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AS WE SEE IT

Dietary Supplements Under Attack

By William Faloon

Near the end of 2008, the media ran headline news stories claiming that **vitamins C, D,** and **E** do not prevent heart attack, stroke, or breast cancer. Within five days, we posted a rebuttal on the home page of our website.

When these biased stories are launched, the media never gives us *prior notice* to prepare a response. That means the public only hears conventional medicine's distorted side of the story.

What follows is a slightly modified version of how we responded to these unfounded attacks:

In the early 1990s, several large population studies showed significant reductions in cardiovascular disease in those who consumed vitamin C or vitamin E.[1-6]

The most widely reported study emanated from UCLA, where it was announced that men who took **800** mg a day of vitamin C lived six years longer than those who consumed the recommended daily allowance of **60** mg a day. The study, which evaluated 11,348 participants over a 10-year period of time, showed that higher vitamin C intake reduced cardiovascular disease mortality by **42%**.[7]

These kinds of findings did not go unnoticed by the federal government, who subsequently invested hundreds of millions of dollars in an attempt to ascertain if relatively modest vitamin doses could prevent common age-related diseases.

In a recent study used by the media to attack dietary supplements, four groups of male doctors were given various combinations of vitamin C and/or vitamin E or placebo. After eight years, there was no reported difference in heart attack or stroke incidence among the groups.[8] This led the media to state that consumers should not buy these supplements.

As you will read, there were so many flaws in this study that the findings are rendered meaningless. Regrettably, consumers who trust their lives to the mainstream media may fall victim to this latest charade to discredit validated methods to reduce cardiovascular disease risk.

DO YOU TAKE YOUR VITAMINS EVERY OTHER DAY?

In the study involving four groups of male doctors, subjects in the vitamin E groups were told to take one 400 IU capsule of synthetic alpha tocopherol every other day.[8] This design flaw raises several issues that are rather obvious to serious supplement takers.

First of all, we don't take our vitamins every other day. Free radicals are constantly being generated in our bodies, and supplement users today seek to take their antioxidants with most meals, as oxidative damage is generally the greatest after eating.[9,10]

It is ludicrous to think that these study subjects would reduce their vascular risk by taking a modest dose, every other day, of a form of vitamin E with inferior antioxidant capacity.

If one were to rely only on *synthetic* alpha tocopherol, the minimum daily dose needed has been shown to exceed 800 IU,[11,12] far greater than the 400 IU ingested every other day by the subjects in this poorly designed study.

Serious supplement users normally take 400 IU every day of natural vitamin E along with a plethora of complementary nutrients. We would not expect 400 IU of synthetic vitamin E taken every other day to produce much of an effect. Yet that is the dose given to these study subjects with the expectation that this would produce a reduction in cardiovascular disease. This is not the only flaw of this study.

NATURAL VERSUS SYNTHETIC VITAMIN E

There was a longstanding debate as to whether natural or synthetic vitamin E is better. For most vitamins, there is no difference between natural and synthetic. In fact, for most vitamins, the only forms available are synthetic. With vitamin E, however, the natural form has proven to be far superior.[4,13-16]

Natural vitamin E is distributed through the body much better than the synthetic form.[12,17-21] The reason is that specific carrier proteins in the liver selectively bind to natural vitamin E and transport it through the blood to our cells. These *carrier proteins* only recognize a portion of synthetic vitamin E and ignore the remainder.[22-25]

Japanese researchers gave natural or synthetic vitamin E to young women to measure how much vitamin E actually made it into their blood. It took only 100 mg (149 IU) of natural vitamin E to produce blood levels that required 300 mg (448 IU) of synthetic vitamin E to achieve.[12]

HOW TO CHECK VITAMIN E LABELS

When checking vitamin labels, natural vitamin E is usually stated as the ***"d"*** form or RRR- [for example ***d-alpha tocopheryl acetate or*** RRR-alpha-tocopheryl acetate, ***d***-alpha tocopherol, and ***d***-alpha tocopheryl succinate]. Synthetic vitamin E will have an ***"l"*** after the ***"d"*** or all-rac- [for example, ***dl-alpha tocopheryl acetate or*** all-rac-alpha-tocopheryl acetate, ***dl***-alpha tocopheryl succinate, and ***dl***-alpha tocopherol]. Remember – ***"dl"*** or ***"all rac-"*** signifies synthetic vitamin E, whereas *"d"* or ***"RRR-"*** signifies natural vitamin E. If you are getting **400** IU of natural ***d-alpha tocopherol*** (***d***-alpha tocopheryl succinate or acetate), it is equal to about **800** IU of synthetic ***dl-tocopherol (dl-alpha tocopheryl succinate or acetate).***

Most studies show that synthetic vitamin E is only *half* as active in the body as the natural form.[17] As it relates to the flawed study claiming that vitamin E does not prevent heart attack, the 400 IU of synthetic alpha tocopherol given every other day equates to only 100 IU a day of the natural form.

We would not expect 100 IU of natural vitamin E a day by itself to reduce vascular disease risk. As you will continue to read, however, there are many *other* flaws in this study that render its conclusions useless.

VITAMIN C POTENCIES TOO LOW

If all you are going to take to protect against free radical damage is vitamin E and/or vitamin C, then you will need far greater potencies than were given to the study subjects in this flawed study.

Published studies that document vascular benefits in response to vitamin C typically use doses of 1,000-6,000 mg each day.[26-31] The authors of the flawed study alluded[8] to this when they stated:

"In a pooled analysis of nine cohorts, vitamin C supplement use exceeding 700 mg/day was significantly associated with a 25% reduction in coronary heart disease risk."[8,32]

Since the doctors who designed this flawed study knew that vitamin C intakes exceeding 700 mg a day significantly reduce heart attack rates,[32] we cannot figure out why they limited their subject's daily dose to only 500 mg.[8]

Two-time Nobel Prize laureate Linus Pauling and his associates advocated daily doses of vitamin C ranging from 10,000 to 20,000 mg to protect against heart attack. Linus Pauling's theory was that atherosclerosis is primarily caused by insufficient vitamin C intake.[33] Dr. Pauling compared the high amount of vitamin C naturally synthesized in the bodies of animals that don't typically die of heart attacks.[34] A 150-pound goat, for example will maintain an ascorbate blood concentration equivalent to ingesting 13,000 mg of vitamin C.[34]

Unlike most animals, humans lack an internal enzyme needed to manufacture vitamin C in their body. If humans don't obtain enough vitamin C from external sources, they die acutely from scurvy, or according to Linus Pauling…slowly suffer atherosclerotic occlusion. Dr. Pauling crusaded to educate humans about the need to take mega-doses of vitamin C.

Dr. Pauling and his associates published papers stating that when vitamin C levels are insufficient, the body uses cholesterol to repair the inner lining of arteries. Dr. Pauling believed that cholesterol's involvement in atherosclerosis was a direct result of insufficient vitamin C.[34-36]

Life Extension has long recommended that its members take at least 2,000 mg a day of vitamin C, along with potent plant extracts to enhance the biological benefits of ascorbate inside the body. The 500 mg daily dose of vitamin C given to the subjects of this flawed study[8] was clearly inadequate. This did not stop the headline-hungry media and many conventional doctors from recommending that aging humans avoid these supplements altogether.

ALPHA TOCOPHEROL USERS NEED COQ10

A number of studies document the ability of *ubiquinol* **CoQ10** to protect against **LDL** oxidation better than **alpha tocopherol** (and other lipid-soluble antioxidants).[79-83]

Some of these studies show that **alpha tocopherol** vitamin E can turn into an LDL pro-oxidant unless **ubiquinol** is also present.[84,85] These studies help explain the inability of the alpha form of vitamin E by itself to significantly reduce heart attack rates in certain populations.

The good news is that most members have been taking **CoQ10** supplements since around **1983** (when Life Extension introduced it to the American public) and have thus protected their alpha tocopherol from converting into a pro-oxidant.

The subjects given synthetic alpha tocopherol in this flawed study were not given CoQ10 supplements, which further explains why there were no reductions in heart attack and stroke risk.

As we noted already, the dose of vitamin E used in this study was also too low to expect a reduction in vascular disease events. While alpha tocopherol vitamin E is a classic antioxidant, its free radical-quenching efficacy pales in comparison to polyphenol extracts[37] from **green tea**, **pomegranate**, **grape seed**, and **blueberry**.

Based on the superior anti-oxidant properties of plant extracts such as **pomegranate**, health-conscious people today are able to obtain greater protection against free radicals and enhance the efficacy of the vitamin C without necessarily having to take the mega-doses recommended by Linus Pauling. On the flip side, to attack the value of vitamin C based on a group of doctors who took only 500 mg a day does not make sense, since this amount does not correspond to the doses that scientific studies show are needed to prevent heart attack.

ALPHA TOCOPHEROL DISPLACES GAMMA TOCOPHEROL

An increasing number of scientists are questioning the wisdom of administering alpha tocopherol vitamin E by itself.[38-42] The reason is that *alpha* tocopherol displaces critically important *gamma* tocopherol in the body.[43] The authors of the flawed study admitted that the failure to include gamma tocopherol may have been a reason that no effect was seen in the alpha tocopherol groups.[8] Here is a quote directly from the flawed study:

"Moreover, PHS II and other prevention trials have used alpha-tocopherol, whereas the gamma-tocopherol isomer also may have a role in cardiovascular disease prevention because it has greater efficacy than alpha-tocopherol to inhibit lipid peroxidation and it may be suppressed in the presence of alpha-tocopherol."[8]

The above admission understates the critical importance that *gamma* tocopherol plays in maintaining arterial health. While *alpha* tocopherol helps protect against lipid peroxidation, *gamma* tocopherol is required to neutralize the dangerous **peroxynitrite** free radical.[44]

Peroxynitrite damages arteries because:

1. Peroxynitrite promotes the degradation of alpha tocopherol, thereby depleting the body of the vitamin E needed to protect the *lipid* (fat) part of LDL against oxidation.[45] LDL is composed of both lipid and protein parts (moieties), and oxidation associated with both moieties has been implicated in atherosclerosis.[46,47] In a fascinating paradox, when alpha tocopherol is given without gamma tocopherol, the result is that alpha tocopherol itself can be neutralized in the body by the peroxynitrite free radical. This in turn promotes oxidation of the lipid moiety of LDL, a major step on the path towards atherosclerosis.

2. Peroxynitrite promotes LDL *protein* oxidation.[48-51] While alpha tocopherol inhibits LDL lipid peroxidation, gamma tocopherol is needed to protect against oxidation of the *protein* moiety of LDL.[42,52,53]

In the absence of gamma tocopherol, which can occur when alpha tocopherol is given without gamma tocopherol, both LDL *lipid* and *protein* oxidation is increased, which reveals the egregious mistake of trying to prevent vascular disease by administering only alpha tocopherol. Health-conscious individuals should be assured that other nutrients such as lipoic acid and polyphenol plant extracts also block protein and lipid LDL oxidation.[9,54-62]

Some studies suggest that only *gamma* tocopherol prevents heart attacks.[6] As it relates to atherosclerosis, gamma tocopherol blood concentrations have been reported to be significantly lower in coronary heart disease patients than in healthy control subjects. While alpha and gamma tocopherols each perform life-sustaining functions, only gamma tocopherol increases endothelial *nitric oxide* protein expression.[52,53,63] As I will describe next, a deficit of nitric oxide in the endothelium is a primary cause of arterial disease.

VITAMIN E BASICS

Alpha tocopherol and gamma tocopherol are the two major forms of vitamin E in human plasma. The dietary intake of gamma toco-pherol is generally two- to four-fold higher than that of alpha tocopherol. Alpha tocopherol plasma levels, however, are about four-fold higher than those of gamma tocopherol.[64] One reason is that there is a preferential cellular uptake of gamma tocopherol over alpha tocopherol, meaning that more *gamma* tocopherol is removed from the blood and assimilated into cells.[65]

Scientific studies consistently show that gamma tocopherol plays a significant role in modulating intracellular antioxidant defense mechanisms.[39,42,66] Interestingly, the presence of gamma tocopherol dramatically increases the cellular accumulation of alpha tocopherol.[67]

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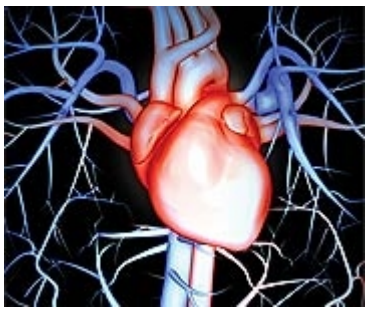
A HIDDEN CAUSE OF HEART ATTACK AND STROKE

Even when all conventional risk factors are controlled, the progressive decline of *nitric oxide* in the arterial wall (the endothelium) too often leads to coronary heart attack and stroke.[68-75]



Seven years ago, Life Extension researchers identified a critical compound (tetrahydrobiopterin) that is an essential cofactor for the enzyme that synthesizes nitric oxide in the endothelium.[76] We spent several hundred thousand dollars trying to develop an affordable way to manufacture this compound as it offered tremendous promise for eradicating atherosclerosis.

We failed to find an affordable way to make tetrahydrobiopterin. The good news is that nutrients that suppress peroxynitrite (like gamma tocopherol and pomegranate) increase endothelial nitric oxide by blocking the oxidation of tetrahydrobiopterin.[77,78]

Indeed, clinical studies show that supplemental gamma tocopherol enhances platelet endothelial nitric oxide synthase activity.[52,53] Furthermore, a diet high in gamma tocopherol-rich walnuts improves endothelium-dependent vasodilation in those with high cholesterol.[63]

By administering only alpha tocopherol as was done in the flawed study, one would expect gamma tocopherol to be suppressed, peroxynitrite levels to increase, and precious tetrahydrobiopterin to be oxidized, thus depriving the endothelium of the *nitric oxide* it needs to protect against heart attack and stroke. Is it any wonder that this study failed to show vascular disease reduction in those given only alpha (but not gamma) tocopherol?

FAILING TO ACCOUNT FOR ALL VASCULAR RISK FACTORS

Numerous independent risk factors are associated with the development of atherosclerosis and subsequent heart attack and stroke risk. A major flaw in this study was expecting low-dose vitamin C and/or E to somehow overcome all of these underlying causes of artery disease.

We know it is *impossible* for vitamins C and E to overcome these many risk factors, but this did not stop the media from recommending that Americans discard their supplements.

The following represents a succinct list of documented vascular disease risk factors:

1. Low testosterone (in men)
2. Excess fibrinogen
3. Low HDL
4. Excess LDL and total cholesterol
5. Excess glucose
6. Excess C-reactive protein
7. Excess homocysteine
8. Hypertension
9. Low blood EPA/DHA
10. Excess triglycerides
11. Excess insulin
12. Excess estrogen (in men)
13. Oxidized LDL
14. Excess platelet activity
15. Nitric oxide deficit (endothelial dysfunction)
16. Insufficient vitamin D
17. Insufficient vitamin K2

The basis for doing this study, as outlined by the study's authors, was to use vitamins C and/or E to:

1. Trap organic free radicals… deactivate excited oxygen molecules… inhibit LDL oxidation
2. Modify vascular reactivity… prevent tissue damage
3. Modify platelet activity and thus reduce thrombotic potential.

As one can clearly see on the previous page, there are **17** documented cardiovascular risk factors. Yet only three of these risk factors are what formed the basis for conducting this low-dose vitamin C and/or E clinical trial. The three most important risk factors the authors of the flawed study expected to favorably influence with vitamins C and E were:

1. LDL oxidation
2. Platelet activity and thrombotic potential
3. Vascular reactivity (another term for endothelial dysfunction).

For every one mechanism the study's authors proposed might enable low-dose vitamin C and/or synthetic vitamin E to work, there are five additional risk factors that would not be corrected. For instance, vitamins C and E in these low doses are not going to reduce C-reactive protein,[86] homocysteine, fibrinogen, or glucose.[87] Vitamins C and E in any dose are not going to increase testosterone, decrease estrogen, or provide cardioprotective EPA/DHA and vitamin D.

On the contrary, as we have already shown, by giving only alpha but not gamma tocopherol, one might expect increased LDL oxidation and impaired endothelial function. That's because alpha tocopherol displaces gamma tocopherol in the body. Gamma tocopherol suppresses the peroxynitrite radical that oxidizes both LDL protein and the tetrahydrobiopterin that is needed to produce endothelial *nitric oxide*.

As far as platelet activity and thrombotic potential (abnormal clotting inside a blood vessel) are concerned, *gamma* tocopherol is significantly more potent than alpha tocopherol in inhibiting platelet aggregation that can lead to a heart attack or stroke.[52,53] By displacing *gamma* tocopherol, the *alpha* tocopherol used alone in this study may have increased abnormal platelet aggregation risk.

From everything we know today, this study was designed to fail. Not only did it not correct for the major causes of vascular disease, but it may have exacerbated some of the more dangerous ones.

NONE OF WHAT I WROTE SO FAR MAY REALLY MATTER

You have just learned why low-dose vitamin C and/or E supplementation would not be expected to reduce heart attack and stroke risk.

I have saved the biggest shocker for last. It turns out that a significant number of the study subjects (who were all medical doctors) who were supposed to take the vitamin C and/or E supplements did not take their pills. Yet when the calculations for heart attack or stroke incidence were made, those who took as little as **66%** of their low-dose vitamin C and/or E supplements were counted as having taken the entire dose.

At the end of the study, **28%** of the study subjects admitted they had not even taken **66%** of their low-dose vitamin C and/or E supplements.

Even more troubling is the method used to track who was really taking their supplements. Participants were asked to remember and track supplement usage for over eight years' time without any verification of actual pill counts, compliance by plasma antioxidant analysis, or in vivo surrogate markers of oxidative stress. Relying upon participants' memory and recollection over a lengthy time period of many years is a rather pathetic way of ensuring adherence, and renders the authors' so-called "sensitivity analysis" meaningless.

The lack of adherence, i.e., the fact that a significant percentage of the study participants were not even taking their vitamins, may be the most significant flaw to this study. No one in the mainstream media bothered to report this, or any of the other flaws that jumped out at us.

Instead, the media's message was don't waste your money on vitamin C or E pills. Many supplement users who are taking the right form and dose of their vitamin C and E nutrients may believe the media's biased reporting.

SHOCKING DEFICIENCIES OF VITAMIN E

The media used this horrific-ally flawed study as a basis to steer Americans away from vitamin C and E supplements. It's as if all of the previous *positive* published studies disappeared overnight.

What was omitted is the fact that **92%** of American men and **98%** of American women do not consume the recommended dietary allowance of **vitamin E** in their diet. The federal government says Americans need **15** milligrams per day of vitamin E, yet even this minute amount is not found in the diets of the vast majority of people.[88]

This means that most Americans require a vitamin E supplement to avoid a chronic deficiency, but this important fact was conveniently left out of the news stories.

Conventional medicine says that severe vitamin E deficiency results mainly in neuro-logical symptoms such as impaired balance and coordination and muscle weakness. These neurological symptoms do not develop for 10-20 years, as it takes time for free radicals to inflict nerve damage in the absence of sufficient vitamin E. The reality is that chronic vitamin E deficiency adversely impacts virtually every cell of the body.[89-94]

DOES DRUG MONEY INFLUENCE HOW MEDICAL JOURNALS REPORT ON DIETARY SUPPLEMENTS?

A group of statistical researchers investigated the relationship between **pharmaceutical advertising** and articles regarding **dietary supplements** in medical journals.[99] The analysis revealed that:

1. Journals with the most pharmaceutical ads published significantly fewer major articles about dietary supplements per issue than journals with the fewest pharmaceutical ads ($P < 0.001$).
2. The percentage of major articles concluding that dietary supplements were unsafe was 4% in journals with the fewest pharmaceutical ads and 67% among those with the most pharmaceutical ads ($P < 0.005$).
3. The percentage of articles concluding that dietary supplements were ineffective was almost twice as high (50%) among journals with more pharmaceutical ads than among those with fewer pharmaceutical ads (27%).

The researchers concluded that increased pharmaceutical advertising is associated with the publication of fewer articles about dietary supplements and more articles with conclusions that dietary supplements are unsafe.[99]

A major reason why many conventional doctors are biased against dietary supplements is that the journals they read seldom publish the favorable studies. Dietary supplements compete directly against prescription drugs in many disease categories. When dietary supplements are properly used to prevent disease, demand for expensive pharmaceutical agents is diminished. It is thus in the financial interest of pharmaceutical companies to encourage negative studies to be published in influential medical journals.

It seems more than a coincidence that mainstream medical journals publish negative editorials against dietary supplements at times of the year that garner the most media coverage. *Life Extension* has long argued that the billions of advertising dollars spent by pharmaceutical companies influences media bias against dietary supplements. This latest study reveals that drug money may also be corrupting medical journals that have a significant impact on professional and public opinion.

A MEDIA COUP FOR PHARMACEUTICAL COMPANIES

The optimal moment of the year to get your message to the masses is the second week of November. This is a time in between holidays, when winter is setting in, and few people are on vacation. The television networks consider this their most important "sweeps week" as it provides the most accurate measurement of their ratings.

The timing of the release of this horrendously flawed vitamin C and E study could not have been more perfect for pharmaceutical interests. It came out less than one week after the November elections, when the media was primed to sensationalize any story that would attract viewers for their all important "sweeps week."

On the very same day the media launched its attack on vitamins C and E, the same news sources reported that very high doses of the statin drug Crestor® reduced heart attack rates by 54% in healthy people who had high *C-reactive protein* levels.[95] Just think, uneducated consumers read on the same day that vitamins C and E are worthless and an expensive statin drug performs miracles.

Financial analysts predict a windfall for the makers of Crestor® based on this widely distributed report. In retrospect, conducting a study only on people with high C-reactive protein (but not particularly high LDL) was a brilliant marketing strategy. It had a high probability of a successful outcome, and if the study failed, Crestor® was never approved to lower C-reactive protein or be used in this population group, so the pharmaceutical company had nothing to lose.

We at *Life Extension* have long warned about the vascular dangers of elevated *C-reactive protein* and even recommended statin drugs if natural approaches fail to reduce C-reactive protein. We don't believe most people have to purchase expensive brand name drugs like Crestor®, as generic simvastatin (name brand Zocor®) or pravastatin (name brand Pravachol®) can provide similar benefit at a fraction of the price.

MEDIA ALSO ATTACKS VITAMIN D

Not content to bash only vitamins C and E, the media the very next day in November 2008 ran a headline story stating that "Supplements don't reduce breast cancer risk." This story was based on a study of women who received *only* **400 IU** a day of supplemental vitamin D.[96]

As has been reported for years in this and other health publications, 400 IU a day of vitamin D is clearly inadequate.[97] To reduce breast cancer risk by around 50%, a daily dose of 1,000 IU and higher is required. The major flaw in this study is that participants in the active and placebo group were allowed to take vitamin D outside the study, which rendered the findings meaningless even if the proper dose had been given.

The fact that the media made this study headline news is regrettable because only about **20%** of the study population achieved a **25-hydroxyvitamin D** blood result at the minimum level required to prevent breast cancer (approximately **30** ng/mL or higher). In other words, most participants in the active or placebo group failed to achieve even the minimal blood concentrations of vitamin D that other studies document are needed to protect against breast cancer.[98] So all this study did was help confirm what vitamin D experts have been saying for over five years now, i.e., a minimum of 800 IU to 1,000 IU of vitamin D a day is required… not the 400 IU used in this study.

DON'T BE A VICTIM OF THIS FLAWED PROPAGANDA

It is in the economic interests of drug companies to steer Americans away from healthier lifestyles and dietary supplements. As more Americans fall ill to degenerative disease, drug company profits increase exponentially.

Enormous amounts of pharmaceutical dollars are spent influencing Congress, the FDA, and other federal agencies. The result is the promulgation of policies that cause Americans to be deprived of effective, low-cost means of protecting themselves against age-related disease.

As a *member* of the Life Extension Foundation, you gain access to scientific information that is interpreted in the context of what health-conscious people are *really* doing to protect themselves against age-related diseases. You also learn how this information is distorted by the government, drug companies, and the media to *discourage* the public from following healthier lifestyles.

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