

 image

The news media has disseminated several articles over the last few months implying that dietary supplements are useless and dangerous. The basis for these articles are press releases from mainstream supported groups such as the American Heart Association and American Cancer Society. These organizations receive financial grants from the pharmaceutical industry, and have openly expressed their bias against dietary supplements in court briefs filed in support of FDA regulatory restriction.

Negative media hype against dietary supplements is nothing new, as the popular press has displayed a historical prejudice against dietary supplements that dates back to the 1940s. For instance, in 1984 the press warned against taking vitamins because conventional doctors said that high potency supplements could cause liver and kidney damage. The Life Extension Foundation reacted immediately to these allegations by testing the blood of 200 members who had been taking massive doses of supplements for years. These blood tests showed there to be zero toxicity in healthy people taking high potency supplements, and the press never again published this fictitious information that had no basis in fact to begin with.

The Life Extension Foundation has continued its reactionary tradition by conducting larger scale blood screening tests of Foundation members. Last year we published an article based on original research at our diagnostic laboratory showing that 50% of our members were not taking enough TMG or vitamin B6 to adequately suppress homocysteine to guard against atherosclerosis. (For specific details, refer to the October 1999 issue of *Life Extension magazine*.) In response to the American Heart Association™s most recent attack on vitamin C, we are proud to present the following article based on actual high resolution carotid ultrasound tests of Life Extension Foundation members who have been taking high potency supplements for many years.

Refer to the Abstracts section for reprint rebuttals to the American Heart Association™s attack on vitamin C from the Linus Pauling Institute, The Vitamin C Foundation and Dr. Robert Cathcart.

A pilot study to ascertain carotid artery status in high potency vitamin C supplement takers

by Paul Wand, M.D. Neurologist

Atherosclerosis is an insidious disease that begins in youth, but often accelerates as humans age resulting in the manifestation of cardiovascular disease. 1,2,92,93 Vitamin C has been explored as an agent that may protect against atherosclerosis and cardiovascular disease. 3-14 The most significant finding came from a published study involving 11,348 adults over a 10 year period. This study showed that males taking the highest amount of vitamin C had a 45% reduction in all cause mortality, a 22% reduction in cancer incidence and a 42% reduction in heart attack risk.15



photo by: Matthew Pace

An in-depth analysis of published studies on vitamin C and cardiovascular disease, however, makes it difficult for the vitamin C user to extrapolate how the results may apply to them individually. For instance, some studies define high-dose as only 250-500 mg a day of vitamin C, 16-19 whereas the serious vitamin user often consumes between 2,000 and 12,000 mg a day of vitamin C.

To put this into perspective, we conducted a Medline search to evaluate published studies showing the effects on humans of various doses of vitamin C as it related to any parameter of cardiovascular disease risk. This database search covered the time period of January 1, 1990 to April 25, 2000. Table 1 reveals the results of this search as it relates to vitamin C dosage and cardiovascular risk factors.

Table 1. Effects of Vitamin C on Cardiovascular Disease Risk

1 study showed favorable response when under 500 mg was administered
53

30 studies showed favorable response when over 500 mg was administered 54-83

3 studies showed no response when under 500 mg was administered 84-86

Based on the published literature over the last ten years, it would appear that higher potency vitamin C supplements have some effect in reducing cardiovascular disease risk, whereas potencies lower than 500 mg a day may have no effect. It is important to note that the human studies presented on Table 1 on the following page do not include the published molecular research of Linus Pauling, Matthias Rath and others who are largely responsible for convincing health conscious people that supplementation with greater than 2000 mg a day of vitamin C reduces cardiovascular disease risk. More on the research of Linus Pauling, et al will appear later in this article.

When attempting to assess the benefits in humans who take very high doses of supplements, such as those taking in excess of 2000 mg a day of vitamin C, a serious gap exists in the published literature. A significant confounding factor is that people taking in excess of 2000 mg a day of vitamin C usually take other nutrients that have been shown to reduce the risk of cardiovascular disease such as coenzyme Q10, 20-25 vitamin E, 91,176,177 vitamin B12, 27 vitamin B6, 28,29 and folic acid. 30-40 It therefore becomes difficult, using epidemiological data, to ascertain the real effects of very high dose vitamin C supplementation on human populations who are taking a wide variety of nutrients in addition to vitamin C.

Why some people take very high doses of vitamin C

An impressive body of research indicates potential health benefits when very high doses of vitamin C are taken over an extended time period. We will define every high dose from here on out as vitamin C intake in excess of 2000 mg a day.

Some of the notable doctors and scientists who have endorsed very high dose vitamin C supplementation include Linus Pauling, Abram Hoffer, Robert Cathcart, Matthias Rath, Irwin Stone, Frederick R. Klenner, Durk Pearson and Sandy Shaw and host of others. These doctors and scientists have authored books and scientific papers that document the benefits of very high dose vitamin C supplementation. In response to these publications, a sub-fraction of the American public has chosen to personally consume 2000 to 12,000 mg a day of vitamin C.

A consistent theory among doctors endorsing very high dose vitamin C supplementation is that it works by specially defined mechanisms to reduce the incidence of artery disease. Linus Pauling, along with his associate Matthias Rath, MD, have published data showing that arteries harden in the absence of sufficient vitamin C. They cite research showing that when the dietary intake of vitamin C is low, collagen production is limited, and arteries tend to become thinner and weaker from wear and tear. Plaque deposits (atherosclerosis) then form to compensate for this weakness. The Pauling/Rath theory, published in both conventional and alternative medicine circles, holds that the root cause of atherosclerotic plaque deposits is a chronic vitamin deficiency. 94-98

Given the credentials of the doctors and scientists advocating very high dose vitamin C supplementation, and the widespread dissemination of their publications in the United States, a sub-fraction of the American population believes that very high dose vitamin C supplementation (along with nutrients such as vitamin E, B6, folate, coenzyme Q10, etc.) will reduce the formation of atherosclerotic plaque and the subsequent development of common forms of cardiovascular disease.

Why conventional doctors doubt the value of vitamin C

The medical profession has traditionally been biased against dietary supplements for a variety of economic and political reasons. As mentioned earlier in this article, there are published studies that show that vitamin C fails to confer a protective effect in reducing cardiovascular disease risk. While the majority of studies (31 favorable studies compared to 7 showing no response) indicate that vitamin C supplements reduce cardiovascular disease risk factors, it appears that the few studies showing no benefit carry great weight in the medical profession. Conventional physicians also tend to be unenlightened about 76 additional human studies published since 1990 showing that vitamin C confers other health benefits such as lowered risks of cancer and other diseases. 99-174

Mainstream organizations have a propensity to look at studies showing no health benefit when vitamin C is consumed in low doses, and then make a public announcement that insufficient evidence exists to recommend widespread vitamin supplementation. The news media is quick to report on studies that show that vitamin C may not protect against cardiovascular disease, without presenting the counter view that not enough vitamin C was consumed in the particular study to provide the expected benefit.

So, despite a rather intensive amount of research that has occurred over the past 10 years, we are still without a scientific consensus as to whether vitamin C is protective against cardiovascular or other diseases, ergo the continued debate over the value of vitamin C supplementation.

Dr. Paul Wand, M.D., Neurologist
photo by: Matthew Pace

At a meeting of the American Heart Association held on March 2, 2000, a presentation was made of an unpublished trial indicating that those who consumed high amounts of vitamin C supplements had increased carotid intima-media wall thickening over an 18-month time period. 41 The doctors who made this presentation

described high amounts of vitamin C as up to 500 mg a day. This presentation contradicts previous published studies showing that vitamin C protects against carotid atherosclerosis and intima-media wall thickening. 42

In response to this unpublished American Heart Association presentation, The Life Extension Foundation asked me to oversee a pilot study of 30 people who had been taking very high doses of vitamin C (and other nutrients) for at least four years.

The objective of this study was to ascertain whether those who have consumed more than 2000 mg a day of vitamin C have a greater or lesser degree of carotid artery wall thickening and atherosclerotic plaque in relationship to their age and other risk factors.

The subjects in our test group ranged from age 45 to 81 years, with a median age of 61. Our test subjects were significantly older than the group tested by the American Heart Association.

The procedure used to evaluate the carotid arteries of these 30 subjects was a high resolution ultrasound of the carotids with doppler evaluation. Multiple sonographic scans were obtained through the area of the right and left carotid systems. This test enabled me to ascertain if there was atherosclerotic plaque present, the degree of intima-media thickening if any, blood flow velocity and the percentage of stenosis (narrowing or blockage), if any. I routinely use this test to help determine if neurologic deficit is caused by carotid artery disease. It is not uncommon for me to detect 60% to 90% blockage in the carotid arteries of patients, along with significant increase of carotid blood flow velocity and severe intima-media thickening. Lay readers should know that increased blood flow velocity is indicative of greater carotid artery stenosis (narrowing).

I was surprised that the doctors who made the presentation at the American Heart Association conference only tested for carotid intima-media thickening. This is only one of four parameters that can be evaluated via carotid ultrasound testing. I believe the American Heart Association doctors should have also checked for carotid atherosclerotic plaque, stenosis and blood flow velocity, in addition to intima-media thickening. Of all parameters that can be evaluated, intima-media wall thickening is the least important factor. Atherosclerotic plaque, stenosis and blood flow velocity are far more important indicators of underlying carotid disease.

The results of The Life Extension Foundation™s four-pronged carotid ultrasound test showed that in 23 out of 30 of these very high vitamin C supplement takers, there was no evidence of carotid plaque formation, obstruction (stenosis) or intima-media thickening. Blood flow velocity through the carotids was completely normal in these 23 subjects.

In seven cases, there was some evidence of carotid pathology, but the extent of disease was insignificant with the exception of two persons who showed carotid stenosis of 30% and 40%. Based on the advanced age of these two subjects, the 30 and 40% stenosis observed was not considered abnormal and was not indicative of a clinically significant disease state.

In the seven cases showing some evidence of carotid pathology, preliminary follow up has at the time of this publication revealed elevated levels of homocysteine, LDL cholesterol and/or glucose as potential causative factors. Additional blood testing of these seven subjects will be conducted to evaluate serum iron, C-reactive protein, LDL particle size, fibrinogen and other potential risk factors for carotid stenosis. When adjusting for age and other confounding factors such as high cholesterol/homocysteine, the slight to moderate carotid pathology detected in these 7 out of 30 subjects is below what would be normally expected.

Overall, this group of very high vitamin C supplement takers showed remarkably healthy carotid arteries, with 23 out of 30 having absolutely no sign of intima-media thickening, blood flow restriction, atherosclerosis or stenosis.

Our pilot study of 30 subjects differed from the American Heart Association study in the following ways

The American Heart Association tested people aged 40 to 60. We thought age 40 was too young to observe significant carotid artery disease in asymptomatic people, so we tested people beginning at age 45. We had no upper age cutoff limit, and tested many people in their 60s, 70s and one 81-year-old.

The American Heart Association only tested for carotid intima-media thickening, while we tested for carotid atherosclerosis, stenosis and blood flow velocity, in addition to intima-media thickening. Atherosclerotic plaque, stenosis and blood flow velocity are far more important indicators of underlying disease than intima-media thickening.

The upper limit for vitamin C intake was apparently 500 mg in the American Heart Association study. Our subjects, on the other hand, consumed well over 2,000 mg a day of vitamin C along with potent doses of other nutrients purported to reduce risk of atherosclerosis and cardiovascular disease.

If we had set a cutoff of 60 years of age like the American Heart Association did, we would have found that none of our test subjects

would have shown clinically significant carotid artery pathology. In other words, had we used the same narrow parameters (under age 60) that were presented at the American Heart Association meeting, we would have had no carotid artery pathology to report in this group of people who take very high doses of supplements.

Since aging is a risk factor in the development of carotid artery disease, we choose to evaluate a much older group (45 to 81 years) of people consuming greater levels of vitamin C and other nutrients. By testing an older age group, we obtained a more clinically significant picture of the carotid artery status of people who have consumed very high doses of vitamin C and other nutrients for long periods of time.

Additional considerations

It is well established that excess iron accelerates atherosclerosis, and one study specifically showed that high levels of iron cause carotid atherosclerosis 43 . It is therefore possible that the people in the American Heart Association study who were taking low potency vitamin C supplements were consuming a multi-vitamin that contained a relatively high level of iron. There is also a possibility that these relatively low-potency vitamin C supplements were causing excess iron absorption from food, but not enough vitamin C to protect against iron-induced LDL cholesterol oxidation that could have contributed to the intima-media thickening observed in the American Heart Association presentation.

Previously published research shows vitamin C as either having a protective effect, or no effect in the development of carotid artery disease. The most significant positive study was published in the American Heart Association™s own journal 42 and measured the relationship between the intake of dietary and supplemental vitamin C, vitamin E and provitamin A carotenoids and average carotid artery wall thickness. In 6,318 female and 4,989 male participants 45 to 64 years old, carotid artery intima-media wall thickness was measured as an indicator of atherosclerosis at multiple sites with ultrasound testing. Among men and women over age 55 who had not recently begun a special diet, those in the high vitamin C intake group showed significantly less average carotid artery wall thickness adjusted for age, body mass index, fasting serum glucose, systolic and diastolic blood pressures, HDL and LDL cholesterol, total caloric intake, cigarette use, race and education. Vitamin C showed an 81% protective effect in women and a 65% protective effect in men. The doctors concluded by stating:

"These data provide limited support for the hypothesis that dietary vitamin C and alpha- tocopherol may protect against atherosclerotic disease, especially in individuals over 55 years old."

Carotid endarterectomy is a surgical procedure used to remove atherosclerotic plaque in the carotid artery. In a study of 45 people undergoing this procedure, the lower the plasma content in vitamin C over a 12-month period, the higher the percentage of vessel re-narrowing after endarterectomy. This study implies that even in advanced cases of carotid stenosis, supplemental vitamin C may be of benefit in preventing further occlusion. 44

Another study involved the feeding of oxidized lab chow along with vitamin C and iron to rabbits for four weeks to induce experimental atherosclerosis. These rabbits had been fed a trans-fatty acid rich diet for 36 weeks prior. Administration of coenzyme Q10 after the feeding of a trans-fatty acid-rich diet showed a decrease in coronary atherosclerosis, artery plaque size and atherosclerosis scores when compared to the placebo group. 45 This study indicates that supplemental coenzyme Q10 may be required when people take vitamin C and iron supplements.

While Linus Pauling, Matthias Rath and others make a good case that vitamin C protects against atherosclerosis, there are studies suggesting that garlic, 46 homocysteine-lowering nutrients folate, 30-38 B6, 28 B12, 26,27 TMG (trimethylglycine), 47-50 and calcium regulating nutrients such as vitamin K 51 provide even greater benefits. One study on people with elevated homocysteine showed that supplementation with folic acid, vitamins B12 and B6 resulted in a regression in carotid artery stenosis within one year as measured by ultrasound testing. 52

Conclusions

Our direct observation, based on carotid ultrasound testing, show that very high vitamin C supplement users have remarkably healthy carotid arteries. When adjusted for other factors such as age, elevated homocysteine, LDL cholesterol and glucose, these very high vitamin C takers as a group appear to have less carotid pathology than the general population. A review of previously published findings indicates that consuming a wide variety of very high potency dietary supplements, combined with blood screening to monitor cholesterol, homocysteine, glucose, iron and other atherogenic risk factors, confers a significant protective effect against the development of carotid artery disease.

Continuation of: The Vitamin C Controversy (*References*)

Abstracts: Rebuttals to the AHA's attack on vitamin C

Continued from: The Vitamin C Controversy

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ABSTRACTS

FEATURED:

Rebuttals to the AHA attack on vitamin C

Rebuttals

Reprint rebuttals to the American Heart Association's attack on vitamin C from the Linus Pauling Institute, The Vitamin C Foundation and Dr. Robert Cathcart.

Rebuttal from the Linus Pauling Institute

Study links vitamin C pills with faster clogging of the arteries? Another unconfirmed study causing unnecessary confusion and fear among the public.

A study reported on March 2, 2000, by Dr. James Dwyer at an American Heart Association meeting in San Diego allegedly raised the possibility that taking vitamin C supplements may speed up clogging of the arteries, or atherosclerosis. Although the researchers themselves called their findings "a surprise" and cautioned that more experiments are needed to investigate whether vitamin C supplements may be harmful, the study was released to the media without discussing its limitations nor putting it in the proper context of the hundreds of existing studies demonstrating the health benefits of vitamin C. Both the researchers and the American Heart Association acted irresponsibly by releasing this unconfirmed study without appropriate background information, causing unnecessary confusion and fear among the public.

Dr. Dwyer reported that subjects taking 500 milligrams of vitamin C daily for at least a year had a 2.5 times greater rate of thickening of the carotid artery wall than did subjects who did not take supplements. These results are in direct conflict with a study published in 1995 in the American Heart Association journal *Circulation*, which found a significant reduction in carotid artery wall thickness in people over 55 years old who consumed amounts of vitamin C greater than 982 mg per day compared to those consuming less than 88 mg per day.

If the results by Dwyer and colleagues were true, people who take vitamin C supplements should die of heart attacks and strokes at a much greater rate than non-supplement users. However, there is no scientific evidence in support of this notion. Many epidemiological studies and some clinical trials have indicated that dietary intake of or supplementation with vitamin C is associated with a reduction in the incidence of chronic disease morbidity and mortality, including cardiovascular diseases. Numerous epidemiological studies have shown a significantly decreased heart attack or stroke risk with increased vitamin C intake.

A large epidemiological study published in 1992 showed a risk reduction for heart disease of 45% in men and 25% in women consuming greater than 50 mg of vitamin C daily from the diet plus regular supplements, corresponding to a total vitamin C intake of about 300 mg per day. Although this study indicated that vitamin C supplements provide cardiovascular benefits above and beyond the vitamin C obtained from the diet, two other large epidemiological studies published in 1996 found no effect on heart disease risk in people who take regular vitamin C supplements. However, not a single epidemiological study nor clinical trial has found an increased risk of heart attacks or strokes in people taking vitamin C supplements.

Over twenty clinical studies since 1996 published primarily in *Circulation* have consistently found beneficial effects of vitamin C, administered either orally or by intra-arterial infusion, on the relaxation of arteries, or vasodilation. Impaired vasodilation is an important risk factor for heart attacks and strokes.

Vasodilation in patients with heart disease is significantly improved following supplementation with 500 mg of vitamin C per day for 30 days, and is comparable to vasodilation seen in healthy people. Beneficial effects of vitamin C supplements leading to normalization of vasodilation were also observed in patients with angina, heart failure, high cholesterol levels, hypertension, diabetes, high homocysteine levels and in smokers. In addition, a recent study in *Lancet* has demonstrated that 500 mg of vitamin C per day given for 30 days lowers blood pressure in moderately hypertensive patients. High blood pressure is a major risk factor for heart disease.

Several limitations of the study reported by Dwyer and colleagues need to be pointed out. First, this was an oral presentation of an abstract, meaning that the study has not been published in the scientific literature after undergoing rigorous peer review. The measurement of carotid artery wall thickness by ultrasound poses significant technical problems and is notoriously difficult.

The differences observed are exceedingly small, and control measurements and strict blinding of the researchers evaluating the data are pivotal. Second, because this is an epidemiological study, the observed associations between vitamin C intake and carotid atherosclerosis do not prove cause-effect relationships, and may reflect differences in diet or lifestyle. There also can be significant confounding by unmeasured risk factors or imperfect statistical adjustments of the data. The vitamin C intakes were estimated, but no actual measurements of vitamin C in the blood of the subjects were made. Third, it is known that in healthy people cells and tissues are saturated at an intake of 100 to 200 mg of vitamin C per day. Therefore, it is difficult to rationalize any effects of vitamin C above these intake levels, as tissue levels would not be altered.

People taking vitamin C supplements should continue to do so, as the known health benefits of vitamin C far outweigh alleged, unconfirmed risks. There is no scientific evidence that vitamin C supplements increase the risk of heart attacks or strokes. Vitamin

C supplements of 500 mg per day have been shown to normalize vasodilation and lower blood pressure, two major cardiovascular risk factors.

Rebuttal to the American Heart Association report by Dr. Cathcart:

The recent story linking vitamin C "pills" with "clogging" of the arteries.

We have been in contact with Professor James Dwyer of the USC Medical School, one of the principal researchers. As expected, this research seems to be good news for elderly vitamin C takers whose carotid arteries have "thinned" with age. There is no evidence of occlusion (or clogging), contrary to the media reports.

Here is what we have confirmed with Dr. Dwyer:

- There is no paper as we suspected. (The USC team's paper is in "peer review" and not available.)
- The USC team used a new "B-mode" imaging technique which is still undergoing clinical trial for accuracy at the NIH.
- This B-mode imaging technique has three indicators. The USC team only studied one; carotid arterial "thickening" or "IMT." (Dr. Dwyer tells us there will be no reference in their paper to the other two occlusion indicators; plaque index and velocity ratio.)
- According to correspondence, Dr. Dwyer and the USC team is unaware that arteries might get thicker with increased vitamin C intake, and that this is entirely predicted by theory. (Increased vitamin C stimulates collagen production, but this is not well taught or well known in medical school.)
- Last year, the same USC research team (Dwyers, et. al) wrote a paper with the opposite findings. Last year they found that stress (some would say a vitamin C deficiency) leads to early atherosclerosis in men (March 1999).

Bottom line: There is no evidence of occlusion, only thickening. Now we need your help repairing the damage caused by the premature release of this unpublished research. Millions of people are now afraid of vitamin C. Please help spread the word. We will post more information as it becomes available at: www.vitaminCfoundation.org.

My experience with 25,000 patients since 1969 indicates that this charge is ridiculous. I know that follow-up is not perfect in private practice but I have had no patient who had a good heart when I first saw them and who took massive doses of C who ever developed heart problems. I have to add that I advise all my patients to avoid sugar, chemicals and highly process foods, and put them on a number of other nutrients.

If it turns out that there is thickening of the carotid, I think it is reversing the thinning that occurs with aging. It is interesting that the effect is so dramatic in the reversing of the effect on smokers. I have to congratulate you at the Vitamin C Foundation on unveiling the other two findings that could have been measured which were not reported.

Probably the finding that C helped would not be publishable.

Dr. Cathcart is a leading expert on treating people with high doses of vitamin C. Visit his website at orthomed.com.

Rebuttal by The Vitamin C Foundation

Here is some technical information on the B-mode imaging process. Note there are three measures, yet the USC paper will only mentions one. The missing two measures are used to infer occlusion.

Detailed B-mode images of the right and left common carotid artery, common carotid bifurcation, and the first centimeter of the internal carotid artery are obtained. Selected images are digitized for later measurement of intima-media thickness. After imaging, the sonographer obtains pulsed wave Doppler measures of blood flow velocity at the mid common (2 cm proximal to the carotid bulb) and in the internal carotid artery at the point of highest velocity distal to the flow divider. These are used to calculate the degree to which plaque may be interfering with blood flow.

The scanning and reading protocols result in three primary carotid disease measures:

- Average wall intima-media thickness
- A measure of degree of focal plaque called the plaque index
- The velocity ratio, a determination of whether or not plaque is interfering with blood flow in the internal carotid artery

Again, the USC team's report will only concern arterial thickness. The occlusion indicators are not reported for reasons unknown.

Owen R. Fonorow
The Vitamin C Foundation
www.vitaminCfoundation.org

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