Multivitamins Reduce Risk for Heart Disease and Diabetes

Vitamins B6, C, and E are associated with lower levels of CRP, a marker of systemic inflammation

By Dr. Edward R. Rosick

"Taking multivitamins is a waste of money." How many times has that opinion been expressed in doctor's offices around the country, or printed in the pages of mainstream medical journals? The answer is "Often." Even today, when it's well known how essential numerous vitamins and minerals are for maintaining optimal health, many doctors still scoff at the idea that most Americans need multivitamin supplements (a term that's generally understood to mean supplements containing multiple vitamins and minerals and, increasingly, plant-derived antioxidants as well).

There is abundant scientific evidence that certain vitamins can help reduce the risk of many chronic debilitating diseases, including heart disease, diabetes, and cancer.1 Current research is producing evidence that a high intake of certain vitamins and minerals may inhibit damage to our DNA, which might help prevent many of the most common diseases seen in industrialized societies.

A recent paper on the relationship between vitamin supplements and optimal DNA functioning stated, "Current recommended dietary allowances for vitamins and minerals are based largely on the prevention of diseases of deficiency . . . because diseases of development, degenerative diseases, and aging itself are partly caused by damage to DNA, it seems logical that we should focus better our attention on defining optimal requirements of key minerals and vitamins for preventing damage to both nuclear and mitochondrial DNA."2

CRP Levels Can Signal a Variety of Diseases

C-reactive protein, or CRP, is a compound produced primarily by the liver in response to acute inflammatory processes, such as bacterial infections. Studies have shown that blood levels of CRP remain chronically elevated, however, in many inflammatory, infectious, and neoplastic (abnormal growth) diseases, including lupus, rheumatoid arthritis, tuberculosis, cancer, diabetes, and heart disease.3

CRP levels are now being used to determine the extent of heart damage during and after heart attacks. One recent study showed that a high CRP level in people who suffer their first heart attack is a strong predictor of future heart attacks, while lower CRP levels suggest less chance of having another heart attack.4 Furthermore, it has now been shown that, even in people who have normal cholesterol levels, high CRP levels can help predict asymptomatic heart disease.5

Statins Reduce CRP Levels—But There Are Alternatives

Some of the top-selling pharmaceuticals in America today are the statins (e.g., Lipitor®, Zocor®, and Pravachol®), which are used to treat heart disease by reducing cholesterol levels. New research has shown, however, that statins also reduce CRP levels, leading scientists to postulate that these drugs' cardiovascular benefits result not only from lower cholesterol levels but also from reduced inflammation. Since heart researchers believe that inflammation in the inner walls of arteries is a crucial factor in the development of atherosclerotic plaque, it makes sense to think that drugs—or supplements—that inhibit inflammatory processes (thus reducing CRP levels) could help prevent heart disease.

Those taking the supplement had significantly lower CRP levels than the controls. The average CRP reduction of 14% was comparable with the reductions that have been seen with statin drugs.

For people who are leery of taking statins because of their high cost or the possibility of unpleasant side effects, or for those who seek more natural ways to improve their health, the good news is that there's exciting new research showing that increased levels of three vitamins (and some antioxidant compounds as well) are associated with reduced CRP levels.

Finding Correlations Is Good . . .

One recent investigation looked at data from 891 participants in the Framingham Heart Study to see if there was an inverse association between CRP levels and circulating levels of vitamin B_6.6 There was. In the authors' words, "These data demonstrate a strong association between decreased plasma PLP [vitamin B_6] and increased levels of CRP, a major systemic marker of inflammation."

CRP Levels May Predict Colon Cancer

Being a marker for heart disease and diabetes has already made CRP (C-reactive protein) a star in the world of medicine—but the star may become brighter yet. Since inflammation has been hypothesized to increase the risk for cancer, a group of researchers recently undertook to investigate whether CRP levels might be useful in estimating a person's risk for two of the most common and deadly forms of this disease: colon cancer

and rectal cancer (commonly lumped together as colorectal cancer).1 The researchers took advantage of the availability of deep-frozen blood samples collected in 1989 from 22,887 men and women (aged 18 or older) who were participating in an ongoing epidemiological study. A survey of their medical records through December 2000 revealed that 172 of them had developed colorectal cancer during the 11-year period. The researchers then selected 342 control subjects (no cancer) who represented a similar profile in terms of age, sex, race, and date of blood draw. When they tested the blood samples of all these individuals for CRP levels, the researchers found a strong correlation with colon cancer (but not rectal cancer): the higher the CRP levels, the greater the risk for colon cancer. Those with the highest levels were 2.6 times more likely to develop the disease than those with the lowest levels. The researchers concluded that the association was real and significant, and they speculated that anti-inflammatory therapy (which would reduce CRP levels) might therefore prove useful as a preventive strategy.

1. Erlinger TP, Platz EA, Rifai N, Helzlsouer KJ. C-reactive protein and the risk of incidental colorectal cancer. *JAMA* 2004;291:585-90.

Another study examined the possible link between a variety of antioxidant compounds and CRP levels in 14,519 American men and women.7 The authors found that CRP levels were inversely related to the concentrations of vitamin C, retinol, alpha- and beta-carotene, lutein and zeaxanthin, lycopene, and selenium. These findings led them to state, “These results suggest that the inflammatory process, through the production of reactive oxygen species, may deplete stores of antioxidants.” In other words, low antioxidant levels favor the proliferation of harmful reactive oxygen species (including free radicals), which is one aspect of the inflammatory process—and high CRP levels are a sign of that.

. . . But Active Intervention Is Better

Those two studies revealed inverse correlations between CRP levels and those of certain vitamin and antioxidant compounds. But what about active intervention? Would supplementing with these compounds reduce CRP levels, which would presumably indicate a decrease in inflammatory processes such as those associated, e.g., with heart disease and diabetes? Two *other* studies have addressed that question.

One study examined the effects of **vitamin E** (alpha- tocopherol) on CRP levels in patients with type 2 (adult-onset) diabetes.8 In this 5-month study, 47 diabetic patients and 25 matched controls with no history of major medical problems were given 1200 IU/day of alpha-tocopherol for 3 months, followed by a 2-month washout phase. The researchers found that the vitamin E supplementation significantly decreased CRP levels in both the diabetic patients and the controls (which means that even the controls had some degree of inflammatory process in their systems).

A Nutritional Alphabet Soup

It has often been said by those in mainstream medicine that Americans don't need to take supplements because the "average" American diet contains enough vitamins and minerals to cover the RDI requirements. Of course, ask an average American what RDI stands for, and you'll get a blank stare. Ask anyone well versed in integrative medicine, however, and you'll get an answer that boils down to "numbers that are designed to prevent disease, not to optimize health." The first set of vitamin and mineral standards, called RDAs (Recommended Dietary Allowances), was established by the National Academy of Sciences in 1941. Its intent was to set minimal requirements for essential nutrients (in a time of possible wartime food shortages) to ensure the basic nutritional needs of the populace. This system underwent many changes over the years to reflect

advances in our understanding of nutritional requirements. Many of the values were scaled down, but a few were scaled up. In 1973 the FDA established its own system, called U.S. RDAs (Recommended Daily Allowances)—not to be confused with just plain RDAs. It was based initially on the highest 1968 RDAs for each nutrient, to ensure that nutritional needs were met for all age groups. The RDAs continued to evolve, however, and so did the U.S. RDAs. Believe it or not, people did get confused! So the FDA clarified things by introducing a new system, called RDIs (Reference Daily Intakes), to replace the U.S. RDAs (but not the just plain RDAs). Then they introduced another system, called DRVs (Daily Reference Values), which was for things such as fats, carbohydrates, proteins, cholesterol, and fiber. And then, to clarify things even more, they introduced another system, called DVs (Daily Values), which is derived from both the RDIs and the DRVs. The DVs are the only ones (mercifully) that appear on food and supplement labels. Are you following this? (There will be a quiz.) Just to clarify things a little more, the latest system is called DRIs (Dietary Reference Intakes), and it was established not by the FDA but by the Food and Nutrition Board of the Institute of Medicine, during the period 1997–2001. In this system, which may be the basis for eventually updating the FDA's RDIs, the values are mostly different from the current RDIs: for the 25 nutrients covered, 14 are lower, 8 are higher, 2 are the same, and 1 is new (choline, which is neither vitamin nor mineral and has no RDI). OK, just one more: there is now also a system called ULs (Upper Limits), which has to do with safe upper limits for vitamins and minerals (in some cases, separate ULs have been established for children). So what does it all mean? Basically, the numbers stand for something necessary and worthwhile, yet misleading: all but the ULs represent *minimal* nutritional requirements for preventing deficiency diseases—but that's often a far cry from *ideal* nutritional levels for optimizing health. We need to know the minimal requirements, because even in our affluent society, many people have specific nutrient deficiencies owing to their junk-

food diets. But we also need to know the ideal levels so that we can be as healthy as possible. *Those* numbers do not appear in these systems. The problem is that the ideals are not nearly as easy to establish as the minimums, especially when the wide variability of "normal" human beings is considered. But scientific research on these matters continues apace, and we will continue to bring our readers the latest and best information on them (using whole words!).

Certain Vitamins Reduce CRP Levels

The other study was a randomized, double-blind, placebo-controlled trial with 87 men and women, aged 30–70, which focused on the relationship between multivitamin supplementation and CRP levels.9 The participants were given either placebo or a daily multivitamin supplement (13 vitamins and 7 minerals, as well as choline, lycopene, lutein, and coenzyme Q_{10}), for 6 months. Their blood was tested, at the beginning and the end of this period, for levels of CRP and for six of the 13 vitamins in the supplement formulation: beta-carotene (a vitamin A precursor), vitamin B_6, vitamin B_{12}, folic acid (a B-vitamin), vitamin C, and vitamin E.

The results showed that those people taking the 24-ingredient supplement formulation had significantly lower CRP levels than the controls; this was especially evident in those whose CRP levels were elevated at the outset of the study. The observed average CRP reduction of 14% was comparable with the reductions (14–28%) that have been seen with statin drugs. The reductions in CRP levels were specifically associated with only two of the six vitamins measured: **vitamin B_6** and **vitamin C.** Whether the reduction was at least in part attributable to any of the other 18 ingredients in the formulation is unknown.

Are Combinations of Compounds Required?

Thus the results of this last study stand in partial agreement and partial disagreement with those of the other three studies cited, but that's not surprising: medicine is not an exact science, and no two research studies are conducted in exactly the same way to begin with. It seems safe to say, though, that certain vitamins (based on good but somewhat conflicting evidence), and *perhaps* certain minerals (no evidence to date), and *perhaps* certain antioxidants (some suggestive evidence) are effective in reducing CRP levels—a highly desirable outcome.

Even at that, however, it's still not clear whether any one compound can do this alone, or whether combinations of compounds are required. It is well known, e.g., that the effectiveness of various vitamins and minerals depends on their cooperative action, without which each individual member of the "team" would be a dud.

Go Multi!

All of the above argues for the idea of taking the best available multivitamin, multimineral, multiantioxidant supplement—the single most important kind of supplement there is—so as to maximize the chances of obtaining all the benefits these marvelous compounds can offer. As we have seen, a new and important benefit—anti-inflammatory action, as evidenced by CRP reduction—has now been added to an already long and impressive list.

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