

## Answering Your Supplement Questions

Today I'd like to answer multiple questions sent to me regarding last week's issue, in which I discussed the supplements that Mr. Mauldin and I are taking. By way of explanation, I didn't include links to the actual products I discussed for the simple reason that I don't want to give the impression that we're recommending these products for financial reasons.

I think that most people know it's possible today for vendors to track where links come from. Some organizations give the linkers a cut of their revenues. Amazon.com does this through its affiliate program, but we're not doing that.

Personally, it always sort of irritates me when organizations appear to be hawking supplements because it makes me question their objectivity; so I didn't include links. I've been convinced to do otherwise, however, in the explanations below. Let me clarify that we have no financial arrangement with anyone regarding these supplements. I write about them, and take them, based solely on the emerging science. Before you take anything yourself, you should always review the latest literature and speak with your physician.

My interest is driven not just by a desire to be as healthy as possible, by the way; I'm also convinced that breakthroughs in biotech analytical tools are making it possible to find rather simple compounds that will have large impacts on health and demographics. Since demographic change is having an enormous impact on our economy and politics, we should be interested in anything with the potential to significantly increase healthspans and alter the makeup of the population.

Since we're talking about supplements, I should start with the most misunderstood: vitamin D. Everybody takes some. What has changed recently, however, is the consensus regarding optimal dosages. In fact, you can't really say how much vitamin D you should take. It's your 25-hydroxyvitamin D blood level that really matters. Different individuals will need very different doses of oral vitamin D to accomplish the target range recommended by the top researchers in this field, which is 40-60 ng/mL.

I realize, by the way, that there are still some people in government science organizations that disagree with me. If you think about virtually any area of nutrition in which government has given guidelines over the past 50 years, there is a near 100 percent record of getting it wrong. Rather than go over the new research again, let me direct you to the University of California project dedicated to increasing understanding about D. ~~It's GrassrootsHealth, which you can access at this link.~~

The thing I really like about this organization is that they offer a test for D levels, which is inexpensive compared to the cost of the average lab test. A superior solution is to find a doctor, like mine, who keeps up with the literature and prescribes a full blood workup regularly. I'm about two weeks late for my blood work now, by the way, but I've been overwhelmed of late.

If you monitor the flood of new studies being published about vitamin D, it's hard not to come to the conclusion that a program of societal supplementation would extend average [healthspans](#) enough to solve most of our healthcare budget problems. This assumes, of course, that people continued working and investing through the years of added health. If, however, they decided to use the extra years collecting retirement

benefits, it would exacerbate the already enormous problem of unfunded entitlements for the aged, which is the main driver behind the debt crisis.

Whenever anybody asks me about supplements, my standard answer is to take vitamin D3 before you worry about anything else. Dr. Michael Holick, who pioneered the new research on vitamin D, suggests that about 4,000 units a day will get most but not all healthy people up to about 40 ng/mL. My blood levels are typically closer to 60 ng/mL, but I live in South Florida and spend a little time in the sun most days.

If you live farther north, however, the sun may not provide much help for much of the year. UVB is missing for most of the day in northern latitudes but is required for D synthesis. Sunshine has benefits other than vitamin synthesis, though. A Scottish study showed that people with greater but not extreme exposure to sunshine had statistically significantly lower blood pressure even when there was no ultraviolet B (UVB) present. This is apparently due to increased production of nitric oxide.

When I got my D levels up where they should be about seven or eight years ago, the impact on my health was immediate and palpable. You can get ~~D3 from Amazon.com here~~, but I take whatever brand my nutritional biologist wife happens to pick up at Walmart. I don't worry about brands and have taken many. I know my serum blood levels are where I want them to be, so all the major brands seem to have worked.

Last week, I concentrated on nicotinamide adenine dinucleotide plus (NAD+) precursors, based on the huge amount of research coming out now about this emerging area of science. Nicotinamide riboside (NR) is getting the most attention. ~~Not only has NR been endorsed recently by several famous scientists~~, the first human studies showed that a single dose raises NAD+ levels.

ChromaDex is the only supplier of nicotinamide riboside, a natural substance found in milk, as it owns the usage and manufacturing patents. It is ~~brand-named Niagen~~, but ChromaDex does not sell the product directly. ~~It's available through Amazon.com~~ and elsewhere. John and I take the High Performance Nutrition brand in the black and blue bottle.

Incidentally, the ChromaDex scientific advisory board is chaired by Nobel laureate Roger Kornberg, a Professor at Stanford Medical School. His Nobel prize in Chemistry in 2006 was for research on the molecular basis of eukaryotic transcription, which my son and I discuss around the dinner table occasionally. When Kornberg accepted the role as chair of the SAB, he specifically cited his interest in NR due to his father's research.

Kornberg's father was also a Nobel prize winner. A professor of biochemistry at Stanford, the late Arthur Kornberg won the prize for physiology or medicine in 1959 and pioneered nicotinamide riboside research while at the NIH.

"Given my father's noteworthy early research of nicotinamide riboside," the younger Kornberg said, "I have been following ChromaDex's progress on developing its Niagen nicotinamide riboside as well as the enormous amount of published research that speaks to the health benefits of NR."

~~The MIT recipe referenced here includes another ChromaDex product, pterostilbene~~, which occurs naturally in blueberry skin. John and I have been taking both of these molecules for several years now. It's available under the trade-name pTeroPure from several sources, ~~including Amazon.com~~. Though others sell pterostilbene, I don't trust other brands that don't use the ChromaDex product.

Another NAD+ precursor that we've both taken for several years is oxaloacetate. As is the case with NR, there is only one supplier which owns usage and manufacturing patents on the heat-stabilized version currently being used by universities researching efficacy in the treatment of neurodegenerative diseases. The company, of course, makes no medical claims as that would bring various government agencies down on its head like granite slabs dropped from helicopters. Free speech? Regardless, it's trade-named benaGene, which you can also get through Amazon.com, but ~~we get it from the manufacturer here.~~

Oxaloacetate is a naturally occurring molecule that plays a critical role in ~~the citric acid cycle~~ and other cellular functions. It increases NAD+ through an entirely different mechanism of action than NR's, so we take them both. It may not be necessary but it will be years before definitive information is generated.

We also take ~~acetyl-L-carnitine~~ because it has been shown in animal studies to work synergistically with oxaloacetate. My wife and doctor have both recommended L-carnitine for a while, but it was ~~this study showing complete restoration of long-term potentiation (LPT) in rats with cerebral ischemia, or stroke~~, that made me start taking it assiduously.

~~Long-term potentiation (LPT)~~ refers to the ability of brain synapses to increase signal transmission based on repeated activity. In other words, the study shows that oxaloacetate and L-carnitine completely restored the ability to learn in rats suffering from induced stroke. This seems like a very good sign to me, since LPT tends to decrease with age in humans. Given the option, I'd like to preserve the ability to learn as long as possible. Maybe, someday, I'll even learn how to spell "rhythm" without a spell checker and remember my in-laws' names.

Anecdotally, a lot of people who use either NR or oxaloacetate report a lifting of mental "fogginess." Dave Asprey, better known as the Bulletproof Executive, sells a coffee with oxaloacetate for that purpose. I don't know, by the way, if his product is cost-effective. I haven't looked that closely at his materials. Coffee on its own, by the way, is incredibly healthful for most people unless they let it interfere with sleep. I'll spend one paragraph on coffee before returning to acetyl-L-carnitine and oxaloacetate.

I've gone into the literature on the subject of coffee and caffeine innumerable times but it's solid science. In previous articles, I've linked to ~~this special issue of the Journal of Alzheimer's Disease that categorized coffee as "disease-modifying" for AD~~. Editor Dr. Mark Smith, one of the world's leading Alzheimer's researchers before his accidental death a few years ago, was so enthusiastic about coffee as therapy that he made the issue free to download. In terms of cost-effectiveness, coffee has got to rank alongside vitamin D in efficacy.

Returning to the subject of acetyl-L-carnitine, this naturally occurring substance breaks down in the blood to transport fatty acids into the mitochondria for conversion to adenosine triphosphate (ATP), which is the only form of energy our bodies can utilize. Acetyl-L-carnitine seems to be particularly important for those who exercise strenuously. It's certainly possible that the same repair of long-term potentiation observed in rats will take place in humans. Anyway, acetyl-L-carnitine is generally considered beneficial on its own, as is oxaloacetate, so there doesn't seem to be much downside to supplementation with both while the upside is potentially dramatic.

Another supplement related to ATP energy production that we take is [ubiquinol](#), a somewhat new and reduced (as opposed to oxidized) form of coenzyme Q10 (CoQ10) that appears to be more active. Ubiquinol is a critical part of the [electron transport chain](#), transferring electrons in the process of synthesizing ATP. It's ~~also available through Amazon.com~~, as is [acetyl-L-carnitine](#), though my wife buys them both at Walmart, I think.

Then, of course, John and I are both using up the last of our anatabine citrate, which is no longer commercially available. I assume, however, that someone is hunting for another NF kappa B moderator. There's an awful lot of unstudied alkaloids out there, and some very smart people know about the unprecedented data generated in the animal and human anatabine trials. Rock Creek Pharmaceuticals is miles ahead on the drug development path as they have permission to begin human trials for arthritis in the UK, but someone else may go after the supplement market.

Hopefully, this answers all the questions I received. This isn't a complete list of the supplements that John and I take, but I think it covers the most important and least known. Let me reiterate once more that we have no financial arrangements with the manufacturers of any of these products.

My hope is you find the above discussion of supplements and the emerging science behind them compelling, and can begin your own research with the data I've provided.

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