

## **Health**

### **Health Journal: The case against vitamins**

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Every day, millions of Americans gobble down fistfuls of vitamins in a bid to ward off ill health. They swallow megadoses of vitamin C in hopes of boosting their immune systems, B vitamins to protect their hearts, and vitamin E, beta carotene and other antioxidants to fight cancer.

It's estimated that 70 percent of American households buy vitamins. Annual spending on vitamins reached \$7 billion last year, according to industry figures.

But a troubling body of research is beginning to suggest that vitamin supplements may be doing more harm than good. Over the past several years, studies that were expected to prove dramatic benefits from vitamin use have instead shown the opposite. Beta carotene was seen as a cancer fighter, but it appeared to promote lung cancer in a study of former smokers. Too much vitamin A, sometimes taken to boost the immune system, can increase a woman's risk for hip fracture. A study of whether vitamin E improved heart health showed higher rates of congestive heart failure among vitamin users.

And there are growing concerns that antioxidants, long viewed as cancer fighters, may actually promote some cancer and interfere with treatments.

Last summer, the prestigious Medical Letter, a nonprofit group that studies the evidence and develops consensus statements to advise doctors about important medical issues, issued a critical report on a number of different vitamins, stressing the apparent risks that have emerged from recent studies. The Food and Nutrition Board of the National Academy of Sciences -- the top U.S. authority for nutritional recommendations -- has concluded that taking antioxidant supplements serves no purpose.

"People hear that if they take vitamins they'll feel better," says Edgar R. Miller, clinical investigator for the National Institute on Aging and author of an analysis that showed a higher risk of death among vitamin E users in several studies. "But when you put (vitamins) to the test in clinical trials, the results are hugely disappointing and in some cases show harm. People think they are going to live longer, but the evidence doesn't support that. Sometimes it's actually the opposite."

Not everybody is buying these results. Consumers remain devoted to their vitamin regimens. Industry groups such as the Council for Responsible Nutrition reject the recent evidence, saying the research is flawed or the people studied were too sick to start with, making it impossible to draw any broad conclusions for the rest of us. "I don't think it's black and white," says Andrew Shao, vice president of regulatory and scientific affairs for the council. "It's important to know that a lot of these studies have been done in diseased populations. I

suppose the expectations are too high. These vitamins are not drugs. They can't be expected to cure or reverse 20, 30 or 40 years of disease."

Everyone needs vitamins, which are key nutrients the body can't make. But micronutrients from foods usually are adequate to prevent vitamin deficiency, which is rare in the U.S. Even so, vitamin B-12 supplements for the elderly and folic acid for women of child-bearing age are recommended.

But the proven benefits of a few supplements pale next to the growing concerns about widespread vitamin use. Nobody knows why high doses of vitamins taken as pills might cause harm. One theory has to do with free radicals, a common byproduct of the normal chemical reactions that occur in cells. Every day cells get damaged due to a variety of factors including sunlight, the foods we eat and natural aging. This creates free radicals, highly reactive molecules that can damage tissues and lead to cancer and heart disease. Although the body has several ways of coping with free radicals, many people believe high doses of vitamins help, mopping up free radicals before they can do much damage.

But the problem is that free radicals may serve an important purpose, sending a powerful signal to the body's immune system, which enlists its own army of soldiers to fight the free radicals and fix the damage. The theory is that by taking vitamins, we undermine that message system and upset the balance of antioxidants and free radicals in the body. It may be that vitamins clean up the free-radical mess, but the immune system isn't alerted to fix the damage, allowing disease to set in.

Another concern is that while vitamins from food sources are necessary and good for you, consumers today often scarf down vitamins at levels that are more like a pharmaceutical dose than something found in nature. In a test tube, high doses of a single antioxidant can turn bad, evolving into pro-oxidants -- meaning they start to oxidize and create free radicals, causing the very problem you were trying to prevent.

Here's a look at what science shows about the risks and benefits of some particular vitamins.

## **VITAMIN E**

Vitamin E has long been touted as beneficial to heart health, based in part on observational studies that have shown diets rich in fruits and vegetables containing E and other vitamins are associated with a decreased risk of coronary disease. Vitamin E also has been studied as a way to help Alzheimer's disease and to prevent prostate cancer.

But research into vitamin E supplements has been disappointing. Most clinical trials in recent years have been inconclusive or shown no benefit -- and some have suggested harm. The University of California-Berkeley Wellness Letter, from the same institution that discovered the vitamin in 1922, last year said it no longer recommended vitamin E supplements because of the data showing no benefits.

Last year, Johns Hopkins University researchers in Baltimore published a shocking finding. After reviewing the data from 19 vitamin E clinical trials of more than 135,000 people, the analysis showed high doses of vitamin E (greater than 400 IUs) increased a person's risk for dying during the study period by 4 percent. Taking the vitamin E with other vitamins and minerals resulted in a 6 percent higher risk of dying.

Not everyone agrees with the methods used in the study. And most of the patients were already unhealthy, so

the results may not apply to healthy people.

Since the analysis was published, another study of about 9,500 patients evaluated long-term use of 400 IUs of vitamin E daily. The study didn't show any statistically meaningful differences between vitamin users in terms of cancer, heart attacks or stroke, but the vitamin E takers had a 13 percent higher risk for heart failure.

The risk of taking vitamin E for cancer is also of concern. Last year, the Journal of Clinical Oncology published a study of 540 patients with head and neck cancer who were being treated with radiation therapy. The patients took 400 IUs of vitamin E or a placebo. The supplement reduced side effects by nearly 30 percent. But recurrence rates among the vitamin E users were 37 percent higher. The finding was not statistically meaningful, but has raised concerns that vitamin intake could hinder the effectiveness of treatments.

Not all the vitamin E news has been bad. Last year, the Women's Health Study evaluated use of 600 IUs of vitamin E every other day by nearly 40,000 healthy women. Overall, there was no benefit of using vitamin E for major cardiovascular events or cancer. But a subgroup analysis found there was a 24 percent lower risk for cardiovascular deaths and a 26 percent reduction in major cardiovascular events among women over 65. The researchers said those findings weren't conclusive, however, in part because they contradict other clinical-trial evidence.

Another study, called Select, is looking at whether vitamin E and selenium lower risk for prostate cancer. The study won't finish for several years, but this summer a safety monitoring committee will review the results to date to see whether any significant risks or benefits have emerged. In February, another study reported in the Journal of the National Cancer Institute showed no clear benefit of vitamin E on prostate-cancer risk, although there was benefit among a subgroup of smokers.

The Select trial already offers a cautionary tale on vitamin use, says Eric Klein, head of urologic oncology at the Cleveland Clinic and a Select investigator. Select was started after a study of smokers in Finland looked at beta carotene and vitamin E to prevent lung cancer. While vitamin E users had an unexpected lower risk for prostate cancer, the beta carotene users had a higher risk for lung cancer. "The psyche of the U.S. population is that a nutraceutical can't be harmful and might be helpful, so why not take it?" says Dr. Klein. "That thinking is just not correct. The message is: Be careful until the data is in."

## **BETA CAROTENE AND VITAMIN A**

Vitamin A is a family of compounds that play a role in vision, bone health, cell division and the regulation of the immune system. Retinol is one of the most usable forms of vitamin A. Several carotenoids, the darkly colored pigments found in many plant foods, can be converted to vitamin A, but beta carotene is the carotenoid that is most efficiently converted to vitamin A.

Although studies have suggested an association between diets rich in beta carotene and vitamin A and a lower risk for many types of cancer, the supplements taken in pill form have proved risky.

The 1994 Finland study of smokers taking 20 milligrams a day of beta carotene showed an 18 percent higher incidence of lung cancer among beta carotene users. In 1996, a study called Caret looked at beta carotene and vitamin A use among smokers and workers exposed to asbestos. The trial was stopped when the participants

taking the combined therapy showed a 28 percent higher risk for lung cancer and a 26 percent higher risk of dying from heart disease.

More recently, a 2002 Harvard study of more than 72,000 nurses showed that those who consumed high levels of vitamin A from foods, multivitamins and supplements had a 48 percent higher risk for hip fracture than nurses who had the lowest intake of vitamin A. Notably, nurses who ate a lot of foods high in vitamin A also had higher risk, possibly indicating that too many foods are now fortified with the vitamin. Milk, margarine and breakfast cereals are fortified with vitamin A. High intake of vitamin A has also been associated with a higher risk of birth defects.

## **VITAMIN C**

Ever since Nobel laureate Linus Pauling extolled the virtues of vitamin C more than 30 years ago, Americans have been taking handfuls of the pills, convinced the vitamins do everything from preventing colds to fighting cancer. But like other vitamin studies, research into vitamin C has been disappointing.

Last summer, the Cochrane Database of Systematic Reviews looked at the clinical-trial evidence for vitamin C supplements in treating the common cold. Among 23 studies, there was no overall benefit to using vitamin C to prevent colds. However, six studies of marathon runners, skiers and soldiers exposed to significant cold or physical stress showed about a 50 percent reduction in colds with vitamin C use. But the investigators warned that these were extreme circumstances and probably don't apply to the general population. Vitamin C may slightly shorten the duration of colds, but the investigators said the small difference may not even be noticed by patients.

There are also concerns about risks associated with vitamin C. A 1999 analysis in the British Medical Journal showed that in three studies, vitamin C didn't lower death rates among elderly people, and may actually have increased the risk of dying slightly. Last year, the cancer journal CA reported that antioxidant supplements, including vitamin C, should be avoided by patients being treated for cancer. Scientists have found that cancer cells gobble up vitamin C faster than normal cells, suggesting that any protection vitamin C gives might be even greater for tumors than normal cells. In 2001 scientists showed that cancer cells may become resistant to chemotherapy drugs after treatment with vitamin C. "It's a mistake to think that cancer cells ... don't like nutrients," says Gabriella D'Andrea, oncologist with Memorial Sloan-Kettering Cancer Center in New York and author of the review.

Whether any of the antioxidant vitamins are cancer fighters or cancer promoters remains an open question. Although some data suggest a benefit, others suggest harm. In October 2004 Copenhagen researchers reviewed seven randomized trials of beta carotene, selenium, and vitamins A, C and E (alone or in combination) in esophageal, gastric, colorectal, pancreatic and liver cancer. The antioxidant users had a 6 percent higher death rate than placebo users.

## **B VITAMINS**

A regimen of B vitamins, including folic acid, vitamin B-12 and vitamin B-6, has been touted as a way to improve heart health by lowering homocysteine, an amino acid thought to be a risk factor for heart attack. But last week, two studies presented to the American College of Cardiology showed that while the vitamins do

lower homocysteine levels, taking them doesn't lower risk for heart attack.

The patients in the studies weren't healthy. They had diabetes, heart disease or a history of heart attack. The New England Journal of Medicine said the consistency of the results "leads to the unequivocal conclusion" that the vitamins don't help patients with established vascular disease.

But the medical community remains divided on whether the vitamins might still be useful for healthy people. "This should not close the book on the investigation of whether B vitamins in a healthy population helps reduce risk of cardiovascular disease," says Dr. Shao of the Council for Responsible Nutrition.

Not all the research into vitamin B is controversial. Folic acid supplements for women of child-bearing age have dramatically reduced the incidence of neural-tube defects in babies. Elderly people can develop an inability to absorb vitamin B-12 from food, so supplements may be recommended as we get older.

## **CALCIUM AND VITAMIN D**

A 2005 study in the British Medical Journal didn't show any reduction in fracture risk among women who took 1,000 milligrams of calcium with 800 IUs of vitamin D a day. But the Women's Health Initiative recently suggested that calcium and vitamin D may lower hip-fracture risk in women over 60. Calcium users, however, had a 17 percent higher risk for kidney stones.

Elderly people, particularly those who have dark skin, get little exposure to sunlight and don't drink milk, are at risk for vitamin D deficiency and are typically advised to take supplements. One study suggests the most benefit comes with about 800 IUs of vitamin D a day.

Most doctors and health experts now suggest that consumers interested in taking vitamins stick to a multivitamin rather than concoct their own cocktails of high-dose vitamins. But even this practice is being questioned because there's little evidence to support it. In August the British Medical Journal looked at multivitamin use among elderly people for a year, but found no difference in infection rates or visits to doctors.

Researchers urge caution when interpreting results from various vitamin studies. Many factors, ranging from the type of vitamin to the age and health of the participants, may influence the results, says Marion Dietrich, postdoctoral associate in the Nutritional Epidemiology Program at Tufts University. What is clear, however, is the important role a healthful diet plays in preventing illness. Large dietary-intervention studies have shown that a healthful diet reduces risk of cardiovascular disease.

But doctors say many patients view vitamins as a quick fix to compensate for poor eating habits, and resist any suggestion that taking them may not be beneficial. "A lot of people are passionate about their vitamins," says Dr. Miller of the National Institute on Aging. "I don't know where they get it from, but it's not based on scientific evidence."