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Folic Acid and Cancer

Every now and then, a study is published that seems to grab everyone's attention for a day or two. Such was the case for a study published in the *Journal of the American Medical Association* (JAMA) titled "Cancer Incidence and Mortality After Treatment with Folic Acid and Vitamin B12" (1). After all the hype, you may wonder if you should be concerned about taking folic acid and vitamin B12. That's why you read the message: to get the Bottom Line on what these studies say and what they don't. Let's take a look.

The Study

Homocysteine is a marker of inflammation in people with cardiovascular disease. Several small studies have shown that supplementation with folic acid, the synthetic form of folate, may decrease inflammation and subsequently, homocysteine. There's also a theory that because folic acid is used in the production of energy, cancer cells will selectively use the folic acid to produce more energy and thus grow faster.

Two large studies conducted in Norway reported that use of folic acid and other B vitamins in high amounts did reduce homocysteine but not the risk of the progression of cardiovascular disease (2,3). In a three-year follow-up, researchers combined the subjects from the two studies and examined the rate of cancer morbidity and mortality among the original subjects (1).

They did the study because the two Norwegian trials indicated a slight tendency for a higher risk of disease progression in people taking supplements versus those taking the placebo. Norway is a good place to do that study to limit confounding sources of folic acid because Norway doesn't mandate folic acid added to foods as is done in the United States; the concern is that with the addition of folic acid to the food supply, primarily cereals and grain products, there might be negative outcomes such as an increase in cancer.

The results of the study showed that when compared to those subjects taking the placebo, there was an increase in cancer and all-cause mortality. Of course, that's inspires all kinds of fears for those of us who live in the U.S., eat grain products, and take supplements that may also contain folic acid. Should we be afraid?

The Problem

There are at least four problems with this study in my opinion. They're complicated, but I'll try to keep it as simple as possible without diluting the science.

Combining Studies

Research starts with a question that you want to answer. Once you develop the hypothesis, you select the subjects and the intervention—whether it's a drug, exercise, etc. That's not what happened in this case. They used subjects who were selected to answer other questions. They just happened to be using identical amounts of B vitamins in both studies as part of the other clinical trial. While that's convenient, there are other age groups and other interventions that might have been better and yielded more pertinent results. The researchers raised the standard for determining whether a treatment was significant or not, but that doesn't change the fact that the subjects were selected for convenience, not because they were the best subjects.

Treatment

The problem with clinicians conducting studies is that they think in terms of one thing: treating a disease. In that way, if the treatment is successful, it can be used as part of treating a disease—in this case, cardiovascular disease.

Here's the question: *whoever said that it was a good idea to use vitamins or any other nutrient as a treatment for a disease?*

That research model is flawed, but it's the only one that makes sense to clinicians. It's not surprising that most large clinical trials that use vitamins and other nutrients as a treatment do not get positive outcomes. I think that a better approach is one I talked about in a message on June 6, 2009. If you've ever heard me speak live, you know I say that vitamins don't cure disease—they may address nutritional deficiencies that can help your body heal itself. That's the role nutrition plays in our health.

Subjects

The subjects in the clinical trials all had significant cardiovascular disease—that's why they were chosen for the original study. They had had heart attacks, were on a variety of medications, and basically were very sick people. That also means that their immune systems were compromised. While the authors state that the percentage of subjects that used every medication and medical procedure was the same in every subgroup which would tend to even out the effects, they did not report other dietary factors or treatment factors which also may have had an effect on the outcomes.

The most significant problem is that there were no healthy control groups—one that took the same supplements and one that took nothing. There's no real way of knowing the effects of the supplements for people before they get a disease when supplementation might have had a preventive effect. We know what happened only to groups of people with significant disease.

Significance

As I reported earlier, there was an increase in cancer, especially lung cancer, in the group that was taking folic acid, vitamin B6, and vitamin B12 in high amounts when compared to the placebo group, but let me remind you these were people with significant cardiovascular disease.

But what were the actual numbers? If you were in the group that took the full range of supplements, there was a 1.7% chance of being diagnosed with cancer over the three year follow-up period. If you took the placebo, it was 1.4%. It was not statistically significant. For lung cancer, it was 3.1% versus 1.9% and was also not significant.

More than that, even if the results were statistically significant, it's not clinically significant and it's not generalizable to other populations of healthy people. An editorial in the same issue of JAMA suggests that if the amounts of folic acid consumed in the U.S. were as high in the study, it could pose a serious health concern (4). While the amounts we consume are not, I disagree for the reason I gave earlier regarding the very narrow, sick subject pool and the lack of healthy controls.

The Bottom Line

Of course, there's always another side to every issue. Since the addition of folic acid to the U.S. food supply, the incidence of neural-tube defects, such as spina bifida, has dropped significantly. So if you're pregnant or trying to get pregnant, your doctor probably recommends taking a folic acid supplement, and that's a recommendation I would heartily support.

But back to the scare tactics. Provocative headlines are not always supported by the data behind them, and I think that holds true for this study as well. There's never a reason to megadose on any nutrient but even if you do, the risk, if it really exists, would be very, very small.

I would prefer to take this in another direction. What would happen to those people who changed their lifestyle by eating better, exercising, losing weight, and taking supplements such as folic acid after a heart attack? Better yet, what would happen to those of us who do those things before we have a heart attack? We might just make studies like these obsolete. It simply depends on one thing:

What are you prepared to do today?

Dr. Chet

References:

1. JAMA. 2009;302(19):2119-2127.
2. N Engl J Med 2006;354:1578-88.
3. JAMA. 2008;300(7):795-804.

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