

Nitric Oxide and Neuropathy

The term Neuropathy refers to damage to the peripheral nerves which causes malfunction and that results in weakness, burning, prickling and pain in the extremities. The two most common causes of neuropathy are diabetes and trauma.

The effects of aging on hormones and Nitric Oxide production

Diabetic Peripheral Neuropathy (DPN), in particular, is a common complication of diabetes. 70% of diabetics develop DPN within 5 years and almost all will develop DPN after 5 years.

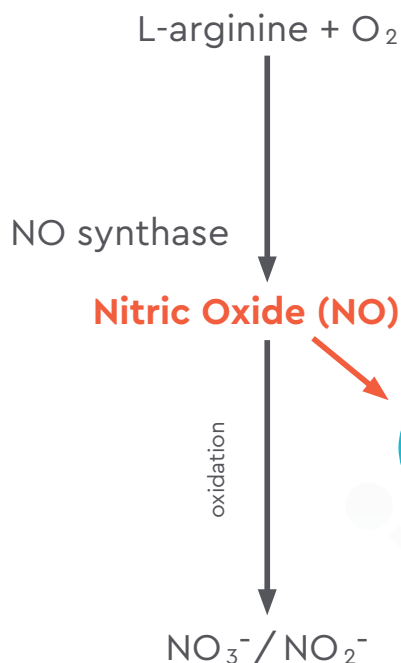
Nitric oxide (NO) is implicated in the etiology of neuropathy and neuropathy linked complications in at least 2 ways.

- 1) Impaired blood flow
- 2) NO is a neurotransmitter in some autonomic fibers

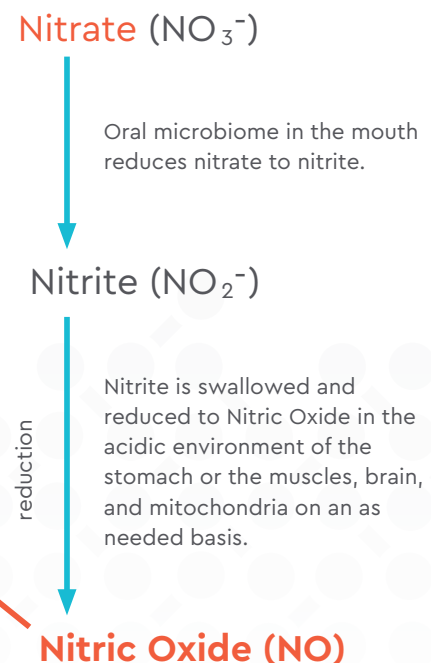
There are 2 different pathways our body has to produce NO:

- 1) Nitric Oxide Synthase (NOS) enzyme system that produces NO from L- arginine.
- 2) Nitrate to nitrite to NO reduction pathway.


The L-Arginine Pathway



The Nitrate Pathway



Biological effects



The L-arginine Pathway is severely impaired by the onset of diabetes in a way that the Nitrate Pathway is not. Here are some of the issues that affect the NOS enzyme pathway's effectiveness:

- The NOS in Pathway 1 is a pH dependent enzyme, which is more active in slightly alkaline conditions and suppressed in acidic conditions. Diabetes will decrease the pH to a more acidic state thus decreasing NOS activity.
- Adequate oxygen is also required for optimal NOS functioning but the circulation that brings oxygen to the cells is fundamentally impaired in diabetics.
- In diabetics, there is an increased production of asymmetric dimethyl arginine (ADMA), which is an inhibitor of NOS function.
- NO binds tightly with HbA1C. With increasing HbA1C levels, more and more NO is bound tightly and not released to support healthy vasodilation important in circulation.
- Oxidative stress is a rampant side-effect of diabetes. This oxidative stress further decreases the functionality of the NOS enzyme system and can diminish available NO, which the body uses in counteracting its affects.

Nitrate supplementation will bypass the NOS enzyme system and support production of much needed NO for diabetics. By the age of 40, our NO production through the NOS enzyme system functions around 50%. Nitrates will bypass the NOS enzyme system as well as helping to recouple NOS, thus enabling improved function. Nitrates are able to scavenge free radicals and improve oxidative stress which is rampant in any chronic condition such as diabetes and neuropathy.

Importance of Nitric Oxide for diabetics:

- NO increases vasodilation and increases delivery of the essential oxygen, nutrients and glucose to the cells.
- Poor circulation and the lack of oxygen, nutrients and glucose can adversely affect the nerves ability to produce ATP (adenosine triphosphate). ATP is the energy molecule driving physiological processes in the body. It is the source of energy that keeps everything functioning.
- Normalization of the NO production can directly impact nerve function by improving the nerve membrane permeability to potassium ions.
- Increasing NO production can mitigate pain because NO mediates the analgesic effect of opioids (endogenous and exogenous) by increasing cGMP (Cyclic guanosine monophosphate).
- Low levels of NO directly contribute to neuropathy.



Berkeley Life is based on a simple premise:

Provide a plant-based equivalency of nitrate that would be found in clinically supported beet juice and leafy greens, allowing the body to convert nitrate — at the appropriate time and at the appropriate place within the body — to NO.

Berkeley Test Strip is a patented salivary Nitric Oxide test strip.

The strips answer the question for individuals:

1. Is my diet or supplementation effective at enhancing my NO status?
2. Is my body converting nitrate to NO as well as ensuring sustained levels throughout the day?

References:

1. Li, Huige, and Ulrich Förstermann. "Uncoupling of endothelial NO synthase in atherosclerosis and vascular disease." *Current Opinion in Pharmacology* 13.2 (2013): 161-167.
2. Cameron N.E., Cotter M.A. (2000) Nitric Oxide, Peripheral Neuropathy, and Diabetes. In: Kalsner S. (eds) Nitric Oxide and Free Radicals in Peripheral Neurotransmission. Nitric Oxide in Biology and Medicine, vol 2. Birkhäuser, Boston, MA.
3. Burke Ph.D., Thomas, (2009, August 7th). Nitric Oxide Series, Part One: Discovery of NO, Nobel Prize, Relevance in Vasodilation. <http://www.diabetesincontrol.com/nitric-oxide-and-its-role-in-health-and-diabetes/>