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Vitamin E: The Forgotten Vitamin

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THE SEX VITAMIN

In 1922 Herbert M. Evans, a researcher specializing in embryology, and his assistant Katharine Bishop were feeding laboratory rats a highly refined diet. The rats appeared healthy but the pregnancies of the female animals were not going well. The pups were either resorbed or born dead.

Altered diets indicated that fresh lettuce or wheat germ prevented the infertility. Testing various extracts the researchers discovered that the unknown nutritional factor was fat soluble.

Other researchers soon discovered that lack of the same nutritional factor, when missing from the diet, rendered male rats sterile. Furthermore, lack caused damaging lesions in both the testes and uterus. In 1925 Evans adopted the name vitamin E for the nutrient.

Dr. George Calhoun, a professor of Greek literature, suggested the scientific name tocopherol to Evans. *Tocos* is Greek for “birth” and *feroin*, means “bringing” while the *ol* designates an alcohol. The first component of the future vitamin E family was isolated by Evans in 1936.

In 1937 Evans successfully isolated beta and gamma tocopherols and it became clear that the vitamin E factor was a family of compounds. An *alpha* was added to the name of

the first discovered member of the tocopherol family.

Eventually it was learned that there were 8 components to a natural vitamin E, four tocopherols and four tocotrienols. Each of the four are preceded by an alpha, beta, gamma, or delta.

Vitamin E was disparagingly referred to as the “sex vitamin” or the “shady lady” of the vitamins, particularly by those who rejected the value of the vitamin.

By 1938 the chemical structure of alpha-tocopherol was worked out. Hoffman-La Roche synthesized the vitamin and began selling it. Others began producing the natural vitamin by processing oils with molecular distillation.

EARLY RESEARCH

Early research on the vitamin E factor revealed that deficiency could lead to paralysis of baby rats, brain damage in chickens, and muscular dystrophy in guinea pigs and rabbits.

Damage from lack of vitamin E was relatively easy to prevent, but very difficult to reverse or repair. The vitamin functioned much more effectively as a preventative of diseases than as a treatment once deficiency symptoms appeared.

Deficiency symptoms developed slowly and by the time they appeared irreversible damage had

often already taken place. Damage to nerve tissue was particularly difficult to reverse.

Another early lesson was that tissues depleted of vitamin E were not replenished rapidly. Assessing the value and potency of vitamin E products by observing the effect on pregnant rats severely limited research until 1939 when a means of measuring vitamin E in foods and in the blood was developed. By 1940 it was clear that vitamin E functioned as a powerful fat-soluble antioxidant, but this was considered of little importance at the time.

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THE FAMILY

Vitamin E is generally thought of as alpha-tocopherol because it is the only member of the family that has been synthesized and it is the most abundant in the bodies of mammals. Alpha-tocopherol is also the most effective in supporting the reproduction of rats which was the only means of assessing vitamin E benefit in the beginning.

The diet usually contains more of the other tocopherols and tocotrienols than the alpha-tocopherol. The reason why the blood contains more alpha-tocopherol than the other members of the family is because the body has a *tocopherol transfer*

protein which selects for natural alpha-tocopherol and moves it into the bloodstream where it finds its way into the "bad" LDL cholesterol and prevents it from oxidizing.

The incorporation of vitamin E into cholesterol is of immense importance for the prevention of heart disease since alpha-tocopherol is very powerful in the prevention of oxidation of cholesterol. This is the beginning of the process of developing heart disease. Oxidized cholesterol has been shown to be 500 times more damaging to blood vessels than cholesterol that has not been oxidized. (All the early studies implicating cholesterol in heart disease were done with the oxidized product.)

Witztum and Steinberg launched the Coronary Primary Prevention Trial in 1979. This was the first large randomized, double-blind study to show that lowering cholesterol decreased heart disease. Their work was published just before the introduction of the statin drugs which reduce cholesterol synthesis. The statin drug bonanza for pharmaceutical firms was built upon this study.

These researchers were aware of the fact that oxidized cholesterol was the problem. Witztum observed that "oxidation of LDL renders it immunogenic....oxidized LDL is recognized by the body's immune system as abnormal, so now we know that atherosclerosis is actually an inflammatory process." It is the inflammatory process that initiates heart disease. Alpha-tocopherol reduces the risk of oxidized cholesterol.

Gamma and Delta

But the question is raised, "Is there any value to the other members of the vitamin E family?"

In 1977 Dr. Ferid Murad found that nitroglycerine released nitric oxide (NO) which dilated the blood vessels and relieved extreme angina pain associated with heart disease.

By 1986 researchers had learned that NO was an important signaling molecule functioning in many places in the body including the inner lining of the blood vessels where it improves circulation, reduces blood pressure, and makes it possible to achieve an erection for the male.

NO is also a weapon used by the immune system to kill infectious microbes and it is also involved in defense against tumors and cancer. This compound is considered so important that a Nobel Prize was awarded for NO research in 1998.

There is a problem with NO however. It is highly unstable and breaks down within 10 seconds which can lead to harmful nitrogen free radicals.

Alpha-tocopherol is not terribly efficient at dealing with nitrogen based free radicals, but gamma-tocopherol and gamma-tocotrienol are.

Stephan Christen conducted a study many years ago in which he fed his laboratory animals large amounts of synthetic alpha-tocopherol. He noticed that gamma-tocopherol blood levels dropped and tumor incidence in the animals increased! With alpha-tocopherol the animals were protected from heart disease, but their risk of cancer increased. Competitive absorption was depleting gamma-tocopherol.

Recent studies have shown that delta-tocopherol has anti-cancer properties similar to those of gamma-tocopherol.

The lesson here is that we need the entire vitamin E family. Tocotrienols have their own unique benefits as well. One of the things they do is slow down the synthesis of cholesterol in the liver.

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THE HEART

Rejection

Evan Shute, a Canadian physician, first became interested in the use of vitamin E to treat heart disease on February 15, 1946 when he gave his mother the vitamin for her angina which was so bad she could not walk across the kitchen without chest pain. She improved dramatically within one week.

He decided to start Roy Bicknell, his barber on the vitamin. Bicknell had such bad chest pain that the weight of his pajamas hurt his chest wall. By March 28, 1946 Bicknell was "virtually back from the dead."

Evan and his brother Wilfrid published on the benefits of vitamin E for heart disease in *Nature* in 1946. These early pioneers utilized vitamin E to treat atherosclerosis, heart attacks, angina, and the tendency to form blood clots.

The medical community was unbelieving and demanded a placebo-controlled trial which was very expensive at the time and very difficult due to the primitive technology available. Evan refused and considered it unethical to deny a victim of heart disease vitamin E. The attacks against the Shute brothers became vicious. Evan continued to publish his research on vitamin E privately until the late 1960's. No respected medical journal would publish his work.

Understanding

A great advance in understanding vitamin E was made in 1998 when Ingold and associates tagged vitamin E so it could be traced through the body in its various forms. At the time it was generally accepted that natural alpha tocopherol was uti-

lized 36% better than the synthetic dl-tocopherol version of the vitamin. This study, however, showed that the natural form of the vitamin was *twice* as bioavailable as the synthetic form of the nutrient in general and three times more bioavailable to an infant in the womb.

Early studies that treated the two forms of the vitamin as essentially equivalent were flawed. This contributed to the fact that many in the medical community rejected the value of vitamin E for heart disease, many at the cost of their own lives as pointed out by Evan Shute in his autobiography.

Turn Around

Many vitamin advocates had accepted the value of vitamin E for heart disease since the 1940's, but acceptance by the medical community began in earnest in 1993. In this year two studies were published in the prestigious *New England Journal of Medicine* showing dramatic benefits from supplementing with vitamin E.

The Nurses Health Study looked at the dietary intake of about 87,000 women. The group was divided into fifths with a range of vitamin E between 2.8 I.U. to 208 I.U. The fifth of the women with the highest intakes of vitamin E had about a 40% reduced risk of heart disease.

Vitamin E is not found in great abundance in many foods. The researchers noted that "Most of the variability in intake and reduction in risk was attributable to vitamin E consumed as supplements."

The researchers also noted that intake of vitamin E for "short periods had little apparent benefit." It was those who supplemented for over two years that experienced the benefit of the vitamin.

The second study was of almost 40,000 male health professionals. All of the males in the upper fifth of vitamin E intake were using supple-

ments of the vitamin. Those who obtained at least 100 I.U. for two years also had almost a 40% lower risk of dying from heart disease.

An epidemiological study of 16 European cultures published in 1991 looked at deaths from ischemic heart disease (IHD) which involves poor blood flow due to narrowing of the arteries. Gey and his associates concluded that "in the present study the cross-cultural differences of IHD mortality are primarily attributable to plasma status of vitamin E, which might have preventive functions."

In 1997 vitamin E made national news. Jason Mehta, a high school student, asked 181 cardiologists what habits they practiced to prevent heart disease. The number one practice was taking antioxidants and the most popular antioxidant was vitamin E. Jason's father, a professor of medicine, helped his son publish his high school project in the *American Journal of Cardiology*. Many cardiologists supplement with vitamin E, but do not recommend it to their patients.

How Does Vitamin E Protect? Antioxidant

Firstly, vitamin E is a potent fat soluble antioxidant. Fats in the body are usually found linked together as in cell walls, the brain and nervous system. This can lead to chain reactions. If oxygen attacks one fat and takes an electron this can then turn that fat to a free radical which will steal electrons from other fats.

Dr. Lester Packer referred to vitamin E as nature's master antioxidant in the March/April 1994 issue of *Scientific American*. Papas explains that the uniqueness of vitamin E is based on the structure of the antioxidant. It has a water loving (hydrophilic) head and a water fearing (hydrophobic) tail similar to the phospholipids in cell membranes. This structure allows vitamin E to anchor itself in cell membranes.

Papas writes, "Vitamin E has a unique structure that comes in very handy. Other antioxidants don't. Its tail is lipophilic (fat loving) and its head is slightly hydrophilic (water loving). This combination gives it unique properties. Like a soldier in a foxhole or a sentry on a wall, it is able to anchor itself in the membrane-its lipophilic tail going deep in the membrane. But its hydrophilic head stays closer to the surface...Each molecule of tocopherol protects a thousand fatty acids. Scientists believe that its position allows it to be regenerated by vitamin C and other antioxidants."

Free radicals can harden cell membranes doing a great deal of damage. One source of damage is alteration of red blood cells so they do not filter through the capillaries and spleen as well. A study on the damage free radical activity could do to red blood cells was conducted in the 1970's exposing the cells to lead and showing this loss of filterability. On a massive scale this can lead to hardening of the arteries, blood clots and other problems.

Protein Kinase C

Protein Kinase C is a signaling molecule that begins to malfunction when blood sugars become elevated. The result is impairment in circulation as illustrated by erectile dysfunction in diabetic males. Vitamin E has been shown to prevent many of the inflammatory and circulatory abnormalities that develop in the function of this cell signaling molecule when blood sugars are elevated. This both protects the heart and circulatory system of diabetics and helps to preserve sexual function.

Nitric Oxide

Gamma and delta-tocopherols increase the presence of nitric oxide in the lining of blood vessels and other places, but also assure that the by-products of its metabolism do not become nasty free radicals.



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ABSORPTION

Vitamin E is a fat soluble substance which means that absorp-

tion is anything but assured. This has proven to be a stumbling block to treatment of some diseases strongly associated with deficiency of the nutrient.

Absorption of fat soluble nutrients requires the production of bile by the liver and the release of bile by the gallbladder at the right point in the digestive process. Thus liver or gallbladder problems can lead to deficiency of a number of fat soluble nutrients like vitamins A and E.

Quality vitamin E complex products are made water miscible. This involves breaking the vitamin E material into tiny little microdots and mixing them with something like lecithin that will keep them dispersed. This is important with vitamin E because it is one of the more expensive nutrients to obtain in its natural form.

The vitamin E complex is a very good candidate for supplementation. It is present in only small amounts in foods and is almost always stripped from processed foods. At the same time the exposure to oxidizing agents in the environment and the presence of oxidized fats in the food supply has never been

higher.

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