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March/April 2009 Vol. 6 No. 2

## **Safety of Nutritional Supplements**

It seems that every week you see an article in a newspaper or hear a report on television about the dangers of taking nutritional supplements. I have been sharing with you throughout this newsletter the health benefits you can receive by taking high-quality, complete and balanced nutritional supplements. So how do you explain why there is so much in the way of negative clinical studies in regard to nutritional supplementation? As a physician, the last thing that I want to do is recommend something that is going to be harmful to my patients. I want to approach the answer to this question from different aspects so that the next time you see a negative report in the media on taking nutritional supplements, you will have some better insight on how this happens.

### **Looking for the “Magic Bullet”**

Almost every study in regards to nutritional supplements from our mainstream medical literature is studying a single nutrient to see if there is a health benefit. For example, they may look at vitamin E or vitamin C or calcium or selenium or magnesium, etc. They look at these individual nutrients as if they were drugs. This is just the way we do our research. However, vitamin E and vitamin C are not drugs. They are simply nutrients that

we get from our foods that our bodies need to function properly. There is almost a universal agreement among researchers that the underlying or root problem of almost all of these chronic degenerative diseases is oxidative stress. Therefore, selecting various antioxidants or their supporting B cofactors or minerals seems like a plausible way to study whether or not there is some protection provided by supplementing these nutrients. There are several problems with this approach.

First, any particular antioxidant only works in a particular part of the body and against particular free radicals. For example, vitamin E is fat-soluble, so it works primarily within the cell membrane. Vitamin C is the best antioxidant within the plasma or fluid-filled areas because it is water-soluble. Glutathione is the best intracellular antioxidant. All of these antioxidants need the so-called antioxidant minerals and B cofactors available in all of their enzymatic reactions to do their job. If these nutrients are not available in adequate or optimal levels, it doesn't matter what dosage of antioxidant you are supplementing, you will get marginal results.

Second, we know that the problem is generally not a particular nutritional deficiency, but instead, it is oxidative stress. It is really all about balance. You want to have enough antioxidants available for the number of free radicals you produce; then there is no oxidative stress. This requires supplementing

a wide variety of antioxidants and their supporting nutrients to accomplish this goal. This creates a positive synergy that gives you the best chance to bring oxidative stress back under control. When you supplement a single nutrient, you are starting out with a major handicap. The most amazing thing that I have observed in reviewing hundreds of clinical trials looking at the health benefits of supplements in various diseases is that the majority show a definite positive health benefit using just one nutrient.

Finally, when you use a single nutrient like vitamin E or beta carotene, there is a possibility that it can become a pro-oxidant. In other words, clinical studies show that it can actually create more free radicals than if you were not supplementing at all. When several different antioxidants and their supporting nutrients are supplemented together, this does not occur. However, there are very few clinical studies where this is done because researchers are continually looking for the “magic bullet.” Here is an illustration of how this happens in the real world and why the results of these clinical trials are so misleading.

### **Alpha-Tocopherol Beta-Carotene Cancer Prevention Study**

Researchers have found in several clinical trials that were looking at antioxidant status of the participant, that those smokers who had the highest levels of antioxidants in their body had the least risk of developing lung cancer. In fact, most of the studies showed that the most important antioxidant happened to be beta carotene. Therefore, researchers in Finland decided to supplement 30,000 participants who were heavy smokers with either a placebo, synthetic beta carotene, synthetic vitamin E, or both synthetic beta carotene and vitamin E. None of the studies demonstrated a decrease in the number of lung cancers these participants developed. However, there was a major concern because

the group that only took the synthetic beta carotene actually had an increase in the number of participants who developed cancer. This was a widely publicized study and their conclusion was that beta carotene was dangerous to take, especially for smokers. This has led most physicians to recommend to their patients to not take beta carotene or any antioxidants because it could be dangerous.

This is a perfect example of researchers being aware of the fact that smokers who have the highest antioxidant levels in their blood stream had the lowest risk of developing cancer trying to find the “magic bullet.” First of all, the use of synthetic antioxidants instead of natural antioxidants creates very little chance of success from the beginning. Synthetic antioxidants have been shown to cause more problems than they help. Synthetic antioxidants are also not absorbed as well as natural antioxidants. These researchers also concluded that using a single antioxidant like beta carotene can actually cause it to become a pro-oxidant (creating more free radicals), especially in heavy smokers. Despite the objections that the study was flawed, this study had a tremendous influence on the medical community and the population in general. The design of the study, which used heavy smokers who had smoked for years, would be a very difficult group to see a health benefit. However, these characteristics in the design of these studies are pretty typical.

However, the rest of the story was not told until July 2004. The same data was reviewed and reported in the American Journal of Epidemiology with entirely different findings. These researchers looked at total antioxidant intake. These researchers concluded that supplementing beta carotene in combination with other antioxidants significantly reduced the risk of developing cancer in these smokers. The authors concluded by stating, “These findings support the hypothesis that a combination of dietary antioxidants reduces lung cancer risk in male smokers.” This is

quite a different conclusion using the same data. However, this was not reported as aggressively in the mainstream media as the original findings were reported.

### **Statistical Manipulation**

A prime example of this type of clinical study was when we were bombarded by sensational news reports about the possible danger of taking higher doses of vitamin E. These reports were based on a review article that was published in the *Annals of Internal Medicine* (4 January 2005; Vol. 142 No. 1) written by Dr. Edgar Miller of the John Hopkins School of Medicine. Miller concluded that a “high” dosage of vitamin E supplements (over 400 IU per day) may increase death rates and should be avoided. Careful evaluation of this study reveals how statistical manipulation can produce whatever results the researcher desires.

#### *The Rest of the Story*

Here are important facts that the media reports didn't mention:

- This is not a new study. It is simply a review of thirty-six controlled trials, with follow-up of longer than one year, done from 1966 to 2004. There is no new research here, just an interpretation of old data.
- Only nineteen trials were considered for statistical interpretation. Out of the original thirty-six, they eliminated seventeen trials that did not have more than ten deaths.
- None of the individual trials noted any statistically significant differences in the mortality between the control group and the vitamin E group.
- The studies involved patients who were already very ill. For example, the CHAOS study (Cambridge Heart Antioxidant Study) involved more than 2,000 patients who had already suffered

a heart attack. The Alzheimer's Disease Cooperative Study (ACDS) involved patients who already had moderate to severe Alzheimer's dementia.

- Many of the patients in both the vitamin E group and the control group died.
- Eight of the nineteen studies actually showed fewer deaths in the vitamin E group than the control group.

The authors were even very careful to point out that their marginal findings of increased deaths from all causes could not be carried over to healthy individuals. But you didn't hear that on the evening news.

#### *Twisting the Numbers*

First and foremost, realize that you can prove anything you desire by simply setting up the criteria of the study to meet the conclusion that you desire to achieve. Out of the original thirty-six trials, the reviewers eliminated twelve trials because there were fewer than ten deaths, three trials were eliminated because there were no mortality data available, and two trials were eliminated because the mortality data were confusing. This left the reviewers with nineteen trials that lasted longer than one year and involved more than ten deaths. They pre-selected trials that supported their conclusions. That's just bad science.

But then the numbers get twisted even more. In order to have results that mean anything, you have to have “statistical significance.” In order to do this, you plug your data into simple formulas that tell you whether your results have a cause or whether they were the result of chance. When all the trials are considered together, or when each study was considered individually, there was no statistically significant connection that could be made between Vitamin E and death. The differences could only be attributed to chance. However, by focusing their analysis on only one or two of the larger studies, they were able to show a very slight statistically significant difference in

deaths between the two groups of very ill patients. These studies used higher dose vitamin E primarily and the researchers came up with a marginally significant difference in deaths between these two groups. But remember, the higher doses were only given to patients who were the most ill, so we would expect a higher death rate anyway.

When they compared the deaths between the control group and the vitamin E group for all nineteen studies, there was no statistical difference in the death rate of either group. Had they analyzed all of the trials and let all the data speak for itself, they would have not found statistical significance.

So the conclusion that higher doses of vitamin E cause more deaths from all causes is absolutely bogus. This is truly a manipulation in the highest sense of the word. They were grabbing at straws for anything they could show statistically. First they had to eliminate seventeen of the trials. Then they eliminated the low dose vitamin E studies and focused on those who were most ill. Even by their own admission they state, "High-dose vitamin E trials were often performed with patients suffering from various chronic diseases, and we could not evaluate or project these findings to healthy adult populations." But you didn't hear that on the news, either.

### **Quality and Amount of Nutrient Used in a Clinical Trial is Critical**

There seems to be a number of recent clinical trials that either have shown no positive health benefits or even negative health benefits. However, as you review them it becomes obvious that they were going to be negative clinical trials from the beginning because of either the amount or quality of nutrient that was supplemented. This was certainly the case involving The Physicians' Health Study, where vitamins E and C were studied in regard to the prevention of cardiovascular disease. The study did involve a large number of

participants for an extended period of time — nearly 15,000 physicians were followed for ten years. The study concluded that neither vitamin E nor vitamin C reduced the risk of major cardiovascular events. However, when you look at what was actually used for supplementation you found that only 500 mg of a synthetic vitamin C was used in one group and 400 IU of synthetic vitamin E was used in another. First of all, I have not seen any significant health benefits in the medical literature with the use of supplemental vitamin C until you get to about 1,000 or 2,000 mg daily. In the case of vitamin E, 400 IU is close to an optimal dose and you would think that there would be a positive result. However, synthetic antioxidants have been found to be inherently poor in quality, and may even have significant harmful effects. Synthetic vitamin E has been shown to only be absorbed at about half the rate of natural vitamin E. To make things worse, in this study the participants were only required to take their supplements every other day. This would be equivalent of taking just 100 IU of natural vitamin E daily. Synthetic vitamin E (dl-alpha-tocopherol) has also been shown to actually displace the natural vitamin E (d-alpha-tocopherol) in the body and decrease its level within the cell membrane. This is actually harmful for the body and clinical trials using these types of antioxidants are destined to fail from the start.

As I was writing this newsletter, a major study came out on the health benefits of multivitamin use by postmenopausal women. More than 150,000 women in the Women's Health Initiative (February 2009) were followed, and those who took multivitamins had no increase or decrease of cancer, heart disease, or stroke. Now, you must realize that all multivitamins are based on RDA levels of nutrients, except possibly for the amount of folic acid they contain (usually 400 mcg). This has been my experience with all the clinical trials that studied the health benefits of taking a multi-vitamin or one-a-day vitamin: They are woefully inadequate in providing those optimal

levels that have been shown by the medical literature to provide health benefits. I agree that taking a multivitamin/mineral is a waste of time and effort. If you are going to supplement your diet, you need to be taking all of these essential nutrients at the optimal or advanced levels.

### **The Economics of Medicine**

I am not really a conspiracy theory advocate. However, I am acutely aware of the true economics of medicine. In my book *Death by Prescription* [Thomas Nelson 2003], I detail the approval process of all pharmaceutical drugs. The average cost for a pharmaceutical company to take a drug from the laboratory to your local drug store is 500 million dollars. Then the amount of money a pharmaceutical company spends to market its drug to the public and physicians is enormous. You can't turn on your television or read a magazine or newspaper in today's world without learning about the newest drug for any illness that you may have. Obviously, the media outlets are going to be supportive of any new major breakthrough in drug therapy because they receive so much in advertising dollars from this industry.

A group of statistical researchers reported that the journals with the most pharmaceutical ads published significantly fewer articles about the health benefits of nutritional supplements compared to the journals with the fewest pharmaceutical ads. They also stated that the percentage of 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.

It appears that any negative study or even slightly negative study is shouted from the rooftops and every media outlet. In general, when I go back and look at the actual clinical trial they have just reviewed, it is obvious that they have a definite bias against

supplementation. I would estimate that eight out of ten clinical trials that evaluate the health benefit of supplements are positive when they use optimal levels and high quality supplements. The other 20% just does not show a health benefit. So these same media outlets just ignore nearly 80% of the clinical trials and rarely report on the positive studies.

The only thing that will ever lower health care costs in the world today is when individuals decide to become proactive in protecting their health. However, you will not receive much support from the medical community because of physicians' bias against supplementation.