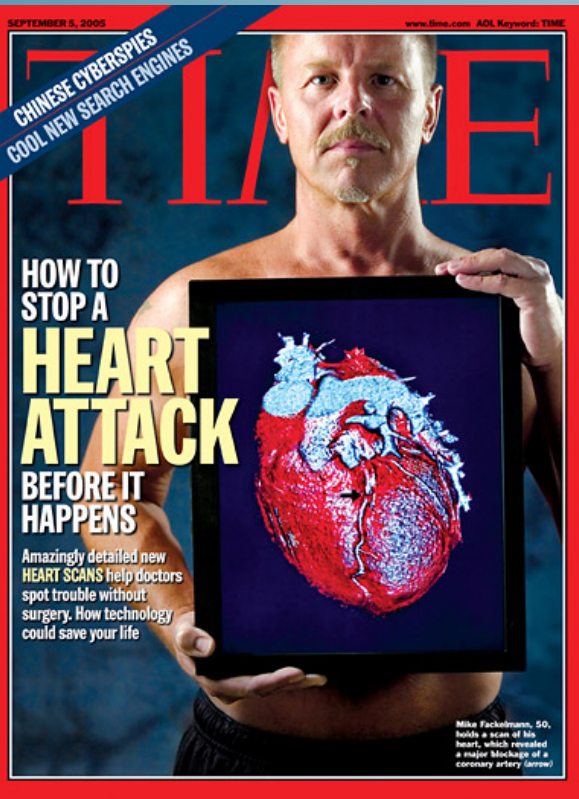
HIP FRACTURE INCIDENCE AND K2 AS MK-7 2008

- *Dietary intakes of calcium, magnesium, vitamin D, and vitamin K were analyzed in nationwide survey (Japan)*
- *Hip Fracture Incidence was much higher in the West*
- *The strongest inverse correlations were found for vitamin K in both men and women*
- *Calcium intake had weak or null associations between the standardized incidence ratio*
- *Mk-7 from Natto – attributed to the reduced risk in Eastern Populations*

VITAMIN K₂ AND VASCULAR HEALTH



Time magazine September 2005: Do you know your calcium score?



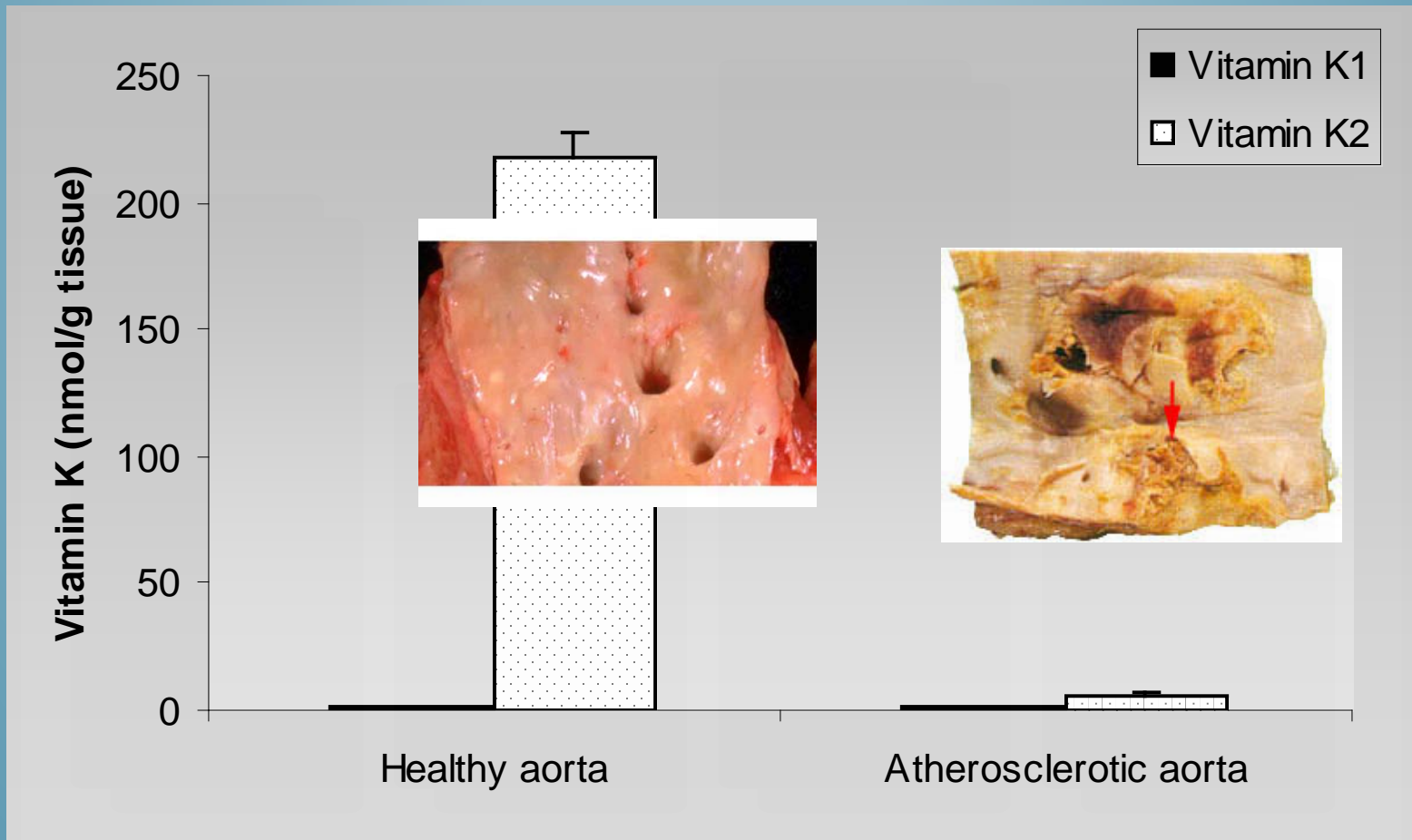
*From the Magazine | Health
The Newest Risk Factor
By ALICE PARK*

Posted Sunday, Aug. 28, 2005

First it was blood cholesterol that could give you an early warning that a heart attack might be around the corner. Then came c-reactive protein. And now that doctors can get a better look at what's inside your heart arteries, they are taking a new interest in something they have always known was present in problem vessels: calcium. Hospitals, clinics and even gyms are touting quick and easy scans that can measure the amount of calcium in your coronary arteries in minutes.

Calcium can then build up in the vessels and stiffen them, laying the foundation for heart disease. Getting one's calcium score is simple, either by electron beam computed tomography (EBCT) or by multidetector CT. Studies show that in every age group people with higher vascular calcium levels have a greater risk of heart attack than do people of the same age with lower scores.

K-vitamins in healthy and atherosclerotic human aorta's (means from 3 donors)



VITAMIN K₂ AND VASCULAR HEALTH

Nutrition, Metabolism & Cardiovascular Diseases (2008) xx, 1–7



available at www.sciencedirect.com



journal homepage: www.elsevier.com/locate/nmcd

Nutrition,
Metabolism &
Cardiovascular Diseases

A high menaquinone reduces the incidence of coronary heart disease in women

Methods and Results: We used data from the Prospect–EPIC cohort consisting of 16,057 women, enrolled between 1993 and 1997 and aged 49–70 years, who were free of cardiovascular diseases at baseline. Intake of vitamin K and other nutrients was estimated with a food frequency questionnaire. Multivariate Cox proportional hazards models were used to analyse the data.

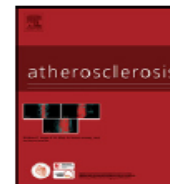
Conclusions: A high intake of menaquinones, especially MK-7, MK-8 and MK-9, could protect against CHD. However, more research is necessary to define optimal intake levels of vitamin K intake for the prevention of CHD.



Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis



High dietary menaquinone intake is associated with reduced coronary calcification

Joline W.J. Beulens^{a,*}, Michiel L. Bots^a, Femke Atsma^a, Marie-Louise E.L. Bartelink^a, Matthias Prokop^b, Johanna M. Geleijnse^c, Jacqueline C.M. Witteman^d, Diederick E. Grobbee^a, Yvonne T. van der Schouw^a

Methods: We investigated the association of intake of phylloquinone and menaquinone, including its subtypes (MK4–MK10), with coronary calcification in a cross-sectional study among 564 post-menopausal women. Phylloquinone and menaquinone intake was estimated using a food-frequency questionnaire.

Conclusion: This study shows that high dietary menaquinone intake, but probably not phylloquinone, is associated with reduced coronary calcification. Adequate menaquinone intakes could therefore be

VITAMIN K INTAKE AND CARDIOVASCULAR DISEASE: THE ROTTERDAM STUDY

- *Objective: to study the association of dietary intake of K₁ and K₂ with aortic calcification, CVD, and total death*
- *Design: cross-sectional analysis in healthy adults*
- *Setting: 4807 men and women aged 55 and older;
10 years follow-up*
- *Measurements: → calcification
 → end point (death)*

VITAMIN K₂ INTAKE AND CARDIOVASCULAR DISEASE

Conclusions:

When consuming daily 45 µg dietary K2 you have:

50% reduction of arterial calcification

50% reduction of cardiovascular death

25 % reduction of all cause mortality

as compared to low intake of dietary K2!

There was no correlation for vitamin K1 in this study!

ADDITIONAL CLINICALLY PROVEN INDICATIONS

- Vitamin K2 shown to reduce diabetes risk by 20% in a Dutch population study over 10 years – 38,000 patients
- Vitamin K2 shown to decrease cancer risk. Study on 23,000 German adults. Showed higher K2 intake associated with a lower likelihood of developing and dying of cancer.
- Vitamin K2 shown to reduce prostate cancer risk by 35% in a epic study in 11,319 men taking part in the Heidelberg cohort.

NEW DISCOVERIES IN VITAMIN K2 FUNCTION



A SEEMINGLY OMNIPRESENT VITAMIN.....

Unitary Hypothesis

**“ Perfusion, Hypoxia, Energy Balance
& Microcirculation Improves
significantly with K2”**

Using a technique of Reverse Pharmacology, we made the following discoveries....

NEW DISCOVERIES

- **Function in Muscle Contraction**
- **Function in Nerve Health**
- **Function in Mitochondria**
- **Redox Function of Vitamin K₂**
- **Function in Cardiac Function and Output**

MITOCHONDRIA FUNCTION

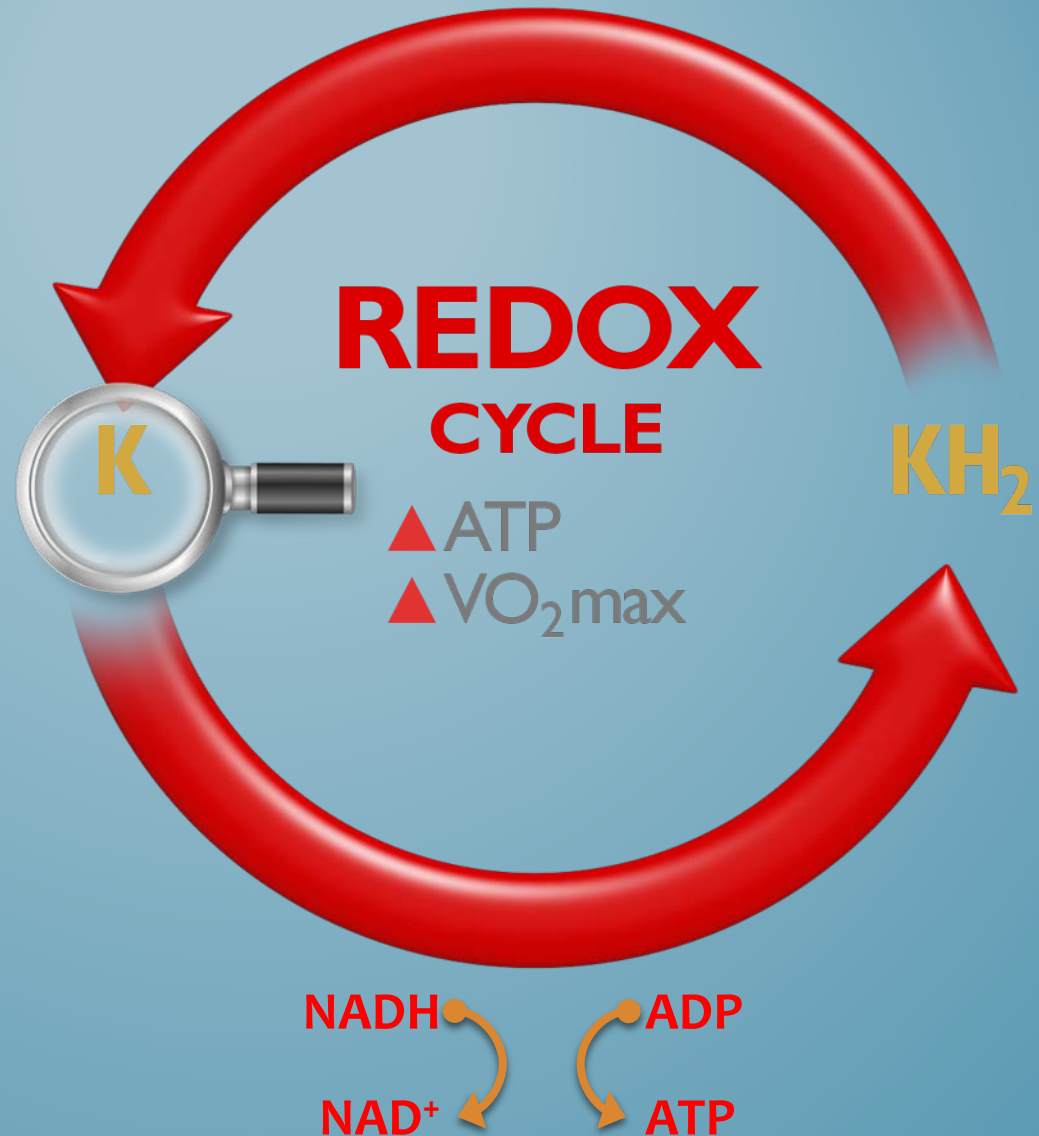
YET ANOTHER MECHANISM

- 1950's

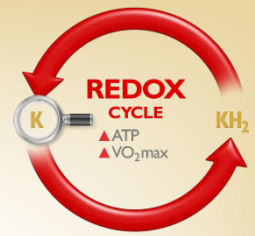
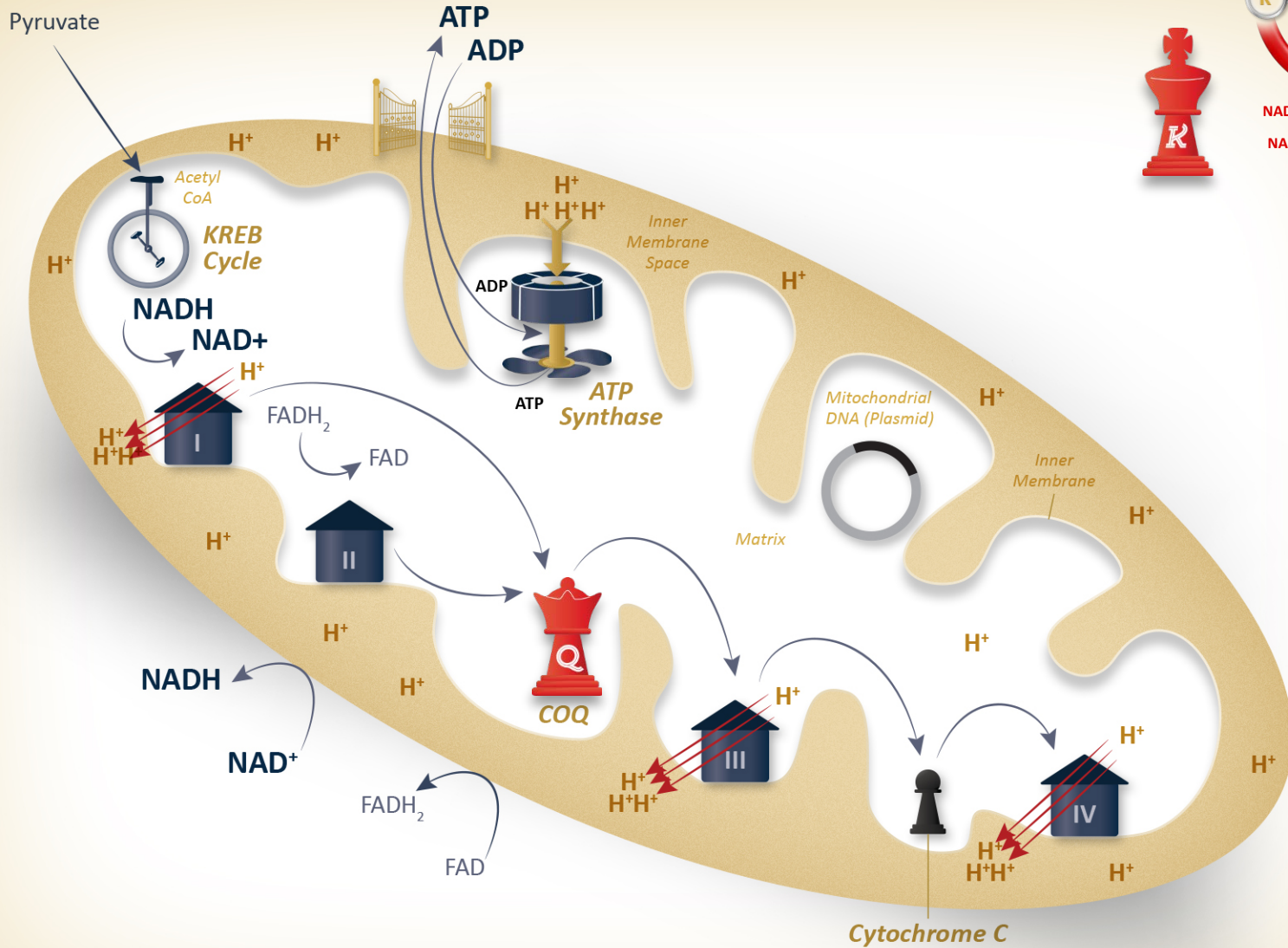
Redox cycle activity of vitamin K was proposed by Martius, *et al.*

- 1960's

At a later date Johnson *et al.*, refuted this claim.

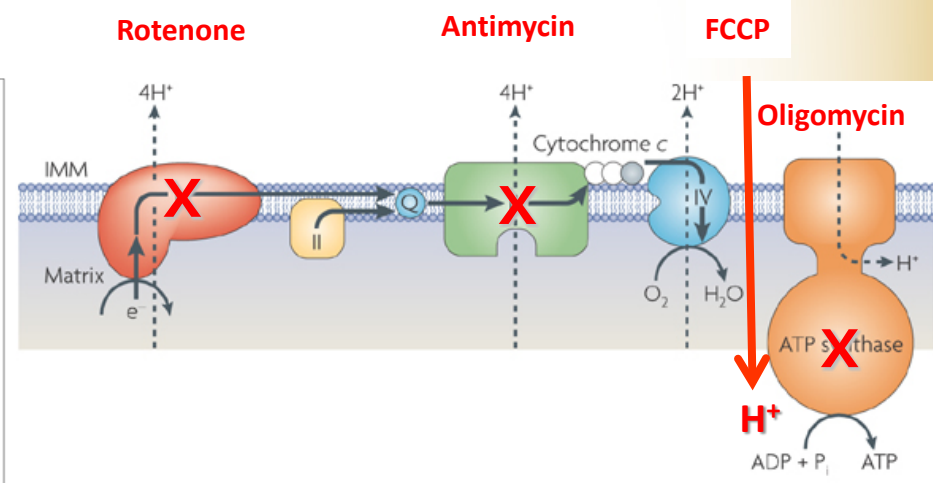
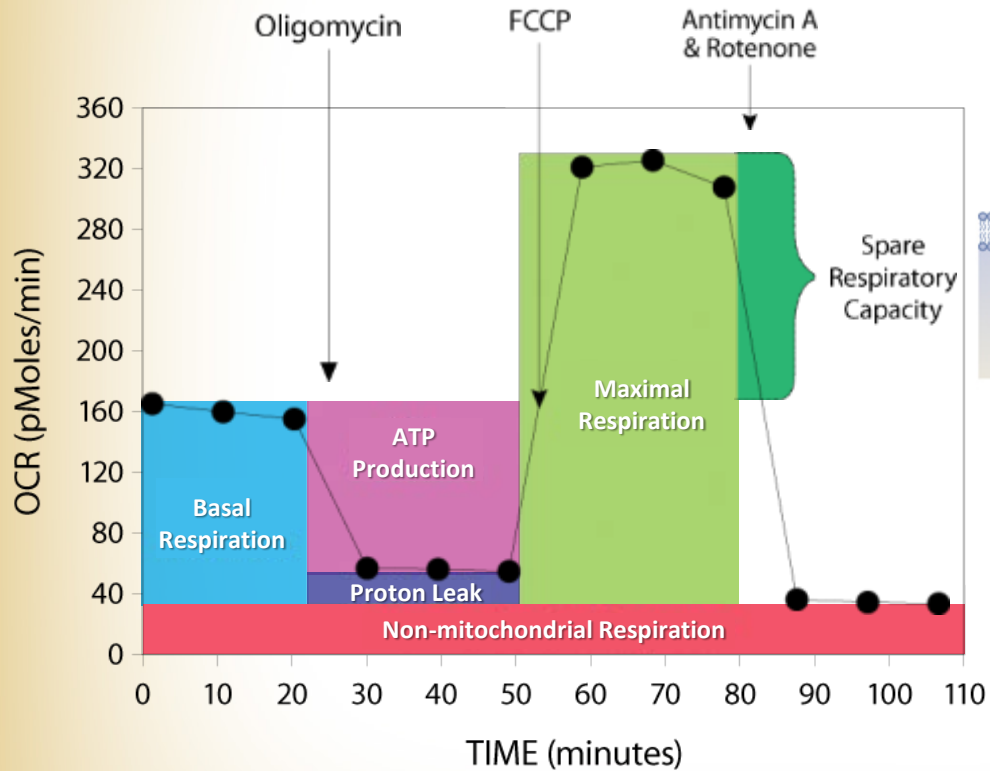
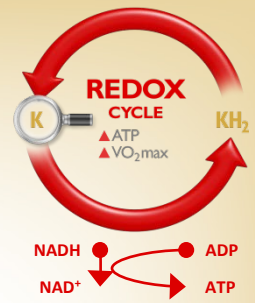


MITOCHONDRIA FUNCTION



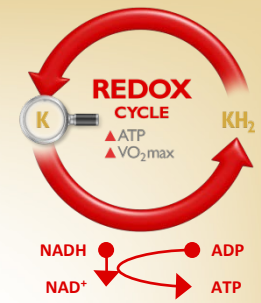
Vitamin K-Mitochondrial Respiration

Mitochondrial Bioenergetics



Nature Reviews | Molecular Cell Biology

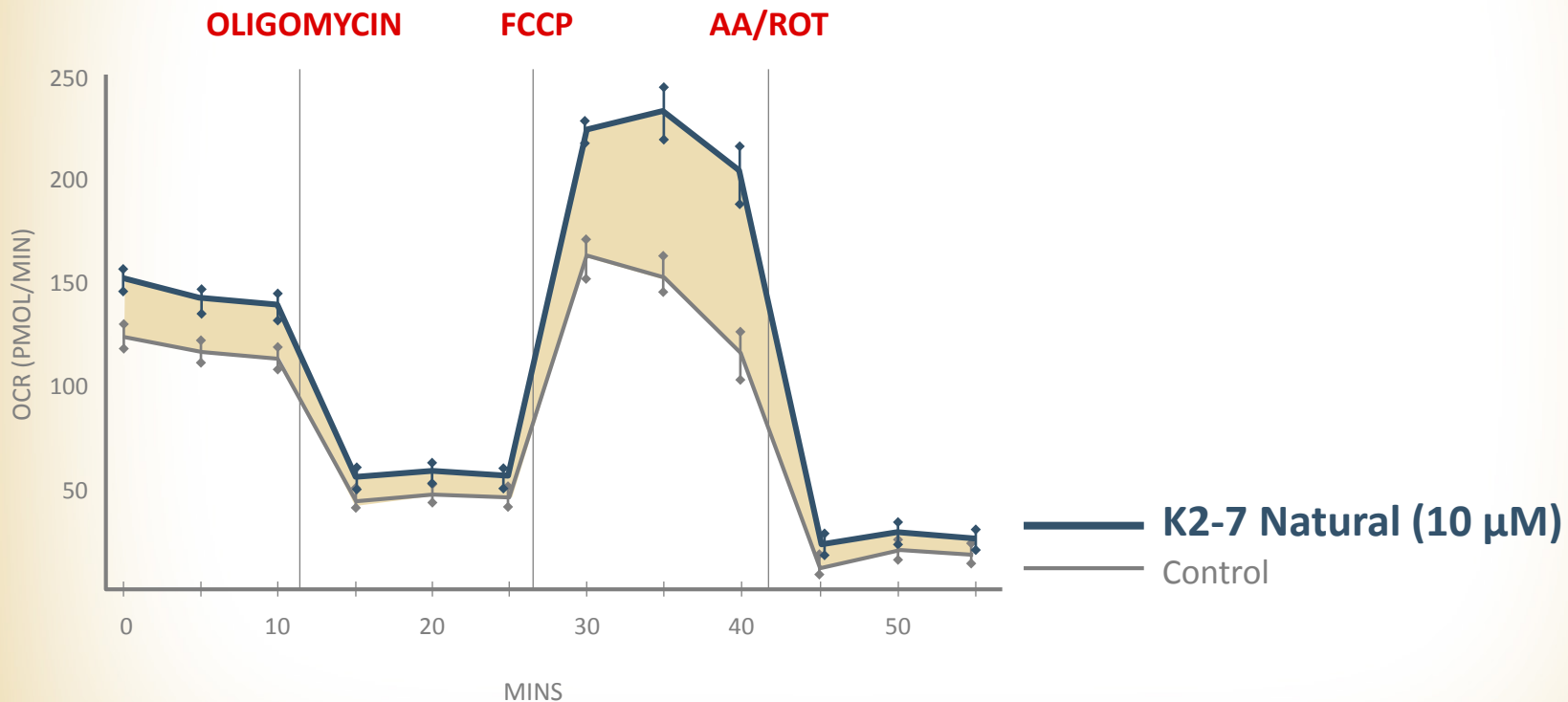
Mitochondrial Respiration: Test sequence in sea horse XF-96 platform



Vitamin K Bioenergetics

Cellular Experiments

Neuroblastoma cell line



Mitochondrial Respiration: Test sequence in sea horse XF-96 platform

NERVE HEALTH

Science. 2012 Jun 8;336(6086):1306-10. doi: 10.1126/science.1218632. Epub 2012 May 10.

Vitamin K2 is a mitochondrial electron carrier that rescues pink1 deficiency.

Vos M¹, Esposito G, Edirisinghe JN, Vilain S, Haddad DM, Slabbaert JR, Van Meensel S, Schaap O, De Strooper B, Meganathan R, Morais VA, Verstreken P.

Author information

Abstract

Human UBIAD1 localizes to mitochondria and converts vitamin K(1) to vitamin K(2). Vitamin K(2) is best known as a cofactor in blood coagulation, but in bacteria it is a membrane-bound electron carrier. Whether vitamin K(2) exerts a similar carrier function in eukaryotic cells is unknown. We identified *Drosophila* UBIAD1/Heix as a modifier of pink1, a gene mutated in Parkinson's disease that affects mitochondrial function. We found that vitamin K(2) was necessary and sufficient to transfer electrons in *Drosophila* mitochondria. Heix mutants showed severe mitochondrial defects that were rescued by vitamin K(2), and, similar to ubiquinone, vitamin K(2) transferred electrons in *Drosophila* mitochondria, resulting in more efficient adenosine triphosphate (ATP) production. Thus, mitochondrial dysfunction was rescued by vitamin K(2) that serves as a mitochondrial electron carrier, helping to maintain normal ATP production.

“Neuroscientist Patrik Verstreken, associated with VIB and KU Leuven, succeeded in undoing the effect of one of the genetic defects that leads to Parkinson's using vitamin K2. His discovery gives hope to Parkinson's patients.”

NERVE HEALTH

Original Article

The effect of vitamin K2-7 in peripheral neuropathy due to Vitamin B12 deficiency and/or diabetes mellitus: A Preliminary Study

Kulkarni VK*, Upase DP*, Dound YA**, Jadhav SS**, Bhave AA***,
Mehta DS**, Valdiya ADB‡

ABSTRACT

Objective: To evaluate the activity and tolerability of Vitamin K2-7 (MK-7) in a series of patients with peripheral neuropathy due to vitamin B12 deficiency and/or diabetes mellitus.

Material and Methods: An open labeled clinical study was conducted in 30 patients presenting with peripheral neuropathy and suffering from either megaloblastic anaemia (vitamin B12 deficient) and/or diabetes mellitus. Vitamin B12 levels in blood were estimated at baseline and during therapy. Vitamin K2-7 capsules (100 mcg / capsule, twice a day) was given orally for 8 weeks. Patients kept a regular record of the intensity of the symptoms during the baseline and throughout the study. Symptoms included tingling and numbness along with weakness, fatigue and cramps. The intensity of the symptoms was assessed on a Visual Analog Scale (VAS). They were followed up to 8 weeks. Blood biochemical and organ function tests were studied at the baseline, at the fourth week and at the end of the eight week. Prior to the study Ethics Committee Approval was obtained from the Ethics Committee of T. N. M. C. & B. Y. L. Nair Ch. Hospital. The trial was registered with Clinical Trial Registry of India (CTRI) (CTRI/2012/08/002930). Informed written consent was obtained from the patients before enrollment.

Results: Depending on the basal VAS score the patients were divided in a moderate group and a severe group. The moderate group had VAS score of 6-8 and the severe group had a VAS score of 8-9. By the end of eight week, the VAS score in both the groups was reduced to 1-2. The intensity specifically of tingling and numbness has reduced to a much greater extent. It was of interest to observe that ten out of 23 patients of Vitamin B12 deficiency group had residual neuropathic symptoms in spite of adequate levels of Vitamin B12 following vitamin B12 administration. The residual neuropathic symptom score reduced following Vitamin K2-7 therapy. Vitamin K2-7 was well tolerated clinically and found to be safe as per the organ functions in all the patients. No adverse events were reported during the period of therapy.

Conclusion: This preliminary study has shown that vitamin K2-7 at a dose of 100 mcg twice a day for 8 weeks was well tolerated and safe with a therapeutic activity for the symptoms of peripheral neuropathy. However, the therapeutic efficacy needs to be evaluated further in a larger sample size, with a placebo controlled randomised double blind trial.

KEY WORDS: Vitamin K2-7, diabetes mellitus, megaloblastic anaemia, peripheral neuropathy, reverse pharmacology.

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** - Viridis BioPharma Pvt. Ltd., V. N. Purav Marg, Chunarbhatti, Mumbai. *** - Consultant Haematologist; ‡ - ICMR Advance Centre of Reverse Pharmacology in Traditional Medicine, Medical Research Center-Kasturba Health Society, Mumbai. Correspondence to: Dr V K Kulkarni, 7, Shefalce, Makarand Society, Veer Savarkar Marg, Mahim, Mumbai - 400016 Email: vitamink2bc neuropathy@gmail.com

Mitochondrial data gave us a clue that perhaps vitamin K2 could regenerate dysfunctional mitochondria in tissue – a great example would be neurodegenerative diseases.

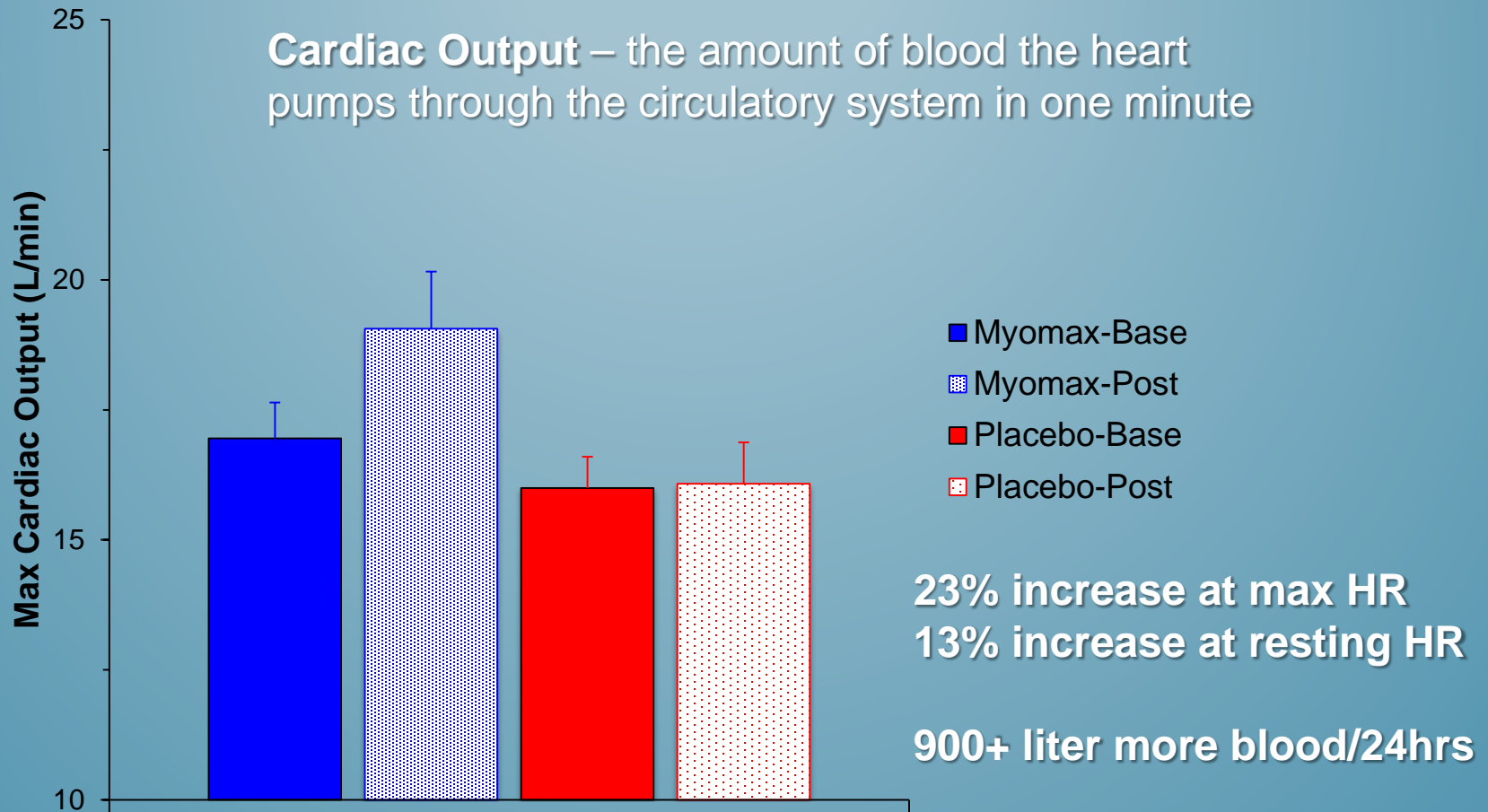
N=30
Dosing: 100mcg/day
Duration: 8 weeks
Results: Well tolerated and significant alleviation of neuropathy

CIRCULATION AND CARDIAC OUTPUT

Consumption of a MyoMax® (Vitamin K2 Containing Supplement) for 8-weeks was Associated with Increased Maximal Cardiac Output during Exercise

McFarlin BK^{1,2}, Henning AL^{1,2}, and Venable AS^{1,2}

¹Applied Physiology Laboratory; University of North Texas, Denton, TX



ARGUABLY THE MOST IMPORTANT ANTIAGING NUTRIENT

The Mitochondrial Free Radical Theory of Aging (MFRTA) proposes that mitochondrial free radicals, produced as by-products during normal metabolism, cause oxidative damage. According to MFRTA, the accumulation of this oxidative damage is the main driving force in the aging process.

Especially Cardiac Mitochondrial Oxidant Production!

“In a revealing study, a team of researchers showed that muscle tissue of a 90-year-old man contained 95% damaged mitochondria compared to almost no damage in that of a 5-year-old.”

By Kirk Stokel

Linnane AW, Kovalenko S, Gingold EB. The universality of bioenergetic disease: age-associated cellular bioenergetic degradation and amelioration therapy. Ann N Y Acad Sci. 1998 Nov 20;854:202-13.

ARGUABLY THE MOST IMPORTANT ANTIAGING NUTRIENT

“studies indicated a decrease of cardiac output with aging at rest and with exercise.”

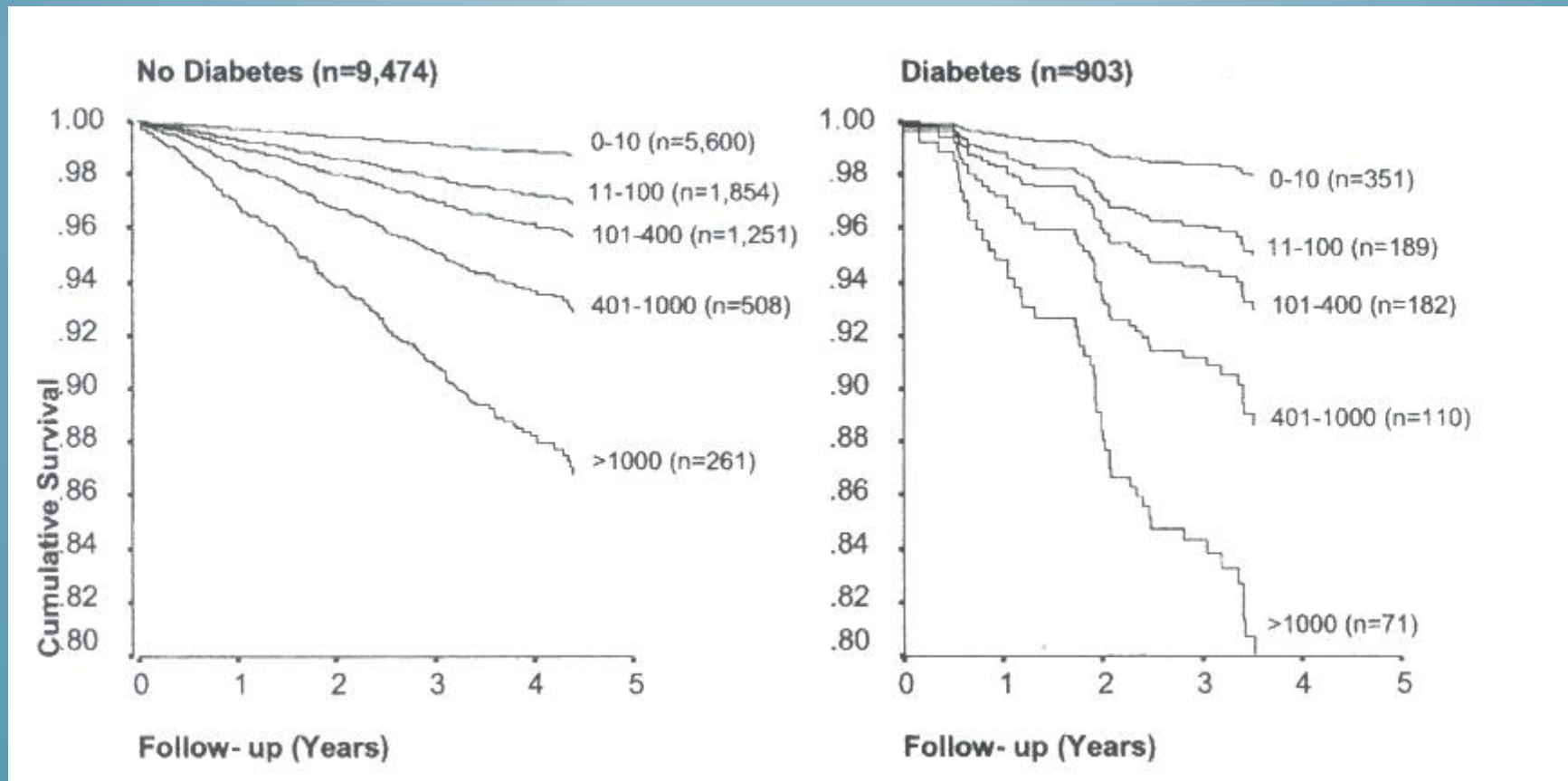
Melvin D. Cheitlin, MD. Am J Geriatr Cardiol. 2003;12(1)

“A substantially reduced output was a consistent finding in older subjects.”

MARTIN BRANDFONBRENER, M.D., MILTON LAN DOW-NE, M.D. AND NATHAN W. SHOCK, PH.D.
CIRCULATION . October 1, 1955

You Are As Old As Your Arteries Are!

Prognostic value of coronary artery calcium screening in subjects with and without diabetes



ARGUABLY THE MOST IMPORTANT ANTIAGING NUTRIENT

Biological aging is a factor of Mitochondrial Health, Cardiac Output and Vascular Health. It is easy to see that all 3 factors are intertwined and vitamin K2 plays a significant role in improving the health of each of these systems.

- *Better perfusion*
- *Removing Calcium from arteries*
- *Slowing down the progression of diabetes*
- *Every cell in the body gets more nutrients and blood supply*
- *Increases mitochondria function, so each cell can produce more energy and we can regenerate dying cells.*
- *Prevents aging related tissue degeneration*

Nature's Fountain of Youth!

Dose required is 100-300mcg and it has a linear dose dependent curve.

WHAT CAN VITAMIN K2-7 DO FOR YOU?

- Heart Disease
- Osteoporosis
- Diabetes
- Cancer
- Dementia
- Joint Health
- Facial/Cranial Development
- Skin Health
- Dental Health
- Muscle Function
- Neuropathy – Neurodegenerative diseases
- Mitochondria Restoration
- Cardiac Function
- Aging

And we are all sub-clinically deficient in this key nutrient!!

-Vermeer C, Shearer JM, Zittermann A, et al. Beyond deficiency: potential benefits of increased intakes of vitamin K for bone and vascular health. Eur J Nutr 2004, 43:325-35

-Cranenburg ECM, Schurgers LJ, Vermeer C. Vitamin K, the coagulation vitamin that became omnipotent. Thromb Haemost 2007, 98(1):120-25

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