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Written by Ann Gerhardt, MD

Fad Supplement: Nitric Oxide Pills

by Ann Gerhardt August 2017

Bottom Line at the Top: Save your money to buy healthy vegetables and protein foods rather than "nitric oxide" supplements which don't contain nitric oxide anyway. Nonetheless, understanding the role of nitric oxide is interesting and important.

You can't buy nitric oxide pills because it's a gas. That doesn't keep pill pushers from labeling their product as nitric oxide (NO), even though what they're selling are ingredients that your body MAY turn into NO. They don't tell you that there is no guarantee that your body will do so.

Ads tell you that their product improves strength and power with weight training and enhances the body's production of nitric oxide, a natural blood-flow enhancer good for a healthy heart, blood pressure and circulation. The labels must say that their claims have not been evaluated by the FDA and that their product is not intended to diagnose, treat, cure or prevent any disease. But that doesn't keep them from scaring the unwary consumer with "signs of NO deficiency," listed as fatigue, unhealthy blood pressure and "No signs at all," meaning anyone. They confirm your need for their product with NO test strips, which measure salivary nitrate, not NO.

The only accurate statement in these ads relates to the fact that NO signals blood vessels to relax and dilate, promoting healthy blood pressure and cardiac function. Arginine, one of the common pill ingredients, might improve muscle building, but by way of a non-NO mechanism.

The main ingredient of most NO products is arginine, an amino acid that we normally get from protein foods. Other products, often made from beets, contain nitrate found naturally in vegetables.

The body has enzymes that turn arginine into NO, but that doesn't happen willy-nilly. If it did, our blood pressure would bottom out and we would pass out from lack of blood to the brain. NO generation is regulated and doesn't automatically surge with an arginine influx from a pill, even though, as a gas, it doesn't last more than a few seconds in blood.

Vegetable nitrate follows a different path to NO. Bacteria in the mouth reduce beet or spinach nitrate to nitrite, which is swallowed. Stomach acid may convert nitrite to NO, or it may be absorbed into the body and flushed out in urine or turned back into nitrate. The salivary glands take up nitrate from blood and concentrate it in saliva, so it can be swallowed and go through the whole process again. Nitrates naturally abundant in water follow a similar fate.

NO actually has an interesting history. Joseph Priestly discovered it in 1774, 2 years after discovering nitr**ous** oxide, or laughing gas. While nitrous oxide went on to intoxicate people at laughing gas parties and later to be used as an anesthetic, NO languished in obscurity.

In 1846, Italian chemist Ascanio Sobrero synthesized nitroglycerin and realized that it was explosive. Why he decided that tasting his explosive compound might be a good idea has been lost to history, but in doing so, he discovered that it causes a blow-your-head-apart type of headache. Scientists attributed the headache to dilated blood vessels. Since angina pectoris, the chest pain often preceding a heart attack, is caused by the heart's arteries not delivering enough blood, nitroglycerin was used for its treatment. It opens the heart's

blood vessels, allowing blood and oxygen to reach heart muscle and alleviate pain.

More than 200 years after Priestly's discovery, scientists finally elucidated how nitroglycerin works and NO's role in the body. They proved that nitroglycerin and other nitrates dilate blood vessels only after their conversion to NO, which is responsible for regulating arteries' relaxation or constriction. They found that cells in blood vessel walls make NO. They identified nitric oxide synthase (NOS) as the enzyme in the cells that generates NO from arginine. NO's role in controlling vascular tone and contributing to heart muscle function led to the journal *Science* naming it the "Molecule of the Year" in 1992. The scientists who figured it out received the Nobel Prize in Physiology or Medicine in 1998.

Since then we've learned much more. Nitroglycerin not only relaxes the walls of blood vessels, but also relaxes heart muscle. It relaxes the main airway into the lungs and inhaled NO dilates the lung's blood vessels in people with lung disease. It relaxes the muscles and sphincters of the gut. Nitroglycerin relaxes just about any spasm except that of skeletal muscles, which are the ones attached to bones. NO also plays a role in energy metabolism, the immune system and brain health. It contributes to memory, vision, pain perception, sense of smell and nerve function throughout the body. NO regulates how prone blood is to clot. Even erectile dysfunction drugs are related to NO: They work by maintaining NO-induced blood vessel swelling in the penis.

Unfortunately, the NO story is not entirely glorious. Too much of a good thing might be bad. Unconstrained blood vessel relaxation markedly drops blood pressure below the level necessary to keep the brain and organs alive. This is called shock, and happens in severe infections in which bacterial toxins stimulate too much NO production. When immune cells in the brain make too much NO, it can be toxic and cause convulsions. NO made by immune cells helps to knock out infectious organisms and tumor cells, but it also turns off white blood cell activation that should be fighting infection.

NO might also be oxidized to 'reactive oxygen species' (ROS), which are toxic. Inflammatory conditions, such as rheumatoid arthritis and colitis, and even mild inflammation, common in obesity and heart disease, favor ROS formation. Diarrhea, fever and infection accelerate NO's oxidation to nitrate.

NOS in cells of blood vessels, heart and brain putters along, constantly making NO in greater or lesser amounts to maintain health. This NOS is highly regulated and in normal people makes just the right amount of NO to maintain health. Other NOS, particularly that in immune cells, turns on and off, kicking into action when needed in response to infection, stress and inflammation. NOS regulation is often abnormal in people with diabetes, inflammatory conditions, high blood pressure, atherosclerosis, high cholesterol and some nutritional deficiencies. They tend to make less NO and are resistant to its beneficial effects.

Because of normal NOS regulation, there is no guarantee that arginine from food or a supplement will be converted to NO. The body just might decide to do something else with it, such as use it to build protein, convert it to creatine in muscle or break it down into urea to be flushed away in urine. Similarly, dietary nitrate may or may not be converted to NO, alternatively ending up in urine or saliva.

Experiments with arginine or beet juice supplements have been rather underwhelming. Normal folks don't derive any benefit with respect to lowered blood pressure or boosted immune function. Beet juice downed by young athletes in a Penn State study did not enhance blood flow to exercising muscles in spite of relaxed vessels at rest.

Supplement effects in people with diabetes, high blood pressure, high cholesterol and heart disease is more complicated. Taking arginine supplements or drinking large amounts of beet juice does relax their blood vessels, but studies haven't shown a survival benefit. In heart attack patients NO helps to grow blood vessels around the clogged ones, so supplements (or a better diet) may be helpful, but

this hasn't been proven. Short-term arginine supplementation relaxes leg arteries in people with poor circulation, but the effect is lost over the long-term. Beet juice may make diabetics' heart muscle less stiff but often without an improvement in blood pressure.

Do we need arginine supplements to make adequate NO? No. The "internet" tells us that the daily arginine requirement is about 4-6 grams, but that is malarky as long as we eat enough protein. Arginine is one of the amino acids that the body can make from other amino acids. Assuming normal intestinal, kidney and liver function, we just need to eat a healthy amount of protein to ingest or synthesize sufficient arginine. Good food sources of arginine are protein foods – meat, fish, poultry, dairy, legumes, corn, nuts, egg and whole grains.

There is no dietary requirement for food nitrates, but everyone should be eating multiple vegetable servings daily. Green vegetables, beets, carrots, cabbage and radishes are good nitrate sources. The Dietary Advice to Stop Hypertension (DASH) diet requires nine vegetable and fruit servings daily. We've credited DASH's high potassium and bioflavonoid content with lowering blood pressure, but perhaps its nitrate content helps too.

Will taking arginine or beet supplements hurt you? People whose kidneys don't work well should not be loading up on extra amino acids like arginine. Those with drug-induced or hereditary methemoglobinemia should avoid high nitrate foods, since they can precipitate a crisis. People with kidney stones should avoid high nitrate vegetables which are also high in oxalate.

So, what to do? Eat a varied diet with adequate protein and plenty of vegetables. If you like beets and spinach, eat them. Avoid infections. Most of all prevent or treat the conditions that cause defective NO regulation, by maintaining an ideal weight and doing regular, moderate exercise.