The Path Ahead

SYNTHETIC OR NATURAL— WHICH SUPPLEMENTS ARE BEST?

I will acknowledge right up front that this is a hot issue, fraught with misinformation, limited research, commercial biases and passionately held beliefs. Nonetheless, this issue affects us every day in our practice.

I've been puzzling over this question since the early 1970s, when I was enrolled in naturopathic medical school. Some of my teachers were inspired by recent advances that enhanced understanding of human biochemistry and were excited by the falling costs of high-dose synthetic nutrients that provided improved clinical success. Linus Pauling was lecturing widely on the wonders of "orthomolecular" medicine and promulgating the benefits of vitamin C at levels difficult to achieve from diet alone. After graduation, I attended 2 inspirational monthly study clubs, one with Jeff Bland, PhD, and the other with Jonathan Wright, MD, and Alan Gaby, MD. Both clubs provided a strong research foundation for nutritional medicine and found favorable results using synthetic supplements.

But then there were the "old timers," who would comment that over time, although the quicker results and lower expense of synthetic nutrients were encouraging, they found those treated with food-derived natural nutrients seemed to fare better. I thought about what they said. They gave interesting anecdotes, but it was difficult to match them against the controlled trials of the time.

So, like most readers of this journal, I kept studying biochemistry and nutrition, treating patients with modest to high-dose, primarily synthetic nutrients and achieving good results. However, I also counseled my patients to decrease sugar and junk-food intake, adopt a whole-foods diet, and to not simply expect health from a pill, no matter how seemingly "natural." Periodically, I would read a study finding that a new nutrient had been discovered in food that was of value to human health. It was exciting to have another tool available, but disquieting that, unless my patients were eating whole-foods diets or supplementing with food concentrates, my supplement plan was coming up short. Patients could be taking all the supplements in the world, but if they were missing those nutrients available only in foods that had yet to be turned into supplements, of what true benefit was it? Even more disconcerting, researchers and epidemiologists were discovering whole classes of nutrients that either had not been detected before or had simply been ignored as unimportant but now were found to be major determinants of health! I also noticed that the recognized importance of a new class of nutrients was limited by the available technology for detection and the increased understanding of human biochemistry. The final indication of the need to re-examine my assumptions on supplementation was the growing number of high-profile supplement intervention failures.

On the one hand, virtually every study shows an inverse correlation between whole foods and most chronic degenerative disease. Cardiovascular illness is a good example in which, for each increase in daily servings of fruits or vegetables consumed, we see about a 4% drop in cardiovascular disease.[1] But what happens when we assert that a single nutrient is responsible for a specific health benefit, then synthesize it (or a close analog) and use the nutrient to treat or prevent a specific disease? The high-profile vitamin E failure studies we discussed in volume 4, issue 1, demonstrate the limitations of this approach. Why did high-dose synthetic vitamin E *not* work the way we expected in cardiovascular disease and actually seemed to increase some forms of the illness? Can it be explained away as a poor meta-analysis, or is the problem really that natural gamma tocopherol—the primary form in human diets—is more important in human health than synthetic alpha tocopherol, which displaces the gamma tocopherol at high dosages? And these are only 2 of the 8 tocopherol stereoisomers. There is the same problem with synthetic beta-carotene in smokers increasing lung-cancer risk. Could it be due to the synthetic beta-carotene displacing other, possibly more-important, carotenoids like lycopene and lutein?

It is not that nutrition is unimportant or that nutritional therapy doesn't work. There are hundreds of studies documenting the efficacy of nutritional therapy. In Table 1, I've prepared a list of the primary reasons why I think nutritional therapy works clinically. The problem, it seems to me, is primarily generated when we try to use isolated synthetic nutrients alone vs natural forms added to a diet of whole foods to try and address the diverse nutrition problems listed in Table 1. I've listed these problems in Table 2. Then, to be fair, I've listed possible advantages to synthetic nutrients in Table 3.

I have not been able to find research that directly addresses the health benefits of isolated synthetic nutrients compared to natural nutrients and/or whole foods. There are a few studies that show the more a food is extracted to a single nutrient, the less clinically effective it is.[2,3]

TABLE 1
WHY SUPPLEMENTAL NUTRIENTS ARE CLINICALLY EFFECTIVE

1. Recent changes in diet have caused a greater intake of foods with lower nutrient densities (eg, more processed and junk foods and less whole foods)
2. All conventionally grown foods have a lower nutrient density than they did in the past
3. When these conventional foods are commercially processed, many of the remaining nutrients are damaged or removed
4. Seasonal and regional variations in food quality provide inconsistent amounts of nutrients (eg, one Washington apple provides differing amounts of vitamin C from season to season and potentially a different amount than that provided by an apple grown in Virginia)
5 People are varying their food choices less, thus basically eating the same nutrient content over and over
6. Recommended daily intakes (RDIs) are suspect
7. There are substantial genomic variations in individual needs
8. Many people have difficulty digesting and absorbing nutrients
9. Enzyme activity, beneficial to nutrient absorption, can be induced by high concentrations of cofactors (typically vitamins and minerals)
10. Toxins (endogenous and exogenous) increase the need for nutrients
11. High nutrient dosages induce direct chemical actions that can be beneficial to health

TABLE 2
POSSIBLE PROBLEMS WITH ISOLATED SYNTHETIC NUTRIENTS

1. May be a different chemical than the natural form (as seen with synthetic vitamin D)
2. May have a different optical structure than the natural form (as seen with synthetic vitamin E)
3. May be only one of several isomers (as seen with synthetic vitamin E)
4. May only be one member of a group of analogs (such as the carotenoids)
5. Contaminants may be introduced through synthesis (as was seen in the Japanese tryptophan fermentation and filtration process in 1989)
6. High levels of one nutrient in a group often inhibit absorption of other group members (as seen in high dosages of alpha tocopherol displacing gamma tocopherols)
7. High levels of one type of nutrient can inhibit absorption of another (as seen with excess calcium intake inhibiting iron and zinc absorption)
8. High levels of a single nutrient can increase or mask the need for other nutrients (as seen in EFAs increasing the need for vitamin E; or as seen with folic acid, which can mask a vitamin B_{12} deficiency)
9. High levels of one nutrient may displace similar nutrients from cell membranes, enzyme systems, etc. (as seen with beta-carotene and lycopene)
10. Nutrients are typically parts of chains, not isolated (eg, antioxidant chains involving vitamins C and E, glutathione and lipoic acid)
11. Genomic proenzyme variations may require different nutrient isomers for activation
12. Many nutrients require other nutrients to be activated (such as pyridoxine requiring vitamin B2 to be converted to the active pydridoxal-5'-phosphate).
13. New nutrients continue to be discovered

TABLE 3
POSSIBLE ADVANTAGES OF SYNTHETIC NUTRIENTS

1. Usually cheaper than natural
2. Available at higher dosages
3. May be more easily absorbed, especially in those with digestive problems
4. Can be provided in activated form (eg, the B vitamin niacin is now available in a coenzyme form known as NADH, and there is an activated form of vitamin D that gets around a person's bodily inability to activate it)

I want to be clear: I am not against high-dose, single, synthetic nutrients—often that is the only option due to cost and dosage requirements, especially when using a nutrient pharmacologically. A good example is high-dose (1,200 mg) CoQ_{10} in the treatment of Parkinson's disease. The success of such an intervention is simply not possible without synthetics.[4] But synthetics alone are not the answer.

For now, this is my bottom line:

1. Encourage our patients to eat a whole-foods. diet (see my latest book with Michael Murray, ND, *Encyclopedia of Healing Foods*).
2. Use nutrients in forms as close as possible to nature, in modest dosages, and in synergistic patterns.
3. Use high-dose synthetics primarily where there is a specific biochemical need.

What are your thoughts? I will address these topics more fully in future editorials.

IN THIS ISSUE

In this issue we begin a new column that, depending on reader feedback (you!), we hope to have regularly appear. For some time, I've wanted to engage the associate editors more frequently in the journal. While they will continue to contribute commentaries, we are now asking them to comment on timely topics. In this issue we are addressing the new US Department of Agriculture (USDA) food pyramid and its weakness and strengths. John Neustadt, ND, wrote an assessment that is followed by cogent comments from our associate editors. Interestingly, after the first draft was written and commented on by the editors,

the USDA serendipitously updated the food pyramid and addressed several of our concerns!

Jeff Bland, PhD, continues his commentary series on deficiencies of the current drug-research paradigm by honoring two intellectual pioneers, Karl Landsteiner, MD, and John L. Jacobs, MD, showing how their thinking helped to evolve our integrative medicine model. Marc Micossi, MD, provides the second part of his series on academia and integrative medicine.

I am very excited by the article on multiple sclerosis by Lynne Shinto, ND, Shannon Sinsheimer (ND candidate), and Dennis Bourdette, MD. Their comprehensive article is extremely sophisticated and an excellent example of the insight and thinking we need to develop algorithms that will provide the best care for our patients. It is interesting to note that this level of quality is the result of a dedicated clinician working on a research fellowship in an integrative medicine research center, convening a panel of experts, and studying the topic for several years. This leads to our interview this month of Drs Shinto and Bourdette—integrative medicine researchers and collaborators. I find it extremely encouraging when conventional and natural medicine professionals work collaboratively to research integrative medicine protocols.

Rick Liva, ND, RPh, continues his series on product quality. I was reminded again of the critical importance of this issue when, at a summit on botanical medicine quality, one of the presenters noted that he found the price of supposedly identical herbal products differing by a factor of 10. You don't always get what you pay for, but you never get what you don't pay for.

The CME this issue is an excellent article, "Inflammation, Pain, and Chronic Disease: An Integrative Approach to Treatment and Prevention" by Tanya Edwards, MD, MEd. I especially like her look at inflammation in the context of specific physiological systems.

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