

# Should Doctors Discourage Nutritional Supplementation?

## A cardiovascular perspective

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Cardiovascular disease is the major cause of death in most western countries, and current preventive treatment is relatively ineffective. There are theoretical reasons why nutritional therapy—antioxidant vitamins, minerals and omega 3 oils—should be beneficial. Because of some negative trials, there is the risk of tossing the baby out with the bath water. This paper reviews how nutritional therapy could assist in a comprehensive preventive approach to reduce heart disease—especially primary prevention. It stresses the need to separate primary prevention—initiated by oxidation of LDL in the vessel wall, and secondary prevention—the consequences of plaque rupture. Because a therapy is ineffective in the secondary preventive role, does not mean that it could not have a primary preventive action. There are many positive studies utilizing nutritional therapies, these are detailed in this paper, and a comprehensive preventive programme including these is suggested.

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### Introduction

Coronary disease remains the number one cause of death in most western countries, despite the billions of dollars spent by health providers. In the grip of an epidemic such as this, it is not surprising that lay people are seeking solace in other approaches beyond allopathic (orthodox medical) therapies. Nutritional supplementation has always been considered unnecessary by medical authorities, and some publications are even suggesting that any further research on some supplements (Vitamin E) should be discouraged.<sup>1</sup>

Does allopathic medicine consider nutritional supplementation on the same level playing ground as pharmaceutical and conventional medical research?

Do doctors make their patients aware of the many real dangers from pharmacological therapy? In USA, the fourth leading cause of death is drugs being used correctly!<sup>2</sup>

In a world where chronic degenerative diseases are increasing, where patients are turning away from conventional medicine and where our current preventative strategies are so blatantly failing, it is surprising that conventional bodies are so reluctant to consider additional therapies which might possibly help reduce disease. This

is also especially surprising when these therapies are unlikely to do any harm.

### Why Supplementation Seems Logical

To operate optimally the body cells require an adequate supply of vitamins, minerals, amino acids and essential fats. If the diet contained sufficient of all of these elements, then supplementation would be unnecessary. The conventional allopathic advice given to a patient considering supplementation is “you receive all you need from your food”. Most health bodies recommend people eat six to eight helpings of fruit and vegetables daily, but how many people actually do? The major beneficial nutrients in fruit and vegetables are vitamins, antioxidants and minerals.

Vitamins have many essential functions and are provided almost exclusively by fruit and vegetables. If these are picked before they are ripe, then processed, stored, chilled, blanched, frozen, and cooked—the nutrient content is greatly reduced.

Small doses of many minerals are necessary for optimal metabolic function. Again these should be available from our diet—especially in vegetables but only if they are present in the soil where the vegetables grow. Unfortunately modern farming techniques have raped many of the nutrients from the soil, and until recently often the only fertilizer replacement was with NPK (nitrogen, phosphate and potassium). At the Earth Summit (1999) it was

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calculated that the minerals in the soil are down 55% in Australia and 85% in the USA.<sup>3</sup> Some countries also have mineral deficiencies in their soils and supplementing with minerals such as iodine, and fluoride is an accepted practice. However, although selenium is very low in the soil of some countries, supplementation with this is rarely if ever considered.

Essential fats are the third of the nutritional supplement groups. The body can make most fats, but two essential fats (linoleic and alpha linolenic) need to be provided in the diet. The value of the omega 3 oils is becoming increasingly appreciated in both prevention and treatment of disease. These oils are found in the fatty tissue of cold water fish.

### How Supplements Could Reduce Coronary Heart Disease

Coronary artery disease involves a number of distinct pathological processes, each one having different causes and thus likely to have differing means of treatment and prevention.

1. *Plaque growth*: This commences in the teen years<sup>4</sup> with LDL cholesterol entering the vessel wall and becoming oxidized. This then leads to a cascade of injurious activity release of chemotactic factors attracting monocytes into the vessel wall, platelet aggregation, endothelial dysfunction, smooth muscle activation, local cytotoxicity and uptake by macrophages to form foam cells. Over the years fibrous tissue and calcium become incorporated into the plaque, presumably in an effort to stabilize it. The initiation factor is oxidation of the LDL.<sup>5</sup>
2. *Plaque rupture and clot formation*: Infarction is usually caused by plaque rupture. The precipitating causes for this are uncertain, but speculation includes mechanical stress, infection, stress and hormones. Rupture results in the sudden creation of an occlusive clot which blocks the coronary artery.
3. *Arrhythmias* develop as the myocardium becomes ischaemic, with ventricular fibrillation being the major cause of death from CAD. It has been estimated that almost 50% of all patients with myocardial infarct develop ventricular fibrillation.<sup>6</sup>

Because coronary artery disease passes through a number of very different pathological phases, therapies which address each stage may differ. For example antioxidants could reduce LDL oxidation and thus reduce plaque growth. However, they may have little effect on plaque rupture or ventricular fibrillation.

In people with established plaque, therapies which could reduce plaque rupture and clot formation or reduce the incidence of ventricular fibrillation could make a significant reduction to the mortality from coronary artery disease. It is therefore essential to clearly differentiate between primary and secondary prevention.

#### Primary Prevention

1. *Plaque growth* is initiated and maintained by LDL oxidation, therefore taking anti-oxidants (Vitamin C, Vitamin E and selenium) could be beneficial. Plaque growth

occurs over many decades, thus only prolonged epidemiological studies are likely to demonstrate benefit. A number of, well-designed studies have in fact confirmed that Vitamins C and E do indeed reduce the incidence of coronary heart disease. There is very little scientific evidence that any of the conventional medical treatments, apart from the statin drugs, actually reduce the development of plaque.

2. *Plaque rupture*: Although the cause is uncertain, it appears from a number of studies that statin drugs, aspirin and omega 3 oils are beneficial. These may act on either plaque rupture or clot formation.
3. *Lethal arrhythmias* are caused by electrical instability and it is likely that electrolyte imbalance could aggravate this. Hypokalaemia is a well accepted foundation for ventricular fibrillation, it is likely that magnesium deficiency could also be an aggravating factor. While few drugs have been shown to reduce the mortality from arrhythmias, omega 3 oils and magnesium have some positive trial results.

#### Secondary Prevention

By definition secondary prevention involves patients with established plaque. Protection from further events mainly involves plaque stabilization and the prevention of fatal arrhythmias. It would be unlikely that anti-oxidant treatment, which mainly affects plaque growth, would show benefit in the 3- to 5-year duration of most clinical trials. Trials involving adults in high risk groups should probably be placed in the same category as secondary prevention because these people are very likely to have established plaque.

#### Problems with Studies Involving Nutritional Supplements

- The double blind trial is superbly designed to assess the benefit of a single agent (such as a drug or operation), but when there are a number of variables, benefit is less easy to demonstrate. Many supplements require other nutritional compounds to achieve maximum benefit. Anti-oxidant action involves a cascade of compounds (Vitamin E works in synergy with Vitamin C and selenium).<sup>7</sup> This means that studying an agent in isolation negates the possible benefit which might have resulted had all the compounds been present together.
- The quality of most nutritional supplements falls far short of the quality of pharmaceutical agents. There are supplements made to pharmaceutical standards, and only these should be used for clinical trials. Most supplements are simply made to food standards, where there is no guarantee of content, dose or degree of contamination. Doctors would never accept the results of pharmaceutical trials if the drugs studied were only made to food standards. Nearly all supplement trials have involved the use of non-pharmaceutical grade products. Few if any supplement trials have measured serum levels.

Some nutritionals have active and inactive forms. Vitamin E has many homologues—a, b, g and d toco-

pherol, and four tocotrienols (also a, b, g and d). These are all formed by plants in the active dextro ('D') form. Synthetic Vitamin E contains an equal amount of the active 'D' form and the inactive 'L' isomer which has much less Vitamin E activity.<sup>8</sup> Most clinical trials have used synthetic Vitamin E.

- Because nutritional supplements are found in food, participants in supplement trials are likely to be taking additional variable doses of the agent being studied in their diet. For example some studies involving anti-oxidants were performed in Mediterranean countries, where the natural intake of antioxidants from fruit, vegetables, grapes and wine is high. Controlling for this is impossible, but it is likely to make the trial results less predictable.
- The effects of taking nutritional supplements will probably take some time to become apparent. Because the development of atheroma takes some decades, trials lasting 3–5 years are unlikely to identify major benefit. For this reason, the classical short-term trials using nutritional supplements are likely to be negative. However, in situations where the disease process is accelerated such as in patients with advanced renal failure, a positive result may be demonstrated much more quickly (e.g. the SPACE trial).<sup>9</sup>

### Nutritional Supplement Studies

The three major nutritional supplement groups which appear to have potential benefit for cardiovascular health are—vitamins (especially Vitamins C and E), minerals (especially magnesium and selenium) and omega 3 oils (fish oil).

#### Vitamins

##### VITAMIN E.

1. Theoretical reasons why Vitamin E should help—The major biologic role of Vitamin E is to protect the lipid components of cell membranes and the low-density lipoprotein (LDL) from oxidation by free radicals. Vitamin E is located primarily within the phospholipid layer of cell membranes.<sup>10</sup> Theoretically by reducing LDL oxidation, Vitamin E could slow or reduce the atherosclerotic process.
2. In animal studies involving many species (rabbits, rats and monkeys),<sup>11–13</sup> Vitamin E does significantly reduce the development of atheroma, however, the presence of Vitamin E in the chow fed to most lab animals has been a confounding factor in some studies.
3. Over 25 epidemiological studies using Vitamin E have been performed, with the majority showing significant benefit. The four major studies, involving tens of thousands of people of all age groups and both sexes are detailed in the following:
  - The USA Nurses study:<sup>14</sup> Eighty-seven thousand nurses followed for 8 years. Those taking the highest level of Vitamin E had a 44% reduction in coronary disease, with the major benefit being seen in those nurses taking Vitamin E supplements. Note

that those taking Vitamin E for less than 2 years showed no positive benefit.

- Post menopausal study:<sup>15</sup> Thirty-four thousand women followed for 7 years. Those taking high amounts of Vitamin E had 60% less heart disease. In this study Vitamin E supplementation did not appear to increase the benefit, although the authors do comment that they had no information on the duration of supplement intake.
  - The USA Health Professional's Study:<sup>16</sup> Thirty-nine thousand and nine-hundred men followed for 4 years. Those men taking more than 100 IU of Vitamin E had 47% fewer cardiac events.
  - Vitamins C and E in the elderly:<sup>17</sup> Eleven thousand people followed for 10 years. Vitamin E reduced coronary mortality by 47% and the addition of Vitamin C enhanced this reduction to 63%.
4. Controlled clinical trials
    - Primary prevention trials: There have been no completed primary prevention studies. The PPP collaborative group trial<sup>18</sup> was stopped early (3.6 years instead of 5) and the number of people recruited was less than intended (4495 instead of 7500). The only other large study (AREDS trial)<sup>19</sup> was never designed to study cardiac events.
    - Secondary prevention trials: Four major trials have been completed in people with demonstrated cardiovascular disease or people at high cardiovascular risk. These people are likely to have established coronary atheroma. While these trials were all reported to be negative, some did in fact show cardiovascular benefit:
      - The ATCB trial:<sup>20</sup> 50 IU of Vitamin E given to 29,000 Finnish smokers. There was no reduction in cardiovascular mortality. The 50 IU dose was far too small—most investigators recommend 400–800 IU/day, but even with this low dose, there was a significant reduction in non fatal myocardial infarction in those taking the Vitamin E.
      - The HOPE study:<sup>21</sup> Nine thousand and five hundred high risk people followed for 4.5 years given 300 IU of natural Vitamin E—no benefit was demonstrated.
      - GISSI-P:<sup>22</sup> Eleven thousand Italians after infarction were given 300 IU synthetic Vitamin E for 3.5 years—there was no reduction in total mortality. However, there was a 20% reduction in heart death and 35% lowering of sudden death and a significant reduction in peripheral vascular disease.
      - The UK Heart Protection Study:<sup>23</sup> Twenty thousand people with known vascular disease received synthetic vitamins (A, C and E) for 5 years with little benefit.
      - The CHAOS<sup>24</sup> study of 1035 people post infarct in Cambridge revealed a 47% reduction in myocardial infarction and sudden death in those taking Vitamin E supplements.
      - The SPACE trial<sup>9</sup> 800 IU of natural Vitamin E was given to 200 patients with advanced renal failure—a population known to develop acceler-

ated arteriosclerosis. These patients were followed for 2 years. Those taking Vitamin E had 70% fewer myocardial infarctions and 54% fewer vascular events.

- Heart transplant patients also develop accelerated atherosclerosis. In a study of 40 patients post-transplant,<sup>25</sup> those patients taking Vitamins C and E had significantly more favourable changes from baseline in maximal intimal thickness, plaque area and intimal index as measured by intravascular ultrasound.

Importantly not one of these well-controlled studies involving tens of thousands of people demonstrated any adverse effect from taking Vitamin E supplementation.

Interestingly all the positive trials used natural Vitamin E and all but one of the negative trials used the synthetic preparation, which is less active.

**VITAMIN C.** This is also an antioxidant, but because it is water soluble, it is unlikely, by itself to have a significant effect upon the lipid oxidation. However, other antioxidants (especially Vitamin E) may be regenerated by donating free radicals to Vitamin C. There are few cardiac studies using Vitamin C alone.

- In Finland 1605 men in the Kuopio study<sup>26</sup> were followed for 8 years following initial blood testing. Those with low blood ascorbate levels had significantly more myocardial infarction (13.2%) than those with higher levels (3.8%).
- A recent publication from the USA Nurses study<sup>27</sup> involving 88,000 women, revealed a 28% reduction in cardiovascular events in women taking Vitamin C supplements but not Vitamin C from food.

**MULTI-VITAMINS.** From the cardiovascular point of view, potential cardiac benefit should come from the B vitamins—B6, B12 and folic acid which beneficially affect homocysteine metabolism and possibly other metabolic pathways. In a recent paper Fletcher and Fairfield<sup>28</sup> reviewing more than 30 years of scientific papers regarding vitamins, stated “Folate, B6 and B12 are required for homocysteine metabolism and are associated with decreased cardiovascular risk” and they concluded “it appears prudent for all adults to take vitamin supplements.”

- In the USA Nurses Study,<sup>29</sup> those nurses who took higher doses of folic acid (greater than 700 ug/day) had 31% less coronary disease and those taking Vitamin B6 (more than 4 mg/day) had a 33% reduction. Interestingly there was no benefit seen at 8 years—the benefits were only seen at 14 years.<sup>30</sup>

### Minerals

This is a more difficult topic to assess, because the level of minerals in the soil differ between countries and even within countries, thus the consequences of ‘deficiency’ are less consistent.

**MAGNESIUM.** This mineral is important for the electrical stability of muscle<sup>31</sup> and also for muscle relaxation. Magnesium

is the treatment of choice for Torsades de pointe and possibly other arrhythmias.

- Magnesium given intravenously has been used in coronary care units to treat patients with myocardial infarction—resulting in a fall in mortality (24%) and heart failure (25%).<sup>32,33</sup>
- A review of published data<sup>34</sup> suggests that sudden death is more common in magnesium deficient areas.
- A study by the Centre of Disease Control<sup>35</sup> of 12,000 people followed for 19 years found those with high magnesium blood levels had 31% fewer cardiac deaths than those with low magnesium levels.
- A recent paper examining the dietary magnesium intake of 7172 men in the Honolulu Heart Study<sup>36</sup> over 30 years revealed that those with high magnesium intake had four cardiac events per thousand per year, while those with the lowest intake had seven per thousand/year.

**SELENIUM.** This is an essential component of the antioxidant enzyme glutathione peroxidase and appears to be essential in the antioxidant defense system. Selenium deficient soils are found in a number of countries including China, Finland and New Zealand.<sup>37</sup> Keshan disease is a cardiomyopathy which is endemic in some areas of China, and people in Keshan, China, where the disease was discovered, treat it with a common herb called Astragalus, which accumulates selenium from the soil. In NZ, most farmers supplement their animals with selenium to avoid liver necrosis and mulberry heart disease in swine and white muscle disease in cattle and sheep.

Because selenium deficiency occurs in only a few countries, there are few studies concerning its use as a supplement. Clark and Combs<sup>38</sup> reported significant reductions in prostate, lung and colorectal cancer with selenium supplements, but few if any controlled studies have been done with selenium in cardiovascular disease.

Coronary disease and heart failure are very prevalent in NZ, especially in the Maori and Polynesian communities. Because selenium deficiency has been shown to cause a cardiomyopathy correctable by supplementing with the mineral, and because in NZ the soil and food selenium levels are very low—it would seem wise for patients with heart disease and especially heart failure to consider taking selenium supplements.

### Omega Fish Oils

These have the potential to make an enormous contribution to coronary heart disease, and it is surprising, with the plethora of positive studies, and complete absence of any adverse effects, that fish oils and fish oil supplementation have not become routine cardiac therapy.

Omega 3 oils are created by algae in the sea and are then concentrated in the fat tissue by the fish which eat them—the fattier the fish, the more omega 3 they contain. Unfortunately fish also store pollutants such as mercury, PCBs and DDT in their fat and bones. Unlike fish fat which is very rich in Omega 3 oils, fish flesh contains more omega 6 and less omega 3. Farmed fish given artificial feed (a combination of fish meal made up of ground fish heads,

bones and some animal meal), have even more omega 6. Thus, purified fish oil supplementation is the safest and most reliable way to achieve a high intake of omega 3 fatty acids.

It has been well-documented that populations which have a high-fish intake, have a low incidence of coronary heart disease and death.<sup>39</sup> Omega 3 oils may act beneficially in a number of ways. They have been demonstrated to reduce sudden death from ventricular fibrillation, presumably by stabilizing the electrical activity at the cell membrane. They also may reduce plaque rupture and clot formation. There have been many studies and trials with fish oils, and most have been spectacularly positive.

### 1.3. Reduction of Cardiac Events

- The USA Nurses study:<sup>40</sup> In comparison with those nurses who ate no fish, those who ate just one fish meal per week had 29% less heart disease, two to four meals per week 31% less and those nurses who ate five or more fish meals per week had 44% fewer events.
- The DART trial:<sup>41</sup> Two thousand and thirty-three men after myocardial infarction who ate more than two fish meals per week had a 26% reduction in coronary events and 29% fall in all cause mortality.
- The USA Health professionals study<sup>42</sup> showed a 26% reduction of cardiac events in men who ate fish versus no fish.
- Chicago Western Electric study<sup>43</sup> of 1822 men followed for 30 years. Those with the highest fish intake had a 42% reduction in cardiac death.

### 1.4. Reduction of Sudden Death

The results of studies looking at cardiac arrest are nothing less than spectacular:

- GISSI-P trial<sup>44</sup> followed 11,000 people after myocardial infarction. Those taking fish oil capsules had a 45% reduction in sudden death.
- The ongoing Health Professional's study:<sup>45</sup> In 22,000 men there was an 81% reduction of cardiac arrest in those who ate fish regularly.
- In the Seattle and King County study<sup>46</sup> patients surviving primary cardiac arrest were compared with a controlled group. Eating one fish meal per week resulted in a 50% reduction in subsequent cardiac arrest and those with high red blood cell membrane levels of omega 3 fats had a 75% reduction in risk.

The best Omega 3 oils are found in oily fish herring, mackerel, ocean trout, salmon, sardines and tuna. Farmed fish is likely to contain less.

## Discussion

There is substantial evidence that optimal dietary intake of many nutrients reduces both the incidence of coronary disease and the mortality. Many of these studies involved the use of supplements; others compared the effects of intake of nutrients between the highest and lowest consumers. There is also an enormous database of patients in

double blind trials confirming that supplements have no adverse effect on coronary artery disease or in fact on any other condition.

While it is undoubtedly best for an individual to receive a full range of the nutrients he or she requires from the diet—for many reasons this rarely happens and even if an individual does eat the requisite volume of fruit and vegetables each day, the preparation of the foods, early harvesting, storage, processing and quality of the soil in which the plants are grown—are likely to mean that the desired intake of nutrients is still inadequate.

The medical profession has been happy to prescribe or recommend supplements in some specific conditions folic acid and iron during pregnancy, multivitamins in alcoholism, potassium with diuretics and sodium chloride in the heat. In situations where there is a soil deficiency, iodine and fluoride have been added to salt and toothpaste. Why is there then such resistance to other supplements?

Fish and omega 3 oils are being slowly and cautiously introduced, but few physicians actually prescribe these, despite the enormous potential benefit which could accrue if everyone who had suffered a myocardial infarction were taking fish oil supplements. All studies have shown a 40–70% reduction in sudden death—and considering that almost 50% of infarcts cause ventricular fibrillation there is a lot to gain.

The B vitamins B6, B12 and folic acid are also being encouraged by some cardiologists, greatly helped by the impressive review by Fairfield and Fletcher. Perhaps the fact that B vitamins lower the known cardiac risk factor homocysteine makes the treatment more acceptable; however, there is little or no data which confirms that lowering the homocysteine does in fact result in a cardiac benefit.

However, when it comes to the use of anti-oxidants, the medical profession has taken a very negative stand. Clinicians do not seem willing to separate out the multiple processes which cause myocardial infarction. Trials on people with advanced atheroma have been negative, suggesting that Vitamin E may not reduce plaque rupture. This does not exclude a role for Vitamin E in reducing the early development of atheroma by reducing LDL oxidation. In fact almost all primary prevention studies using Vitamin E have been strongly positive.

Minerals also, have been ignored. Magnesium is slowly being considered for cardiac arrhythmias and perhaps for cardiac failure.

Even though NZ is known to have very low soil selenium levels and all farmers supplement their animals, it is rarely if ever considered as cardiac therapy. Because selenium is deficient in only a few countries, there is little data on its use. Because the cardiomyopathy of Keshan disease in China may be reversible by selenium supplementation, it is surprising that it has not been studied in New Zealand, especially in the Maori and Polynesian people where heart failure is very common.

One of the major objections to the use of dietary supplements is the concern that if people take supplements they will not bother to eat well. This should never be entertained because good foods contain many other unknown ingredients which have possible health benefits. A respon-

sible proponent of supplementation would recommend that a person eat as well as he or she possibly can, and supplement simply to ensure optimal levels of the known beneficial nutrients are included in the daily diet.

## Conclusion

In an era where coronary heart disease remains at epidemic levels and where current approaches have made only a small improvement, the medical profession should be encouraging an overall comprehensive preventive programme which commences in childhood, when the atherosclerotic process starts. Because young people are unlikely to make major changes in their eating habits and lifestyle, the introduction of supplementation with a good multivitamin/multimineral preparation and fish oil capsules could be introduced—similar to the cod-liver oil and malt given to many of today's adult generation when they were young. When people reach an age where they are likely to consider additional lifestyle changes, then an overall comprehensive programme should be considered.

### A Comprehensive Cardio Protective lifestyle

- Optimal nutrition including a generous daily intake of fruit and vegetables, reduce saturated fat, eliminate trans fats, and increase the mono and polyunsaturated fats, especially the omega 3 oils. Reduce refined carbohydrates and increase the whole grains and other carbohydrates with a low glycemic index. Quality low fat protein, including cold water fish, game, whey, soy and other vegetable proteins.
- A good nutritional supplement containing anti-oxidant vitamins, minerals and fish oil capsules. This will ensure that the body cells have all the nutrients required to enable them to function optimally and also to neutralize excess free radicals. In NZ selenium supplementation should be included.
- Alcohol in moderation one to two glasses per day (preferable red wine) should be permitted, and in fact if the data is to be believed, should probably be encouraged—but more than two per day should be resisted.
- A regular exercise programme not necessarily strenuous. An activity that the individual enjoys and so is likely to continue long term.
- Stress reduction—modern life has eliminated the 'time out' which most other civilizations have found not only desirable, but form a major part of their culture. Meditation, contemplation, yoga, prayer, tai chi etc may not be the Western way, but stopping to let the stress of life flow away and allowing the flight/fight autonomic changes to subside, results in many benefits.
- Aim for ideal body weight (BMI < 25 kg/m<sup>2</sup>).
- Dental hygiene is probably more important than is currently appreciated, as the inflammatory basis of plaque rupture could start from some infected focus. Good dental hygiene and especially the avoidance of gingivitis would seem wise. The jury is still out on the possible dangers of root fillings, which create a dead tooth encouraging anaerobic bacteria and toxin produc-

tion. The dangers of mercury fillings is still being hotly debated.

- Tobacco in all its forms should be eliminated, including exposure from an early age to second hand smoke.
- Risk factor control aim to have all risk factors optimal, preferably with non pharmacological means, at least initially. Aim for blood pressure less than 120/80, LDL cholesterol less than 3 mg/dl and HDL greater than 1mg/dl, homocysteine less than 12 mg/dl and fasting blood glucose less than 6 mg/dl.

The many manifestations of atherosclerosis have multiple causes and so many means by which these could be reduced. Only an overall strategy involving lifestyle, dietary and other changes are likely to be successful. The effect of each individual intervention may be small, but in many cases they are synergistic, and the combined effect of their introduction could be major.

To return to the title of this paper should doctors be discouraging their patients from taking nutritional supplements?

- Nutrition is very important for cardiovascular health.
- Most people do not (and probably cannot) get the optimal doses of essential vitamins, minerals and fat necessary for long term cardiac health from diet alone.
- There is considerable evidence that supplements do provide cardiovascular health benefits, and there is strong biological rationale for believing these results.
- The safety profiles of the essential nutrients have been categorized and are fully safe for long term use. It seems hard to justify the current negative approach made by the medical profession, especially in light of the fact that many clinicians and cardiologists do themselves take nutritional supplements.<sup>47,48</sup>

## References

1. Vivekananthian DP, Penn MS, Sapp SK, Hsu A, Topol EJ. Use of antioxidant vitamins for the prevention of cardiovascular disease: meta-analysis of randomized trials. *Lancet* 2003;361:2017–23.
2. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA* 1998;279:1200–5.
3. US Senate Document No. 264 and the Earth Summit Report 1999.
4. Strong JP, Malcome GT, McMahon CA, Tracy RE, Newman WP, Herderick EE, et al. Prevalence and extent of atherosclerosis in adolescent and young adults. Implications for prevention for the pathobiological determinants of atherosclerosis in youth study. *JAMA* 1999;281:727–35.
5. Steinberg D, Parsatharathy S, Carew TE, Khoo JC, Witztum JL. Beyond cholesterol, modifications of low density lipoprotein that increase its atherogenicity. *N Eng J Med* 1989;320:915–24.
6. Evans T. Cardiac arrests outside hospital. *BMJ* 1998;316:1031–2 (Editorial).
7. Chan AC. Partners in defense, Vitamin E and Vitamin C. *Can J Physiol Pharmacol* 1993;71:725–31.
8. Houston MC. The role of antioxidants in the prevention and treatment of coronary artery disease. *JAMA* 2003;6(2):17–23.
9. Boaz M, Smetana S, et al. Secondary prevention with antioxidants of cardiovascular disease in end-stage renal dis-

- ease (SPACE): randomized placebo controlled trial. *Lancet* 2000;356:1213-8.
10. Simons LA, Von Konigsmark M, Balasubramanian S. What dose of Vitamin E is required to reduce susceptibility of LDL to oxidation? *Aust NZ J Med* 1996;26:496-502.
  11. Kazdova L. Protective effect of Vitamin E on aortic lipid peroxidation and atheroma formation in hypercholesterolaemic rabbits. *Atherosclerosis* 1995;115:S47.
  12. Keegan A, Walbank H, Cotter MA, Cameron NE. Chronic Vitamin E treatment prevents defective endothelium relaxation in diabetic rat aorta. *Diabetologia* 1995;38:1475-8.
  13. Verlangieri AJ, Bush MJ. Effects of D-alpha-tocopherol supplementation on experimentally induced primate atherosclerosis. *J Am Coll Nutr* 1992;11:131.
  14. Stampfer MJ, Hennekens M, et al. Vitamin E consumption and the risk of coronary artery disease in women. *N Eng J Med* 1993;328:1444-9.
  15. Kushi LH, Folsom AR, Prineas RJ, Mink PJ, Wu Y, Bostick RM. Dietary antioxidant vitamins and death from coronary heart disease in post menopausal women. *N Eng J Med* 1996;336(18):1156-62.
  16. Rimm EB, Stampfer MJ, Ascherio A, Giovannucci E, Colditz GA, Willett WC. Vitamin E consumption and the risk of coronary heart disease in men. *N Eng J Med* 1993;328:1450-6.
  17. Losonczy KG, Harris TB, Havlik RJ. Vitamin E and Vitamin C supplement use and risk of all cause and coronary heart disease mortality in older persons. *Am J Clin Nutr* 1996;64:190-6.
  18. de Gactano G. Low dose aspirin and Vitamin E in people at cardiovascular risk, a trial in general practice. Collaborative group of the Primary Preventive Project. *Lancet* 2001;357:89-95.
  19. A randomized placebo controlled, clinical trial of high dose supplementation with Vitamins C, E and beta carotene for age related cataract and vision loss. *Arch Ophthalmol* 2001;119:1439-52.
  20. The effect of Vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *N Eng J Med* 1994;330:1029-35.
  21. Yusuf S, Dagenaga G, Pogue J, Bosch J, Sleight P. Vitamin E supplementation and cardiovascular events in high risk patients. The heart Outcomes Prevention Evaluation Study Investigators. *N Eng J Med* 2000;342:154-60.
  22. Dietary supplementation with n-3 polyunsaturated fatty acids and Vitamin E after myocardial infarction: results of the GISSI Prevenzione trial. *Lancet* 1999;354:447-55.
  23. MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20,536 high risk individuals: a randomized placebo controlled trial. *Lancet* 2002;360:23-33.
  24. Stephens NG, Parsons A, Schofield PM, Kelly F, Cheeseman K, Mitchinson MJ. Randomised control trial of Vitamin E in patients with coronary disease, Cambridge heart Antioxidant Study (CHAOS). *Lancet* 1996;347:781-6.
  25. Fang JC, Kinlay S, Beltrame J, Hikiti H, Wainstein M, Behrendt D, et al. Effects of Vitamin C and E on progression of transplant associated atherosclerosis: a randomized trial. *Lancet* 2002;359:1108-11.
  26. Nyyssonen K, Parviainen MT. Vitamin C deficiency and risk of myocardial infarction: prospective population study of men from eastern Finland. *BMJ* 1997;314:634-8.
  27. Osganian SK, Stampfer MJ, Rimm E, Spiegelman D, Hu FB, Manson JE, et al. Vitamin C and risk of coronary heart disease in women. *J Am Coll Cardiol* 2003;42(2):253-5.
  28. Fletcher RH, Fairfield KM. Vitamins for chronic disease prevention in adults: clinical applications. *JAMA* 2002;287:3127-9.
  29. Rimm EB, Willett WC, et al. Folate and vitamin B6 from diet and supplements in relation to risk of coronary heart disease in women. *JAMA* 1998;279:359-64.
  30. Stampfer MJ, Hennekens CH, Manson JE, Coditz GA, Rosner B, Willett WC. Vitamin E consumption and the risk of coronary heart disease in women. *N Eng J Med* 1993;328:1444-9.
  31. Dyckner T, Wester PO. Magnesium in cardiology. *Acta Med Scand* 1982;661(Suppl):27-31.
  32. Horner SM. Efficacy of intravenous magnesium in acute myocardial infarction in reducing arrhythmias and mortality: meta analysis of magnesium in acute myocardial infarction. *Circulation* 1992;86:774-9.
  33. Woods KL, Fletcher S, Roffe C, Haider Y. Intravenous magnesium sulphate in suspected acute myocardial infarction: results of the second Leicester intravenous magnesium intervention trial (LIMIT-2). *Lancet* 1992;339:1553-8.
  34. The National Health and Nutritional Examination survey epidemiological follow up study. *Int J Epidemiol* 1999;28:645-51.
  35. Ford ES. Serum magnesium and ischaemic heart disease: findings from a national sample of US adults. *Int J Epidemiol* 1999;28:645-51.
  36. Abbott Rd, Ando F, Masaki KH, Tung KH, Rodriguez BL, Petrovitch H, et al. Dietary magnesium intake and the future risk of coronary heart disease (The Honolulu Heart Program). *Am J Cardiol Sep* 2003;92(6):665-9.
  37. Robinson MF. Selenium in human nutrition in New Zealand. *Nutr Rev* 1989;47:99-107.
  38. Clark L, Combs G, et al. Effects of Selenium Supplementation for Cancer Prevention in Patients with Carcinoma of the Skin. *J Am Med Assoc* 1996;276:1957-62.
  39. Dyerberg J, Bang HO, Stofferson E, Moncada S, Vane JR. Eicosapentaenoic acid and prevention of thrombosis and atherosclerosis. *Lancet* 1978;ii:117-9.
  40. Hu FB, Bronner L, Willett WC, Stampfer MJ, Rexrode KM, Albert CM, et al. Fish and omega-3 fatty acid intake and risk of coronary heart disease in women. *JAMA* 2002;287(14):1815-21.
  41. Burr ML, Fehily AM, et al. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet* 1989;2(8666):757-61.
  42. Ascherio A, Rimm EB, et al. Dietary intake of marine n-3 fatty acids, fish intake, and the risk of coronary disease among men. *NEJM* 1995;332:977-83.
  43. Daviglius ML, Stamle J, Orenca AJ, Dyer AR, Liu K, Greenland P, et al. Fish consumption and the 30-year risk of fatal myocardial infarction. *NEJM* 1997;336:1046-53.
  44. Marchioli R, Barzi F, Bomba E, Chieffo C, Di Gregorio D, Di Mascio R, et al. Dietary supplementation with n-3 polyunsaturated fatty acids and Vitamin E after myocardial infarction: results of [Gruppo Italiano per lo Studio della Sopravvivenze nell'infarto] GISSI-Prevenzione. *Lancet* 1999;354:447-55.
  45. Albert CM, Campos H, Stampfer MJ, Ridker PM, Manson JE, Willett WC, et al. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. *NEJM* 2002;346:1113-8.
  46. Siscovick DS, Raghunathan TE. Dietary intake and cell membrane levels of long-chain n-3 polyunsaturated fatty acids and the risk of primary cardiac arrest. *JAMA* 1996;275(11):836-7.
  47. Coombes JS, Gore P. Antioxidants, exercise and Australian and New Zealand cardiologists. *Int Med J* 2001;31:501-4.
  48. Meta J. Antioxidants among American cardiologists. *Am J Cardiol* 1997;79:1558-60.