April 2, 2006

Dear Friends and Colleagues,

Several of you have asked me to respond to the recent negative story on food supplements that appeared in the March 20, 2006 issue of the Wall Street Journal and was repeated in news outlets across the country. Let me start on a philosophical note.

Science consists of a series of experiments designed to test previously accepted hypotheses. Furthermore, most of the experiments are designed to disprove previously accepted hypotheses. There is no fame in being the 10th person to prove that a hypothesis is correct. Fame comes from being the first person to disprove a previously accepted "truth" and establish a new paradigm. This is the strength of the scientific method, because it means that no idea goes unchallenged. It is only through this rigorous process that truth can eventually emerge. The consequence of this approach is that individual studies often disagree. Sometimes when you analyze the studies closely enough, you will find that one of the studies is flawed in one way or another. Sometimes, however, we never can actually figure out why the studies disagree. That is why scientists like to go with the majority of studies. If 10 or 12 show a benefit and 1 or 2 do not, we usually assume that the 1 or 2 are probably wrong. However, scientists like to keep an open mind, so if the contradictory study was performed in a different manner than previous studies, we like to design additional studies to resolve the conflict. That is why when contradictory studies come out, scientists invariably say something like "That's interesting, but we need to do more studies to see if that is correct".

The problem is that some experts have their biases and like to hype any study that suits their bias. This cuts both ways, of course. Many food supplement companies make inflated claims for their products based on very skimpy evidence (I will note that I have always respected Shaklee for their very cautious approach to product claims). Similarly, skeptics of food supplements jump on every negative study even if most studies show a clear benefit. The press, of course, is simply focused on creating controversy so that they can sell subscriptions and/or ads. For the most part, the Wall Street Journal article was simply a compilation of many previous media reports. Thus, much of what was contained in that article is a perfect example of the GI/GO principle (garbage in/garbage out). I have pointed out that many of the previous reports were either poorly designed or were inconsistent with the vast majority of previous studies and had been overly hyped by some experts and/or the media. You can find these details in "Science by Press Conference", "Soy Isoflavones & Breast Cancer Risk Revisited", "Part of the Story" and "The Rest of the Story – Part 2" on www.bobsfiles.net. These same studies have been critiqued by many other experts and that information can be found under the "Health Information " section of the www.shaklee.com website. I won't go into those details in this letter.

While I am waxing philosophical, I also would like to point out that the modern scientific method is often ill-equipped to evaluate the benefits of individual food supplements. The scientific method works best when you can analyze a single variable over a short time period. This works well when you are trying to

analyze the effect of a drug for treating a specific disease. However, to the extent that we can extrapolate animal studies to humans, individual nutrients are important in preventing disease, not in

treating it. To test food supplements properly, one would need to design a study with thousands of subjects to have enough subjects so that a significant number of them would develop the disease that you are evaluating. The study would also need to be done over a 20 to 30 year period to see if supplementation prevented the onset of that disease. Such studies are clearly not economically feasible. Thus, the studies that are actually done usually start with a very sick population to see if a single supplement can prevent further progression of the disease. These kinds of studies show positive results occasionally, but they are not ideally designed to measure the ability of supplementation to prevent disease.

The other point I would like to make is that supplementation is only one part of a holistic approach to wellness. It is not logical to think that one can eat MacDonald's and Twinkies, lay in front of the TV and achieve health just by taking food supplements. Diet, exercise and supplementation are all equally important for achieving optimum health. However, the modern scientific method is designed to test one variable at a time, and it is quite expensive to really evaluate holistic approaches to health. For example, one recent epidemiologic (population) study showed that lifestyles that involved high fiber intake, adequate calcium intake, adequate B vitamin intake (the high fiber, adequate calcium and B vitamin intake were usually achieved through supplementation), low fat, weight control and exercise substantially decreased the risk of colon cancer, but that none of those variables alone could be shown to have a significant effect. How do we interpret studies like that? Do we tell people that none of those things matter if you want to prevent colon cancer (which some of the headlines did say) or should we tell people that lifestyles that include all of those things are important in reducing your risk of developing colon cancer? As I said, it is very difficult and expensive to evaluate the efficacy of holistic approaches to health. However, in the few instances in which holistic approaches have been evaluated, they have been extremely effective. For example, if you start with people who are pre-diabetic, a holistic approach is more effective than drug therapy in preventing them from becoming diabetic. Similarly, a holistic approach (the DASH diet) is as effective as drug therapy in lowering blood pressure. So, if I can get up on my soapbox for a minute, all of us should be pursuing a holistic approach to health for ourselves and should be recommending a holistic approach to health for others.

Now that I have put things in perspective, I will respond to the Wall street Journal article.

Vitamin E: The article referred to a study from Johns Hopkins that suggested that people who supplemented with more than 400 IU of vitamin E actually had a higher risk of dying than those who didn't. This comes under the heading of what I would call a flawed study. That is unfortunate, because this study was what we call a meta-analysis that combines the results of many studies. Meta-analyses are supposed to attain greater statistical power by combining multiple studies, so this had the potential of being a very good study. However, the investigators chose to include only those studies that had adverse outcomes and completely ignored the hundreds of studies with vitamin E that had no adverse outcome. With a selection criterion like that, the results were predictable.

Even so, the negative results were almost totally due to a single study starting with very sick patients and using a combination of vitamin E and hormone replacement therapy, which is now known to increase the risk of heart disease. This study has been thoroughly critiqued by many experts (For example, there is a discussion of vitamin E benefits and risks in the March 2005 issue of Environmental Nutrition. You will also find commentaries on vitamin E benefits and risks in the Health Information section of the www.shaklee.com website).

The Wall Street Journal also mentioned a second report, which suggested that Vitamin E supplementation might increase the risk of heart failure. That study is one that I think has been over-interpreted and over-hyped. The authors actually found that vitamin E lowered the risk of heart attacks, but discounted that finding. They then reported that their data suggested a slight increase in heart failure, admitted that no other study had seen that effect, and concluded that we needed to pay attention to the risk of heart failure. Most objective scientists would consider this study interesting and worthy of further investigation. However, in light of the many other studies that did not see any increased risk of heart failure, it is far too early to be making any recommendations based on this one study. The article then mentioned a recent study suggesting that while vitamin E significantly decreased the side effects of cancer chemotherapy, it may have decreased the effectiveness of the therapy as well. This is an area of research that is crying out for good clinical studies. On the one hand, some antioxidants and B vitamins could interfere with chemotherapy. On the other hand, cells of our immune system desperately need nutrients to recover from the ravages of chemotherapy, and a strong immune system is essential if our bodies are going to defeat the cancer. I should also point out that the few other studies that have been reported in the scientific literature show that supplementation produces a reduction in side effects with no decrease in the efficacy of chemotherapy. I definitely do not subscribe to the hypothesis that supplements should be avoided because they will “feed the cancer cells”. If you want to starve the cancer cells, the way to do that is to use drugs that block off their blood supply (such drugs now exist). You can’t starve cancer cells by withholding nutrients without starving the normal cells in your body, and those normal cells, especially the cells of your immune system, are vitally important if you are going to destroy the cancer. My personal recommendation is to use food supplements such as vitamin E to minimize the side effects of chemotherapy, but to stop their use a couple of days before to a couple of days after each round of chemotherapy to avoid possible interference with the chemotherapy.

Finally, there is the whole question of whether vitamin E is effective in preventing heart disease and cancer. There is substantial evidence that vitamin E is effective in preventing heart disease. The CHAOS (Cambridge Heart Antioxidant Study) and the Men’s Health Professional Follow-Up Study both showed substantial reduction in heart disease risk in men supplementing with vitamin E. In addition, the recent Women’s Health Study suggested that vitamin E reduced the risk of heart disease in women over 65. (No effect was seen in women under age 65 in that study - which was the only part of that study to actually make the headlines. It is important to note that heart disease develops later in women than in men, so there may not have been enough heart attacks in the younger group to see a significant effect of vitamin E). However, several other studies of vitamin E and heart disease have come up empty. Thus, I and most experts feel today that vitamin E has not been proven to be a “magic bullet” that is capable

of significantly reducing the risk of heart attacks by itself in a population that already has advanced heart disease. However, vitamin E does clearly reduce certain risk factors for heart disease (It reduces cholesterol oxidation, stimulates nitric oxide production and may reduce inflammation). Thus, I feel that vitamin E supplementation definitely has a place as part of a holistic approach to reducing the risk of heart attack (See my earlier comments about holistic approaches). Other experts feel similarly. For example, Drs. Eric Rimm and Meir Stampfer of Harvard Medical School and the Harvard School of Public Health recently concluded in a broad review of the evidence that "results from observational and experimental studies consistently support an effect of vitamin E supplementation on reducing risk of coronary heart disease."

As mentioned in the Wall Street Journal article, the jury is still out with respect to vitamin E preventing cancer. However, if I were a betting man, I would bet that vitamin E will not prove to be a "magic bullet" for preventing cancer either, at least not in the relatively short-term studies that are economically feasible. With cancer, like heart disease, I would recommend a holistic approach that included antioxidants like vitamin E.

Finally, this article, along with similar news articles in recent years, fails to note the many published papers showing benefits of vitamin E supplementation, such as studies showing that vitamin E supplementation helps prevent macular degeneration (along with vitamin C, zinc and beta-carotene) and the decline in immune function that occurs as we age. How much vitamin E is enough? I don't know of any experts currently recommending megadoses of vitamin E. For most of the studies showing beneficial effects of vitamin E supplementation, the amount of vitamin E found in Shaklee Basics should suffice. While I am skeptical of claims that higher amounts of vitamin E are harmful, I am also not convinced that they offer additional benefit for most people. I should add the disclaimer that I am reviewing the literature from the point of view of a scientist interested in the prevention of disease in healthy people. I am aware that clinicians sometimes recommend higher amounts for the treatment of specific diseases, but I do not feel qualified to evaluate those recommendations.

Beta Carotene and Vitamin A: The article referred to two studies showing that beta-carotene may actually increase the risk of lung cancer in smokers and people exposed to high levels of asbestos. Most experts now agree that it is prudent not to supplement with megadoses of beta-carotene if you are a smoker or have had extensive asbestos exposure, but there is no indication that beta-carotene supplementation presents any risk for non-smokers. More importantly, the beta-carotene studies occurred long enough ago that follow-up studies have begun to unravel the cause of the effect. It turns out that a high concentration of pure beta-carotene actually interferes with the absorption of other carotenoids in the diet that may be even more beneficial than the beta-carotene itself. Thus, most experts feel that beta carotene in foods is actually quite safe. This is why most food supplement manufacturers now make mixed carotenoid supplements like Shaklee's CarotoMax.

The article also mentioned the Nurses study which suggested that high levels of vitamin A might increase the risk of bone fractures. I have serious doubts about that study, because it is essentially saying that we cannot take the recommended dietary allowance of vitamin A without increasing the risk

of bone fracture. You can find critiques on that study by other experts on the Health Information portion of the www.shaklee.com website. However, until the issue is fully resolved, most food

supplement manufacturers (including Shaklee) have cut the levels of vitamin A in half in their multivitamin/multimineral supplements and replaced the other half with beta carotene.

Vitamin C: The Wall Street Journal article was correct in saying that vitamin C supplementation does not prevent the common cold, and that vitamin C requirements are increased in people who are experiencing physical stress (Vitamin C requirements are also increased in smokers). I also agree with the article's statement that vitamin C has been shown to decrease the duration of the common cold. This effect varies considerably from individual to individual, but can be significant in some people. I generally increase my vitamin C intake, along with Shaklee's Defend & Resist and Nutriferon, when I first experience the onset of cold symptoms. My critique on the discussion of vitamin C supplementation and cancer is the same as for vitamin E (see above). Several years ago, Dr. Gladys Block of the National Cancer Institute and U.C. Berkeley reported that 33 out of 46 studies relating to non-hormone-dependent cancers found a significant protective effect of vitamin C. However, I, and most experts, do not recommend vitamin C supplementation as a magic bullet to prevent cancer, but rather as part of holistic approach to reduce the risk of cancer. As with vitamin E, supplementation with vitamin C and other nutrients can help our immune system recover from the ravages of chemotherapy, but I recommend that it be avoided during the administration of the chemotherapy because it could interfere with some of the drugs being used (This has not actually been demonstrated, but I recommend erring on the side of caution). Finally, the article discussed a recent study looking at the effect of vitamin C supplementation on death rate in the elderly. There have been a few studies of this type, most showing no effect and some showing a slight decrease in death rate. None of the studies showed significant effects. Again, I would point out that it is highly unlikely that vitamin C by itself will be either a "magic bullet" that will prolong life or a "magic gun" that will shorten life. Finally, as with vitamin E, the article neglected to mention the many studies showing the benefits of vitamin C supplementation. The amount of vitamin C found in the Basics should be sufficient and safe for almost everyone. Higher intakes are probably safe, but may not be needed by most people. However, I again need to add the caveat that I am looking at this from the point of view of reducing disease risk in a healthy population.

B Vitamins: The Wall Street Journal was correct in saying that folic acid supplementation has been shown to decrease the incidence of birth defects and is now recommended for women of child-bearing age. It also pointed out that B12 supplementation is often important in older people. Finally the article noted that supplementation with B6, folic acid and B12 has been shown to lower homocysteine levels, which appears to be a risk factor for heart disease. However, the article then went on to point out that a recent study didn't find any lowering of actual heart attack risk in patients taking those B vitamins. This is clearly a case of a study asking the wrong question. Simply put, what the study did show was that B vitamins were not magic bullets capable of preventing heart attacks in a very sick population over a relatively short time period. The study did not address the more important question, which is whether B vitamin supplementation as part of a holistic approach can reduce the risk of heart disease in a relatively healthy population over a 10 to 30 year time frame. In my opinion, B vitamin supplementation has been shown to decrease at least one probable risk factor for cardiovascular disease and is, therefore,

appropriate as part of a holistic approach to reduce the risk of cardiovascular disease. In a similar vein, B vitamin supplementation has been shown to reduce risk factors associated with some forms of cancer. Again, I am not advocating megadoses of B vitamins. The amount of B vitamins in the Shaklee Basics will suffice for many people. In addition, B vitamins should not be taken when chemotherapy is administered without consulting your oncologist because folic acid can interfere with some commonly-used chemotherapeutic drugs.

Calcium and Vitamin D: The Wall Street Journal article also mentioned the recent headlines saying that supplementation with calcium and vitamin D did not prevent hip fractures. Those headlines were highly misleading, and I have addressed this study previously (see “Part of the Story” in www.bobsfiles.net ). The misleading aspects of those headlines are also thoroughly discussed in the April 2006 issue of Nutrition Action.

Omega 3 Fatty Acids: While not in the Wall Street Journal article, there were a series of headlines recently saying things like “Omega-3 fatty acids found to have no effect on heart disease or cancer”. However, in actuality when you look at the published studies carefully it becomes clear omega-3 fatty acids were effective and that the paradigm was very different than in most other supplement studies. In this case, omega-3 fatty acid supplementation does significantly reduce the risk of heart attacks in people who have already had heart attacks, but could not be shown to be effective in people who were relatively healthy at the start of the trial. This may simply indicate that omega-3 fatty acids are not magic bullets that can single-handedly reduce the risk of heart attack in otherwise healthy people. However, it more likely is a reflection of the fact that heart disease requires many decades to develop in healthy individuals, and it is simply not possible to perform a long enough study to demonstrate an effect of omega-3 fatty acids on heart disease risk in a healthy population.

I hope that this is helpful.

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