

Vitamin E—Understanding Tocopherols and Tocotrienols and What They Mean to Your Health!

ABSTRACT: A Johns Hopkins study of Vitamin E supplementation has called attention to erroneous assumptions by the supplementation industry. The conclusions we can draw from that study is that "more" is *not always better* when it comes to dietary supplementation. In the case of Vitamin E, too much can increase your chances of death from coronary heart disease (CHD).

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However, the right dosage of the right kinds of Vitamin E (such as that found in the famous "Mediterranean Diet") may just be the single best thing you can do for your health.

vitamin e remains the master antioxidant, protecting your body from serious conditions such as CHD, cancers, and premature aging. You can still reap the benefits from Vitamin E if you know the correct types and amounts you should be using on a daily basis.

SMART PUBLICATIONS RESEARCH TEAM, Petaluma, CA—Researchers at Johns Hopkins unleashed a storm of controversy recently when they released a report on the safety of Vitamin E supplementation.

The report was released in the Annals of Internal Medicine on November 10, 2004. It stated that people taking mega-doses of Vitamin E in excess of 400 IU/day had a 5% increased chance of death from coronary heart disease (CHD).

Most Vitamin E supplement capsules contain 400 IU to 800 IU.

In the current Johns Hopkins study, the research team analyzed raw data from 19 previous studies involving more than 136,000 patients in North America, Europe, and China.

The Vitamin E Paradox ... Why Vitamin E Protects Only Some People

The Vitamin E study from Johns Hopkins brings up serious questions about the effectiveness and safety of this powerful antioxidant. But it also brings into focus a paradox that has befuddled nutritional scientists for years.

The paradox is this: People who take high levels of Vitamin E supplements don't gain anywhere near the benefit nutritionists predict. But people who follow a diet high in Vitamin E enjoy much better general health.

The health-boosting capabilities of dietary Vitamin E were beautifully illustrated in a 12-year study of over 88,000 female nurses in the United States (known as the "Nurses Health Study"). Nurses who ate a diet high in Vitamin E had fewer heart problems ... lower rates of breast and cervical cancers ... lower cholesterol levels ... and generally much better health than those who didn't.

Other studies have shown that men who eat this type of diet have a similarly high level of good health, lower PSA scores, lower incidents of prostate and other cancers, significantly lower LDL (bad) cholesterol levels, improved heart function, and decreased incidence of heart disease.

In other words, men who eat a diet higher in Vitamin E are healthier than men who don't.

So why is a typical high Vitamin E diet—a diet containing foods such as nuts like walnuts and pecans, whole grains, extra virgin olive oil, and dark green vegetables—a diet that can help extend life and improve health ... while typical Vitamin E supplementation has little or no effect (or worse) on your health?

The solution to this paradox means a huge difference in your health.

The solution is this: Most Vitamin E supplements—indeed, the Vitamin E supplements used in the clinical studies in the Johns Hopkins analysis—are not really Vitamin E at all. They are only one part of a complex mixture of similar molecules, all of which are present in foods high in Vitamin E.

Let us explain.

A Little Science to Keep You Healthy ... What Vitamin E Really Is

Vitamin E is not one thing. It is eight similar but different compounds. These eight compounds exist naturally in your body and in a well-balanced, whole-food diet like the Mediterranean Diet.

Unfortunately, most of the attention Vitamin E has received is focused on just one of these compounds—alpha-tocopherol. The reason is alpha-tocopherol is the most easily isolated and synthesized of the eight constituents of Vitamin E—and by far the most commonly used form in supplementation.

But all of these components are important in keeping you safe from the ravaging effects of free radicals. (More about free radicals in a moment.)

Studying just one of these eight compounds in isolation from the rest—and arriving at conclusions about Vitamin E—simply does not make sense. It's like trying to judge all Ford trucks based on just the F150.

There are two classes of components in Vitamin E: tocopherols and tocotrienols—each class with four distinct compounds (for your total of eight). Figure 1 shows you the structure of these four compounds.

A good diet or supplementation program contains all eight of these compounds. But for this discussion, we'll focus primarily on two of them: alpha-tocopherol and gamma-tocopherol.

(The other six compounds are called beta-tocopherol, delta-tocopherol, alpha-tocotrienol, beta-tocotrienol, gamma-tocotrienol, and delta-tocotrienol.)

Figure 1 shows the structure of alpha- and gamma-tocopherol molecules. You will notice that the only real difference is in the "head" (or the chroman ring) of the molecules. This is also the active part of the molecule, the part that protects against free radical damage and oxidation.

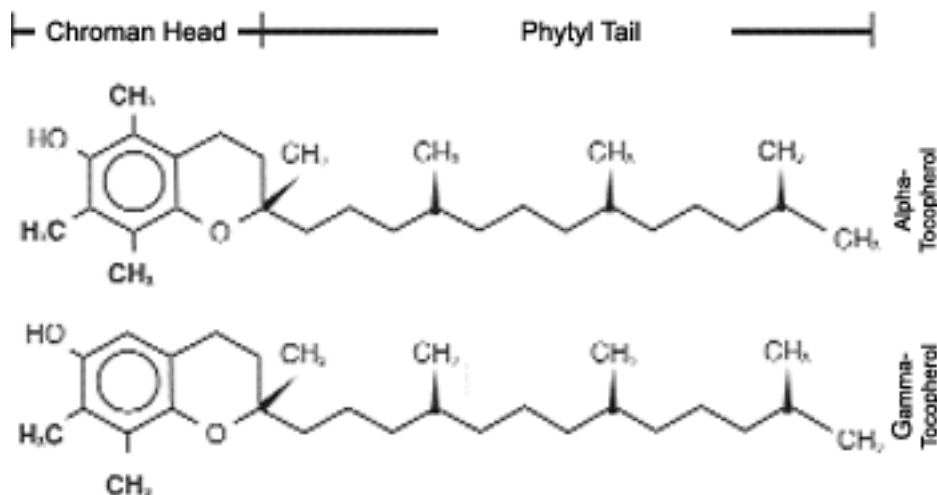


Figure 1: Alpha-Tocopherol & Gamma-Tocopherol Molecular Structure

The tail (or the phytyl end) in all the four tocopherols is identical.

The structural difference between the two molecules may be small, but that difference makes a huge difference in the way the compounds act in your body. It's like looking at two different old-fashioned keys.

The inactive tail of the molecule is the stem of the key. The head is the bit or active part of the key. Keys with just slightly different shapes open different locks.

Table 1: Antioxidant Activity of Selected Tocopherols

Kind of Tocopherol	Antioxidant Activity
<i>d</i> -alpha tocopherol	100
<i>d</i> -gamma tocopherol	130

It's the same with the components of Vitamin E. Alpha-tocopherol's major chore is to neutralize the effects of reactive oxygen in your body. Gamma-tocopherol's main job is to neutralize reactive oxygen and reactive nitrogen. It also has higher antioxidant activity than alpha-tocopherol.

Gamma-tocopherol complements the activity of alpha-tocopherol ... and works together with the other six components of Vitamin E. These eight key components protect you from the ravages of free radicals and damaging oxidation at a cellular level.

Vitamin E—complete eight-component Vitamin E like that in the

Mediterranean Diet—is an insurance policy. It ensures you will be strong, healthy, and active ... for yourself, for your family and loved ones, and for those who depend on you.

We've mentioned free radicals and antioxidants quite a bit here ... and we're sure you've heard a lot about them in the past. But if you want to understand how important Vitamin E is to your overall health, we think that you'll appreciate a clearer picture of these two critical aspects of your health.

Free Radicals: Are They the Real Villains?

You've heard so much negative press about free radicals (and their partner "oxidation") you might have been left with the impression that they are terrible villains whose sole purpose is to destroy your body. (Confused about what oxidation really is? See the sidebar "The Inside Story on Oxidation".)

This image could not be further from the truth.

Free radicals are normal by-products of a normal metabolism. In fact, they are a necessary part of a normal metabolism. Free radicals are also an important part of your immune system's arsenal against infection and disease. It's when they run amok that serious problems like cancers, heart disease, diabetes, and premature aging occur.

What Are Free Radicals?

Think back to high school chemistry for just a moment.

Molecules are made up of atoms linked together by chemical bonds. Every atom consists of a nucleus at the center and electrons that travel around the nucleus. The important thing here is that electrons like to be paired.

Molecules are usually neutral. That is, every electron is paired with another one. But sometimes one of the outer electrons gets stripped away. This can happen as a result of normal metabolic activity. Or it can be due to environmental conditions like radiation, smoke, and pollution.

When an outer electron gets stripped away, the result is a free radical. The molecule doesn't like being in this state. It becomes very unstable and reactive and frantically seeks a way of neutralizing itself. It neutralizes itself

by stealing an electron from another molecule.

You can see how this can start a chain reaction inside your body. One free radical steals an electron from another molecule, converting it into another free radical. That new free radical goes on and strips away an electron from yet another molecule. And so on.

Creating Damage Like a Runaway Train

The dangerous free radicals are the ones that are the most reactive. They steal electrons from any place they can get them such as your DNA or the natural fats in your body (called lipids).

DNA is a huge, twisted molecule that carries all your genetic information. It is the master library in your cells that not only tells what your offspring are supposed to look like. It also tells each and every cell in your body what to do.

ANTIOXIDANTS

- Prevent the formation of excess free radicals
- Scavenge free radicals after they have formed and before they damage other molecules like your DNA and lipids ... and before they can attack and damage your cell membranes
- Repair damaged molecules or replace the damaged ones with new, healthy molecules
- Protect you safely and without causing more damage themselves

DNA tells your heart muscle cells to act like heart muscle cells and to grow into other heart muscle cells. It tells the marrow in your bones how to make red blood cells. It tells your lung cells how to grow and develop into fully functional lung cells.

So, when an electron gets stolen from your DNA, the DNA becomes damaged. If it isn't repaired or protected by an antioxidant, it will carry the wrong information. That wrong information can cause the cell where the damage is to develop into something its not supposed to be—Cancer. The cell then—develops faster than it should and doesn't reproduce as it should.

When free radicals interact with lipids in cell membranes, something called lipid peroxidation occurs. This is just a fancy way of saying your lipids become rancid. Rancid, damaged membrane lipids are a major cause of blockages in your veins and arteries ... leading, of course, to coronary heart

disease.

Free radical damage is so invasive that it's been fingered as a cause of almost every major chronic illness.

"Free radicals are cellular renegades; they wreak havoc by damaging DNA, altering biochemical compounds, corroding cell membranes, and killing cells outright. Such molecular mayhem, scientists increasingly believe, plays a major role in the development of ailments like cancer, heart or lung disease, and cataracts. Many researchers are convinced that the cumulative effects of free radicals also underlie the gradual deterioration that is the hallmark of aging in all individuals, healthy as well as sick."

Time Magazine, April 6, 1992

Antioxidants to the Rescue

As we said before, free radicals are highly reactive molecules that are looking to gain stability by stripping an electron from another molecule—that is, oxidizing it.

What if we could find a molecule willing to give up an electron that was not as reactive as the free radical. A sort of "protector" molecule willing to give its life to protect yours. A molecule that as a free radical could easily and quickly be disposed of or safely metabolized back into another protector molecule. With such a molecule, the problem of free radicals could be solved. Your body could go on producing necessary free radicals while preventing unnecessary damage.

This is the perfect description of an antioxidant molecule—a molecule whose molecular structure counteracts the effects of runaway oxidation produced by uncontrolled free radicals.

"This is the first time gamma-tocopherol has been shown to induce death in lab-grown human cancer cells while leaving healthy cells alone. The study shows that the anticancer effect is enhanced when mixed forms are used."

Qing Jiang
Assistant Professor
Purdue University

The Master Antioxidant: Vitamin E

Nature has devised numerous antioxidants, but Vitamin E is one of the most powerful and works so effectively on a number of different levels that it's been dubbed the "Master antioxidant" by Andreas Papas, PhD—renowned adjunct professor at James Quillen College of Medicine at East Tennessee State University.

Vitamin E fights against free radicals in a number of different cellular arenas. But one of its most important functions appears to be protecting your cell membranes from free radical damage.

A thin membrane that acts as a cellular protector surrounds every cell in your body. But the cell membrane's function is much more complex than that. It also must transport nutrients and vital substances into the cell while transporting cellular waste products out.

Figure 2 shows a simplified diagram of a small piece of cell membrane. Phospholipids—a special type of lipid molecules—make up a major part of the membrane. Alpha- and gamma-tocopherol are strategically placed in the cell membrane to act as guardians against free radicals.

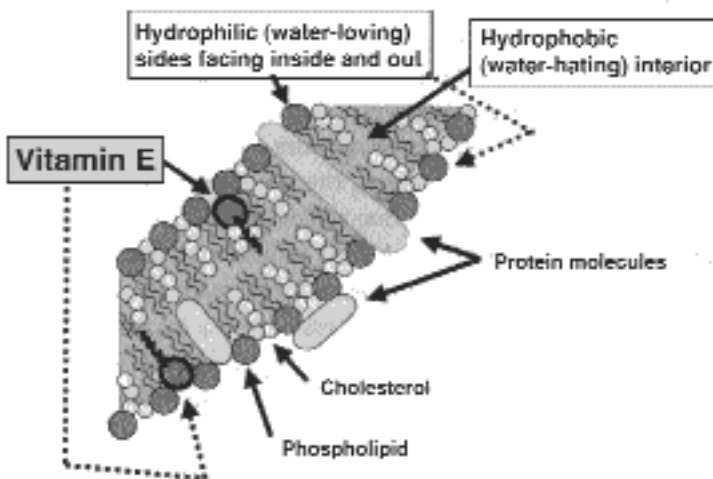


Figure 2: Vitamin Protects Cell Membranes from Free Radicals

If a free radical attacks one of the lipids, a near-by tocopherol can take the brunt of the attack saving the phospholipid from having an electron removed (being oxidized) and becoming rancid. Or, if the phospholipid is oxidized, the tocopherol molecule quickly reverses the oxidation before long-term damage

is done.

Similarly, the tocopherol molecules protect the cholesterol portion of your cell membrane.

It's important at this juncture to point out that both HDL ("good" cholesterol) and LDL ("bad" cholesterol) are important structural components of many parts of your cells including the membrane. They are also building blocks of many hormones and other physiologically important compounds.

It is only when LDL cholesterol becomes oxidized that it becomes a problem. Oxidized LDL cholesterol is the most important factor in getting blocked arteries. This blockage is the cause of coronary heart disease, heart attacks, phlebitis, and even strokes!

If not protected by Vitamin E, cholesterol in membranes and throughout your body will become oxidized by free radicals. The survival of a cell depends on the integrity of its membrane. If a phospholipid becomes oxidized, it migrates to the surface of the membrane.

The membrane structure loses its integrity and becomes leaky ... a death sentence for the cell.

Vitamin E's Special Powers

As mentioned earlier, free radicals don't attack just one other molecule and fall over dead. They start a chain reaction of destruction. Vitamin E has special powers to disrupt that chain reaction, especially in the membrane. By disrupting the chain reaction at the membrane, Vitamin E keeps the membrane fluid. A fluid membrane is necessary for it to do its critically important jobs in keeping your cells—and you—alive. Other chain reaction breaking antioxidants are not able to do this.

By sitting near the surface of the membrane, Vitamin E's active site (the chroman head) is available not only to fight free radicals. It is also easily accessible for regeneration by other antioxidants like vitamin C. Since Vitamin E can be so readily restored to its full fighting capacity, a single molecule can protect thousands of phospholipid molecules by deactivating attacking free radicals.

Vitamin E and Cell Communication

Your cells "talk" to each other. They have to or else the wonderfully complex, interactive thing called "you" could not exist. Without cellular communication, no multi-celled organism could exist. In fact, even the cells in the most primitive organisms communicate between each other.

The Special Role of Nitric Oxide in Cell Communication

Your cells communicate in a number of ways, but one of the most surprising is by using the nitric oxide molecule (NO).

In 1998, the Nobel Prize for Medicine was awarded to two scientists—Dr. Robert Furchgott and Dr. Louis Ignarro—for their groundbreaking work in determining how this simple and unstable molecule conveys signals among cells.

Since Furchgott and Ignarro's pioneering work, NO has been found to have a wide range of very important functions:

- NO—produced in the lining of arteries—dilates them as a way of regulating blood pressure. In atherosclerosis the lining loses its ability to produce NO.
- White blood cells counter bacterial and fungal infections and parasite infestations by releasing enormous amounts of NO.
- White blood cells use NO to defend against cancerous tumors.

NO is an unstable molecule with a life span of less than 10 seconds. It breaks down to form nitrates and nitrites—two very reactive forms of nitrogen.

So nitric oxide's role in your body is a case of good news-bad news. The molecule allows cells to carry on important communication that is essential to your staying alive. And it breaks down into molecules that speed up your death.

Gamma-Tocopherol Referees the Fight

This might seem like an un-winnable situation, but nature has once again provided an elegant solution in the form of gamma-tocopherol. Gamma-tocopherol has the ability to change highly reactive nitrogen back into safe NO. Or it can change it into a variety of harmless compounds.

Alpha-tocopherol lacks this ability!

Purdue Study Points to Potent Cancer Protection

A recent Purdue University study led by Qing Jiang (pronounced "ching zhang") has indicated that gamma-tocopherol—the form of Vitamin E found in many plant seeds but not in most manufactured nutritional supplements—might halt the growth of prostate and lung cancer cells.

The research team found that gamma-tocopherol inhibits the proliferation of human prostate and lung cancer cells in lab tests. The vitamin's presence interrupts synthesis of certain fatty molecules called sphingolipids in cancerous prostate cells. However, the gamma-tocopherol leaves healthy human prostate cells unaffected, which could give it significant value as an anticancer agent.

"This is the first time gamma-tocopherol has been shown to induce death in lab-grown human cancer cells while leaving healthy cells alone," said Jiang, who is an Assistant Professor of Foods and Nutrition in the College of Consumer and Family Sciences.

"This could be wonderful news for cancer patients if the effect can be reproduced in animal models. But because most nutritional supplements contain only alpha-tocopherol, a different form of Vitamin E that alone does not have these anticancer properties, it may be better to supplement the diet with mixed forms of Vitamin E. The study shows that the anticancer effect is enhanced when mixed forms are used."

A Quick Peek at the Other Tocopherols and Tocotrienols

The two most dominant forms of Vitamin E in the Mediterranean Diet and other whole food diets high in Vitamin E are alpha-tocopherol and gamma-tocopherol. Beta-tocopherol is present in lower quantities than either the alpha and gamma forms. And its antioxidant power is also lower.

Delta-tocopherol has the strongest antioxidant power of all four tocopherols, but like beta-tocopherol, it is in lower quantities in a Vitamin E rich diet.

Tocotrienol's Vital Role

The main components of Vitamin E are the tocopherols. But the tocotrienols mentioned earlier are also important guardians of good health. The four

tocotrienols differ from tocopherols by having double bonds in the tail of the molecule. The active chroman head structure remains the same as its analogous tocopherol.

Most of the research into Vitamin E has been done on alpha- and gamma-tocopherols, but research on the tocotrienols is increasing and showing their importance in maintaining good health. For instance, research indicates that tocotrienols can clear atherosclerotic blockage in the carotid artery, a condition that can lead to stroke. (*Lipids* 1995 Dec; 30(12); 1179-83)

Cholesterol levels have also been lowered by the tocotrienol fraction of Vitamin E. One particular study involved 25 high cholesterol patients in a double blind study. The treatment group was given four capsules daily of tocotrienols mixed with palm oil, while the control group was given corn oil.

After eight weeks, total cholesterol and LDL levels decreased significantly in the 15 subjects given the palm tocotrienols, while the control group exhibited no change. (*Am Journal of Clinical Nutrition* 1991 Apr; 53 (4 suppl.): 1021S-1026S)

Tocotrienols are showing promise in the battle against cancer. Tests show tocotrienols have the ability to kill cancer cells by inducing programmed cell death (known as apoptosis). While doing this, it leaves healthy cells alone.

Human breast cancer cells have also responded positively to tocotrienol treatment as noted in a study of cancer cells in culture whose growth was inhibited. (*Lipids* 1995 Dec; 30 (12): 1139-43).

Other in vitro study cases have effectively demonstrated the ability of tocotrienols to hold back the growth of estrogen receptor-positive and estrogen receptor-negative breast cancer cell reproduction. (*Lipids* 1998 May; 33 (5): 461-9). Interestingly, in these studies, it was the gamma- and delta-forms of tocotrienols that did the trick, not alpha-tocopherol—which actually proved ineffective.

A Closer Look at Alpha- and Gamma-Tocopherols Putting the Puzzle Together

There can be no doubt that Vitamin E is a powerful and much-needed antioxidant and guardian of health. Or, perhaps we should say that the eight different forms of Vitamin E are. But most studies of the efficacy of Vitamin

E—including the recent Johns Hopkins study—have concentrated on alpha-tocopherol.

Likewise, most Vitamin E supplementation regimens involve only using alpha-tocopherol. Focusing only on this one, most dominant form of Vitamin E is a mistake. Living systems are in fact ecosystems. All the parts work together, and excessive interference with the natural balance can cause problems. Supplementation programs should seek to rebalance the internal ecosystem, not to overwhelm it.

Alpha-Tocopherol: Strong Fighter but Bully to Gamma-Tocopherol

A good example of this is the delicate balance your body maintains between alpha- and gamma-tocopherol.

When in proper balance, alpha- and gamma tocopherols work in coordination with each other. Alpha-tocopherol's particular specialty is protecting your cells against the ravages of reactive oxygen. It is the main player in protecting your cell membranes against free radicals.

Gamma-tocopherol attacks and neutralizes both reactive oxygen and reactive nitrogen. It forms a second line of defense against attacks on cell membranes. But it also protects NO from becoming cancer-causing nitrites and nitrates—something alpha-tocopherol does not do.

This is just one example of the subtle interplay between all eight components of the master antioxidant we know as Vitamin E.

However, while alpha-tocopherol is a strong fighter, it is also something of a bully. High levels of alpha-tocopherol (above 150 IU) suppress gamma-tocopherol levels. It is not known whether alpha-tocopherol also suppresses the other six components, but it is reasonable to suspect that it does.

By suppressing gamma-tocopherol, high levels of alpha-tocopherol suppress gamma's ability to protect you against heart disease, cancers, and other free radical related illnesses. In other words, if you take too much alpha-tocopherol, you are destroying gamma-tocopherol's ability to protect you from cancer and heart disease.

If you want Vitamin E to work for you, you need all the components in the

correct amounts. Or you could be wasting your time ... or worse, your health.

The lesson to take away from this—and the lesson that seemed to go unnoticed in the Johns Hopkins study—is that Vitamin E is a powerful antioxidant and health protector. But it's one whose special balance and "ecology" must be respected—an ecology that is close to the balance of tocopherols and tocotrienols found in a whole foods, Mediterranean Diet.

Getting All Eight Tocopherols ... In the Correct, Natural Amounts

Probably the single best way to get your Vitamin E is through food sources high in the different tocopherols and tocotrienols. These sources represent a balanced mix of the necessary Vitamin E components to give you the most antioxidant protection against free radicals.

Whole grains, nuts, dark green vegetables and some fruits are generally good sources. The following list represents the best sources of complete, dietary Vitamin E:

OILS (Unrefined)

- Wheat germ oil
- Sunflower oil
- Safflower oil
- Corn oil
- Soybean oil
- Extra virgin olive oil

VEGETABLES & FRUITS

- Spinach
- Broccoli
- Asparagus
- Kiwi
- Mango
- Olives

NUTS & NUT PRODUCTS

- Almonds
- Sunflower seeds
- Hazelnuts
- Peanut butter
- Peanuts

- Pecans
- Walnuts

Has All the Antioxidant Power Been Scoured Away?

A diet rich in the necessary tocopherols and tocotrienols represents the best theoretical source of Vitamin E protection. However, reality falls short of theory. A reality of our modern life is that it is often difficult or impossible to get enough of the required oils, nuts, fruits, and vegetables on a daily basis to supply the Vitamin E your body needs for optimum health.

For starters, your busy life means you often have to skip well-balanced meals. Food taken on the run is usually food devoid of nutritional value.

Second, most of our food—even that which passes itself off as fresh—has been robbed of much of its nutritional riches. When you buy fresh broccoli, for instance, it is virtually impossible to guarantee that it has not been subjected to conditions that have depleted its supply of Vitamin E (and other crucial nutritional factors).

So, unless you are growing and picking your own food (without chemical fertilizers and bug sprays), you're probably only getting the very minimum your body needs to "keep going."

And you're not getting the full antioxidant, cancer and heart disease-fighting capabilities Vitamin E—complete 8-component Vitamin E—can bring you.

Is Supplementation Safe? Yes ... with a WARNING

So it comes to this: if you're hoping to get the full benefits of Vitamin E from dietary sources alone, you will fall far short of what you need. You are not getting what you need to give yourself the optimum health you and your loved ones deserve.

Your choice ... the only healthy choice you can make if you want to get the full antioxidant power of Vitamin E ... is to start on or continue a Vitamin E supplementation program.

But with a warning! Your supplementation program must follow the recommendation of Qing Jiang:

"Because most nutritional supplements contain only alpha-tocopherol, a

different form of Vitamin E that alone does not have these anticancer properties, it may be better to supplement the diet with mixed forms of Vitamin E."

To ensure your Vitamin E supplementation program brings you the optimum anti-cancer, anti-heart disease benefits, you must:

1. Use a supplement with all 8 Vitamin E components (tocopherols and tocotrienols).
2. Use only the natural (*d*-) forms of tocopherols and tocotrienols ... and avoid the mixed *dl*-synthetic forms.
3. Keep your daily intake of alpha-tocopherol well below 100 IU, preferably near 30 IU.
4. Use a supplement with at least 40 mg gamma-tocopherol, preferably 60 mg.
5. Be careful of "so-called" mixed tocopherol supplements, which usually contain mostly alpha-tocopherol and provide more than 100 IU of alpha-tocopherol daily.

By following these guidelines, you will gain the full benefits of Vitamin E's master antioxidant power ... while protecting yourself from possible problems from alpha-tocopherol's suppression of gamma-tocopherol's strength and protection.

Do not wait. You should begin this safe, highly effective way of protecting your body from free radicals and other life-damaging oxidants right now! And you must do it completely with properly balanced, mixed tocopherols and tocotrienols.