

# Be All the Man You Can Be

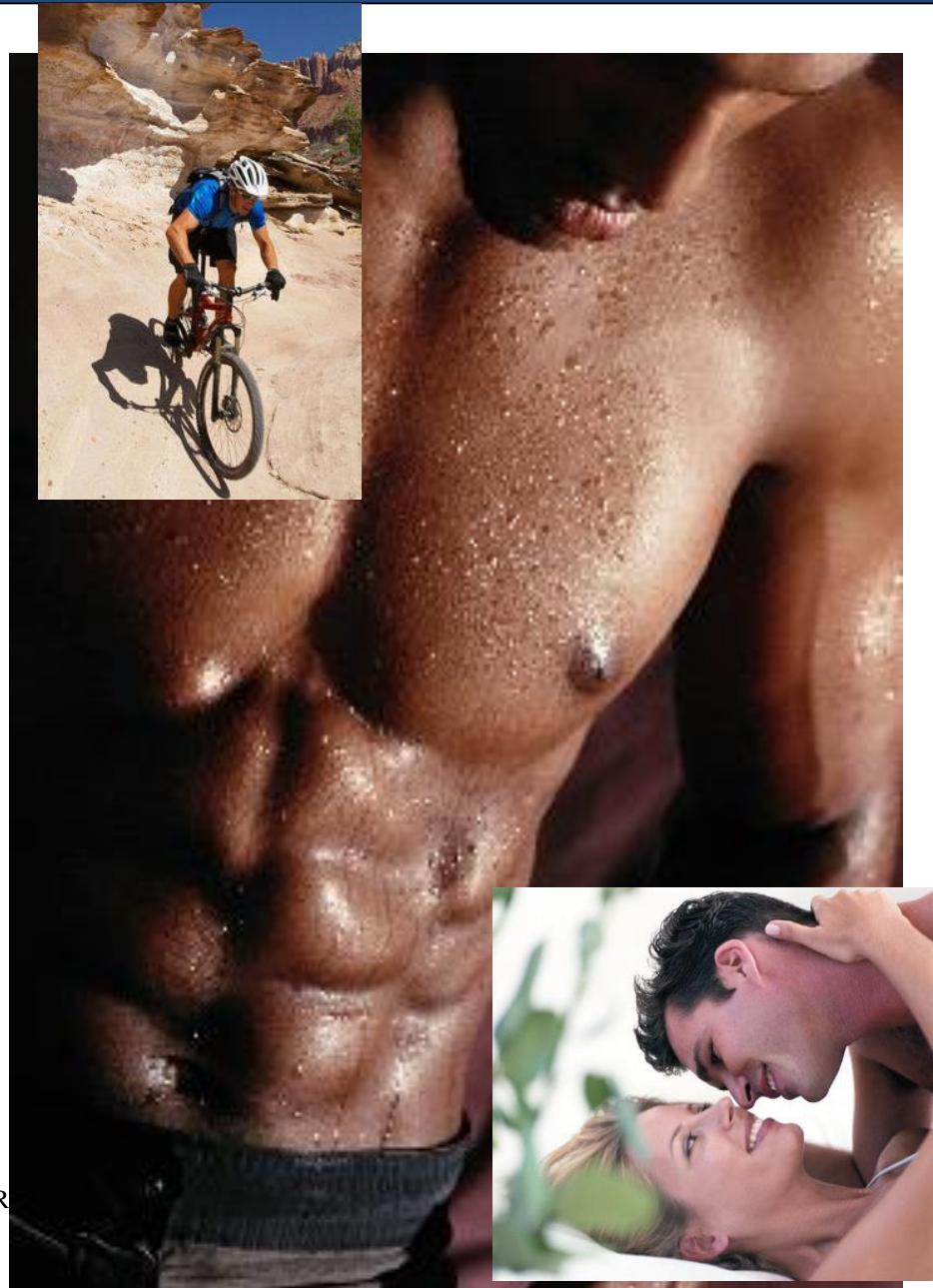
*Discover the Secret of Optimum Cellular  
Health and Maximum Male Vitality*

**Your Cellular Health  
Handbook and  
Definitive Guide to:**

**Nitric Oxide Assessment  
and Supplementation**

**Lasting Solutions for  
ED and Cardiovascular  
Disease**

**NO and Improved  
Athletic Performance**



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# The Power of Cellular Health

How would you like to experience true VITALITY?

And I don't just mean sexual vitality. I mean the boundless energy to do ALL the things you want to do. I mean the unlimited ability to act spontaneously, stay focused, motivated, and alert; to enjoy peak physical performance and quicker, more complete recovery.

While these benefits sound strikingly similar to those that come from achieving and maintaining a high, balanced level of testosterone, there's another piece to the male performance puzzle that most men—and their doctors—miss.

**That missing piece is optimum CELLULAR HEALTH.**

73 TRILLION CELLS  
YOU ARE ONLY AS HEALTHY AS YOUR CELLS!



Deep inside your body, there are trillions of different cells carrying out more than 200 specialized functions. And in order for the systems of your body to work efficiently, these cells must be able to communicate with each other well. If your cellular health is poor, your physical (and mental) systems will decline regardless of how high your testosterone level is.

Testosterone is an important hormone, but hormones are simply messengers that tell your cells what to do. The beneficial effects you experience from testosterone are dependent upon the health of your cells. And the health of your cells is dependent upon how well their basic, biological needs are being met.

**1. Your cells need support.** Because they are constantly dividing and growing, your cells need a steady supply of raw materials to work with. Just as you could not build a strong house without adequate amounts of wood, concrete, and nails, you cannot build a healthy cell without adequate amounts of essential amino and fatty acids, which must be derived from cholesterol and saturated fats. That's right—the RIGHT kinds of fat are actually GOOD for you! Without sufficient amounts of these critical building blocks, your cells will be weak, function poorly, and make mistakes when attempting to communicate with each other.

**2. Your cells need to be nourished** with a wide spectrum of nutrients including vitamins and minerals. If these are deficient, the functional capacity of each individual cell will suffer. Just as you cannot fuel a car with water, you cannot fuel your cell with nutritionally-deficient foods.

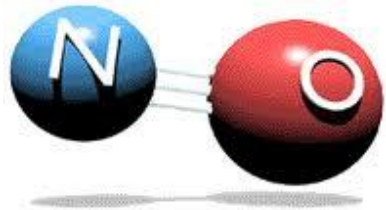
**3. Your cells need to eliminate waste.** The human body is approximately 70% water, which is used as a transport mechanism by each and every cell. Drinking an adequate amount of pure, clean water is essential as it will allow your cells to rid themselves of metabolic waste.

**4. Your cells need to be protected.** In order to protect themselves from the damaging effects of free radical activity (the inevitable end result of any metabolic process), your cells need antioxidants. If left unchecked and unaddressed, excessive free radical activity will result in reduced cellular energy and pre-mature aging.

**5. Your cells need to be kept clean.** You wouldn't walk into your house wearing a pair of shoes coated in mud or toxic waste, but many of us don't think twice about exposing our bodies (and our cells) to toxins. While we all know that chemicals, metals, radiation, and medications can be harmful to the body, it's easy to forget that the toxic load we carry can include excessive physical and mental stress; and a variety of commonly-ingested substances we mistakenly call food—artificial sweeteners, chemical additives, processed fats, hybridized grains, refined sugars, and genetically modified foods such as soy, corn, and canola.

**6. Your cells need to be properly fueled.** Even if everything else is in your physiological house is in order, your cells must have the necessary energy to carry out their tasks. Their most basic source of energy is oxygen. You can live without water for a week and without food for more than a month, but you cannot live without oxygen for more than 15 minutes.

**And this is where the big picture story of optimal cellular and maximum male health both begin**—with oxygen and a simple, yet relatively secret, gas molecule called Nitric



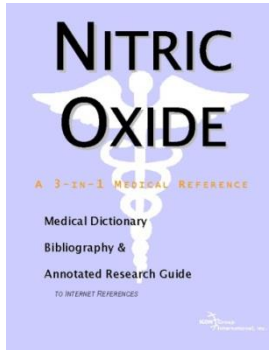
Oxide (NO). Nitric Oxide is the key player responsible for delivering oxygen-rich blood to every cell, tissue, and organ system in your body.

As you read on, you will discover how this male vitality secret can greatly increase your health and performance by directing more oxygen to every cell in your body.

**Just a few of the functional benefits of NO supplementation include:**

- Better circulation
- Improved lung capacity
- A stronger, more powerful heart
- More energy and greater endurance
- Improved mental capacity
- More youthful, on-demand sexual function.

# Nitric Oxide: The Miracle of Life



In the 1970's, medical researchers made a Nobel Prize winning discovery: the existence of a short-lived gas called Nitric Oxide (NO) that acts as a powerful, messenger molecule inside the body. Because NO diffuses rapidly across cellular membranes, it is involved in virtually all physiological (and pathological) processes in the body. Learn more about the 1998 Nobel Prize award [here](#).

The idea that a short-lived gas (50% of NO disappears less than a second after it's released) plays such a pivotal role in virtually every physiological function took the scientific community by surprise. And the realization that such a molecule is being produced within our bodies, acting as a cell to cell communication agent, has revolutionized scientific and medical reasoning.

Now, almost 15 years after the Nobel Prize award and more than 120,000 scientific papers later, we are finally beginning to appreciate the foundational role NO plays in both health and disease—and the critical importance of having enough of this vital compound in your body.

## The effects of Nitric Oxide are fleeting but powerful.

When created and released, this gas quickly and easily penetrates nearby membranes and cells, initiating its myriad signals. Most notably, it relaxes the smooth muscle lining of the blood vessels, promoting better blood flow (and therefore more oxygen) to the cells.

It also acts as powerful antioxidant by neutralizing the free radical superoxide and promoting the formation of glutathione, a critical antioxidant. It facilitates the transmission of messages between nerve cells contributing to improved memory and learning capacities, better sleep, and a more positive mood. It supports the immune system by helping the body fight off infections and the potential development of cancer cells.

And as bodybuilders have known for years, it contributes directly to glucose uptake, muscle velocity, power output, gene expression, and muscle growth.

**“There may be no disease process where this miracle molecule does not have a protective role”**

– Louis J. Ignarro, PhD, a 1998 Nobel Laureate

# The Famous Three

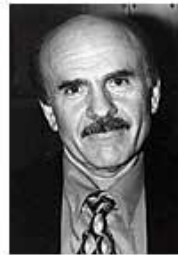
NO was first discovered by Dr. Robert Furchgott in 1980 as a substance produced by the cells lining our blood vessels, or endothelial cells, that allows our arteries to vasodilate (relax and open). He first described the substance as an “endothelium derived relaxing factor” or EDRF. Dr. Louis Ignarro later discovered that EDRF was actually a gas molecule—Nitric Oxide. Doing further research, Dr. Ferid Murad confirmed that the life-saving heart medication Nitroglycerin actually works through the release of NO.



The Nobel Prize  
in Physiology or  
Medicine 1998



Robert F.  
Furchgott



Louis J. Ignarro

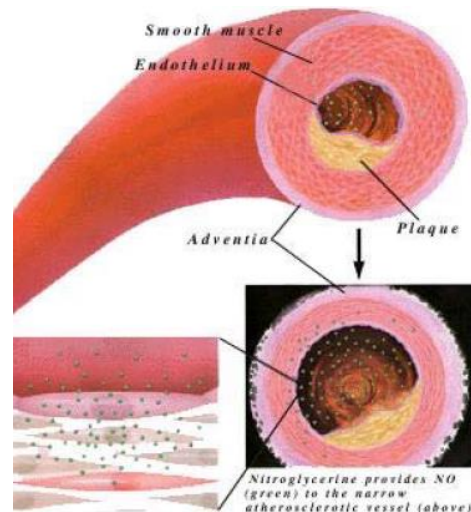


Ferid Murad

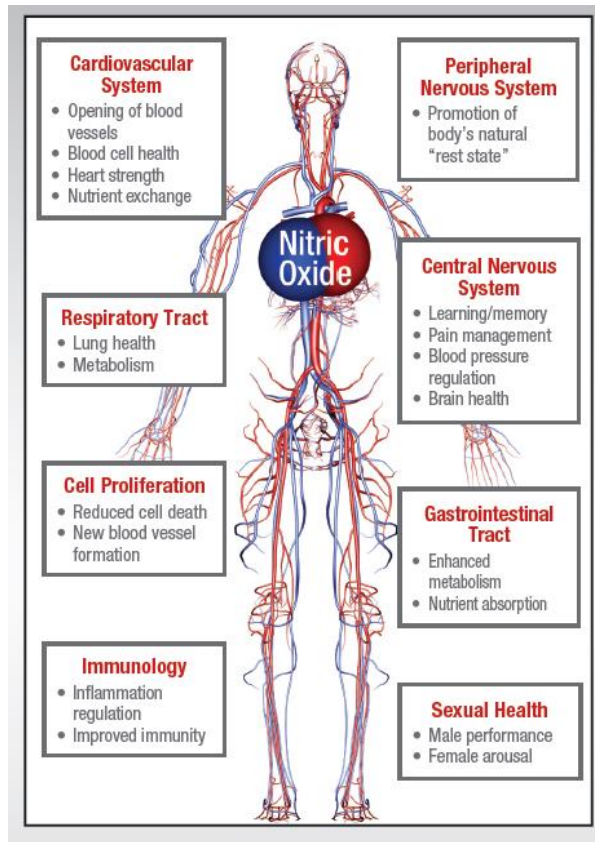
## Nitroglycerin relieves chest pain via Nitric Oxide

In atherosclerosis, plaques that form reduce blood flow in the arteries. This reduced blood flow decreases oxygen supply to the heart muscle causing chest pain. For more than a century, we have known that Nitroglycerine reduces this pain by dilating the vessels and increasing blood flow.

With the discovery of NO came the knowledge that Nitroglycerin acts as Nitric Oxide donor, causing the affected blood vessels to dilate in nanoseconds.



# Nitric Oxide: The Key to Unlocking Your Personal Health Potential



**Take control of your health and well-being. Assess and optimize your Nitric Oxide level!**

Nitric Oxide plays a vital role in the functional health of virtually every cell, tissue, and organ system in the human body. And because of this, diminished NO levels will lead to a wide variety of physical, mental, and sexual problems.

It's most powerful effects are on protecting and strengthening your heart and vascular system.

**To protect yourself from heart disease, you need more Nitric Oxide. NO will:**

- Reduce and prevent high blood pressure
- Keep your arteries young and flexible
- Prevent or reverse artery-clogging plaque
- Stop the formation of artery-clogging blood clots
- Reduce internal inflammation

**But the benefits of NO don't stop there. This life-enhancing substance will:**

- Improve penile erections and enhance both male and female sexual sensitivity
- Reduce the risk of diabetes and diabetic complications.
- Promote a healthy immune system as it attacks and kills unwanted bacteria
- Improve your digestion
- Limit the swelling and pain of arthritis
- Calm the inflammation of asthma
- Enhance wound healing
- Protect your bones from osteoporosis
- Allow for an easier adaption to low oxygen at high altitudes
- Limit skin damage from over exposure to the sun
- Promote deeper, more restful sleep
- Improve your mood and memory
- Act as a powerful antioxidant regenerator.

# Nitric Oxide: The Proven Performance Edge



Increased NO levels have been scientifically shown to enhance athletic performance and endurance—even among athletes who were already fit and healthy.

This makes sense given that Nitric Oxide contributes directly to blood flow, oxygen delivery, glucose uptake, muscle velocity, power output, and muscle growth; it's really only logical that increased NO levels will enhance an athlete's overall performance.

***Studies on foods rich in nitrates (especially red beets and kale), which enable NO production, have shown that Nitric Oxide can increase an athlete's endurance capacity by at least 16%. (Murphy M, et al. J Acad Nutr Diet. 2012;4:548-52)***

***Other studies have shown that the use of NO-enhancing supplements have reduced the oxygen cost of moderate-intensity exercise and extended athletes' time to exhaustion during high-intensity exercise. (Bailey SJ, et al. J Appl Physiol. 2010;109(5):1394-403)***

**Increases in Nitric Oxide also explain, at least in part, the benefits in performance seen by endurance athletes living and training in high altitudes.**

Your Nitric Oxide level will increase in low oxygen content locations in order to improve oxygen delivery to your cells. This natural, physiological response is the reason why Tibetans living at high altitudes have ten times the amount of NO in their blood compared to those living at sea level.

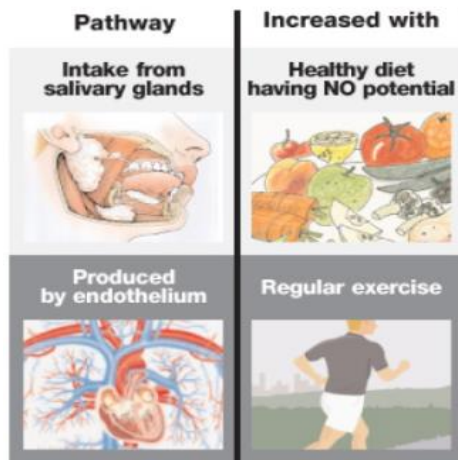




# Nitric Oxide: Production Pathways

Our bodies continuously produce NO from specific amino acids, oxygen, vitamins, various enzymes, and certain foods. Although Nitric Oxide is manufactured by many cells in the body, the greatest area of its production occurs in the single layer of cells lining your blood vessels (the endothelium) and from the conversion of the nitrates found in certain foods.

**There are two primary pathways the human body uses to produce NO.**



In the **classical eNOS pathway**, NO is produced from L-arginine (an amino acid) found in the healthy endothelium (the tissue that forms a single layer of cells lining various organs and cavities of the body) under the direction of an enzyme called endothelial Nitric Oxide Synthetase (eNOS).

Production of NO in the eNOS pathway declines with age, and when the endothelial lining becomes damaged due to cardiovascular disease. Moderate physical activity, regular exposure to sunlight (or vitamin D3 support), antioxidants, and an anti-inflammatory diet rich in omega 3 fats can be very powerful in protecting the endothelium and raising

NO production. In addition, in many men, supplementation with an L-Arginine Cocktail (described later) will also raise NO levels.

A second, more recently-discovered **nitrate-NO pathway** operates independently from eNOS. This production pathway relies on the health bacteria in your mouth to convert the naturally-present nitrates found in certain foods to Nitric Oxide. This pathway is now known to produce the majority of NO found in the body. The nitrate-NO pathway confirms the importance of eating foods rich in nitrates—dark green vegetables, red beets, berries, wine, and dark or raw chocolate.

Production of Nitric Oxide in the nitrate-NO pathway will decline for a number of reasons, including poor oral and stomach health. In addition to improving your oral and gastro-intestinal health, the consumption of vegetables rich in nitrates such as kale, chard, spinach, and arugula and in polyphenol-rich foods such as red beets, pomegranates, blueberries, grapes, and chocolate will help support this pathway. Supplementation with a natural, nitrate-rich NO lozenge can also greatly enhance the conversion of nitrates to NO.

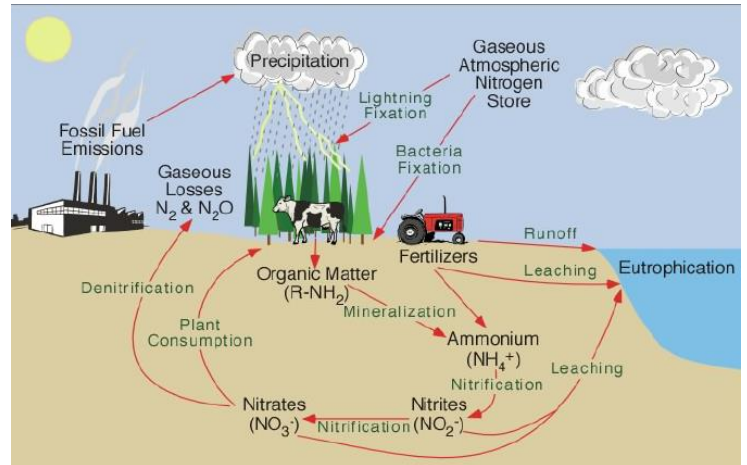
# The Nitrogen Cycles

Nitrogen is used in many ways by life on our planet. In order for the nitrogen cycle to work properly, both the Earth and its inhabitants convert nitrogen into many different organic forms that are then used and recycled on a continuous and repetitive basis.

## The Environmental Nitrogen Cycle

Our atmosphere consists of over 75% nitrogen gas (primarily N<sub>2</sub>). It is this gaseous nitrogen that serves as the precious resource all life on Earth depends upon.

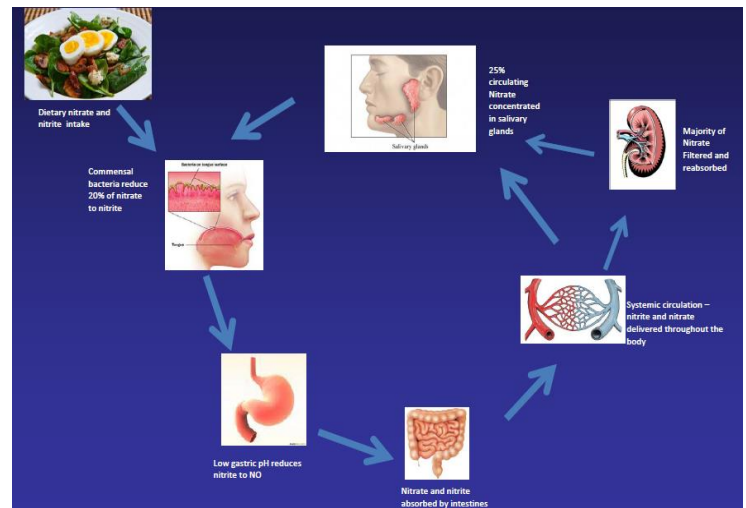
Through a multi-step process that involves precipitation, lightening, solid waste, and soil bacteria, nitrogen is naturally recycled into formats that plants can use and incorporate into their own, living matter. It is this form of nitrogen that fuels the NO production process.



## The Human Nitrogen Cycle

Through a multi-step process that involves healthy bacteria in your mouth, salivary glands, stomach acid, and gastrointestinal absorption, dietary nitrates from plants are first converted to nitrites, then to NO which directly supports all cellular health and function.

This short-lived gas (which is produced either from dietary nitrates or from L-arginine in the cell lining) is physiologically converted back to nitrate, which either re-enters the circulatory system or is excreted in the urine.



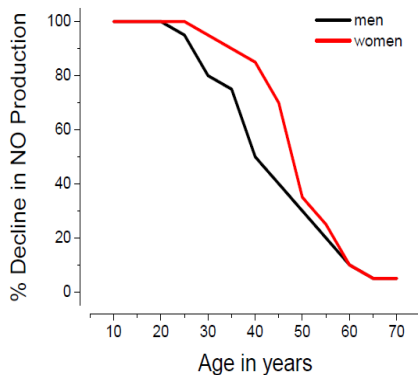
# Nitric Oxide Production: Age is the Enemy

Do you frequently feel fatigued? Find yourself falling asleep in the afternoon? Losing your car keys or your interest in sex? Do you want to have a stronger, more resilient immune system? Are you concerned about the health of your heart, blood pressure, or blood sugar?

**Then you are probably getting older—both chronologically and biologically.** And the older you are, the more difficult it becomes for your body to produce adequate amounts of NO.

An adequate amount of oxygen is an essential requirement for optimum physiological health; powered by Nitric Oxide, your arteries are responsible for transporting it. When you are young, your body produces large amounts of NO in the endothelial lining of your internal organs which keep your arteries supple and expandable (to accommodate variable blood flow requirements).

While NO levels decline for a variety of reasons including endothelial damage, a lack of dietary nitrates, low stomach acid, imbalanced mouth bacteria, insufficient physical activity, and excessive physical and mental stress, the greatest threat to your NO level is your age. As your NO production begins to decline after the age of 40, your cardiovascular health and health risks exponentially increase.

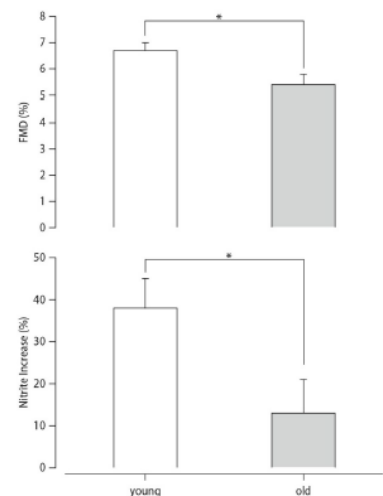


**The aging process interferes with the body's ability to make enough Nitric Oxide.**

By the age 40, your body will produce half the NO it did at the age of 20. By the time you reach 70, it will be capable of producing only 25% of the Nitric Oxide it needs. That means your NO level will be at its lowest right when you need it the most!

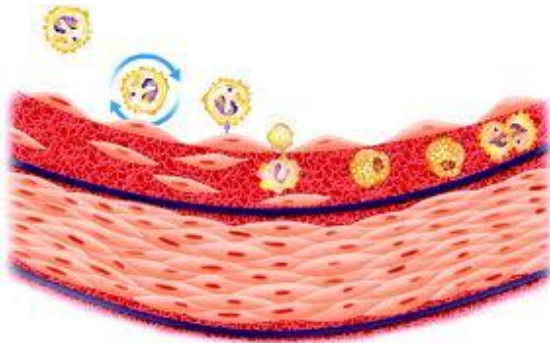
## Reduction in blood flow and nitrate levels in younger versus older athletes, after the same exercise stimulus.

The amount of nitrite found in your body following physical exercise is a reliable predictor of your overall fitness capacity. With age, the amount of NO your body can generate after exercise is reduced. This is why older athletes lose their responsiveness to training; they have to work harder in order to derive the same training-related benefits.



# Nitric Oxide and Cardiovascular Health

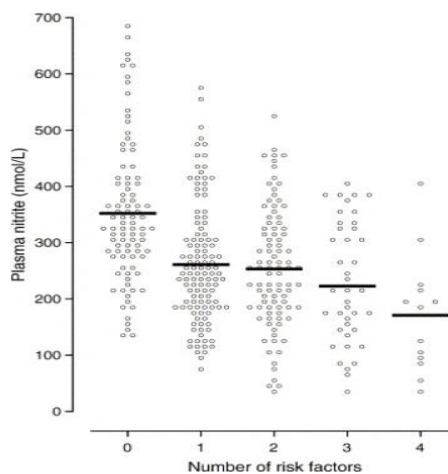
Over the past two decades, it has become evident that decreased levels of bioavailable, endothelial NO (produced from endothelial NO synthase or eNOS) play a large role in the development and progression of atherosclerosis. Medical science now recognizes that the dysfunctional eNOS pathway as one of the most important cellular imbalances and a powerful indicator of future cardiovascular disease and many other health disorders.



**Endothelial dysfunction is a disruption of the normal biochemical processes carried out by the endothelium—the cells that line the inner surface of the body’s internal organs including the heart, arteries, and veins.**

**Experimental and clinical studies provide evidence that endothelial dysfunction is linked to every major cardiovascular risk factor. It is now considered a reliable predictor of both atherosclerotic disease and its progression.** (Schachinger, Britten et al. 2000; Halcox, Schenke et al. 2002; Bugiardini, Manfrini et al. 2004; Lerman and Zeiher 2005)

**Loss of NO-related endothelial function is associated with a number of cardiovascular disorders including atherosclerosis, resulting from decreased NO production and/or utilization.** (Davignon and Ganz 2004)

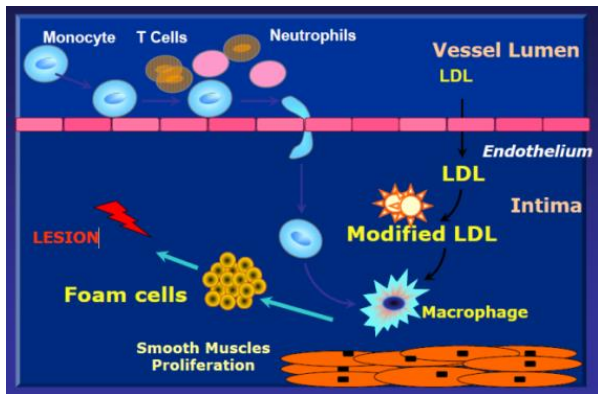


## **NO Concentrations and Endothelial dysfunction:**

The average plasma nitrate and subsequent NO response is directly related to conventional, vascular disease risk factors including high lipid levels, high blood pressure, and age.

**Optimizing your NO level will protect your endothelial lining and dramatically reduce your risk of cardiovascular disease.**

While there are many factors that contribute to the onset of cardiovascular disease, the health of your entire vascular system depends upon healthy endothelial function and an adequate NO supply. Nitric oxide deficiency will lead to reduced blood flow and tissue oxygenation and lead to increased inflammation and free radical activity which will injure the cells, damage the endothelium and further reduce Nitric Oxide production.



***Over time, the effects of internal inflammation (caused by stress and poor dietary and lifestyle choices) injure the inner, arterial walls. This damage is the underlying cause of atherosclerosis.***

***Despite what you might have read or been told, cholesterol is only an innocent bystander; it does not cause heart disease.***

**If your approach to cardiovascular health has been cholesterol-centered and does not address your endothelial health and Nitric Oxide status, you will lose the battle.**

Instead, you must adopt an anti-inflammatory diet—primarily, grass-fed meats, fresh vegetables, and HEALTHY FATS including those that come from wild fish, olive, coconut, avocado, and grass-fed dairy products. You must also reduce or eliminate your intake of most grains, processed sugars and fats; make more positive lifestyle and fitness choices; and supplement your diet with food-based micronutrients and antioxidants. Finally, you must optimize your NO, vitamin D3 and omega 3 fatty acid levels.

# Nitric Oxide and Sexual Health

**Erections are naturally triggered by the body's release of NO.**



When you are sexually stimulated, Nitric Oxide is produced in the penis to signal the blood vessels in the corpus cavernosum to dilate in order to accommodate an increase in blood flow. It is this increased blood flow that causes engorgement and a sustained erection. Without sufficient NO production, there is poor circulation which results in either no erection or a poor erection that cannot be sustained. The same applies to women. Without proper blood flow to the clitoris, women cannot have orgasms or experience enhanced sexual sensitivity.

**You need both testosterone and NO.**

As men and women age, their sexual performance and enjoyment often suffers. It is important to understand that it is only through the combination of testosterone and NO signaling working together that the natural vasodilation required for erections and sexual sensitivity will occur.

So if your eNOS and/or nitrate-NO pathways are impaired, even if you have adequate hormonal and dopamine triggers, you will not have a strong erectile response. On the other hand, you can still have a good erectile response, even if your testosterone levels are declined if your NO pathways are healthy.

**Note:** Your testosterone and dopamine levels (the brain chemical responsible for drive and passion) will be at the highest upon waking, which is what causes your morning erections. Both testosterone and dopamine influence the release of Nitric Oxide.

**New research shows that, for many men, erectile dysfunction (ED) is an early warning sign of cardiovascular disease (CVD), cancer, Alzheimers disease, diabetes, and other chronic illnesses.**



Over 50% of those who suffer a heart attack have no traditional risk factors for heart disease. Quite often, their first sign of heart disease is a heart attack!

If you are suffering from ED, be forewarned: Sexual dysfunction is linked to an NO insufficiency, which contributes to the onset of heart disease. In a 10-year study, men who had ED at the beginning of the study were 80 percent more likely to develop CVD by its end.

# The Age of Viagra

**ED drugs such as Viagra, Levitra, and Cialis capitalize on NO function to increase blood flow and enhance erections in men and sexual responsiveness in women.**

Interestingly, Viagra was initially designed to be a heart medication. But instead of having its strongest effect on the heart, researchers discovered that it improved blood flow more dramatically in other areas of the body.



Viagra and other ED drugs improve blood flow by binding to an enzyme called PDE-5 that is involved in the breakdown of NO in the body. By blocking this enzyme, NO is metabolized much less rapidly, causing its levels to accumulate more slowly—even when Nitric Oxide production is low do to an unhealthy endothelium.

As with any medication that functions by inhibiting an intricate natural function in the body, the PDE-5 inhibitors are ineffective for some and can create serious problems for others.

Let's look at why PDE-5 inhibitors are NOT your long-term solution to Erectile Dysfunction:

- 1. They are ineffective in many people whose NO levels are too low.**
- 2. Their effects diminish over time;** they become ineffective for over 50% of all users after three years.
- 3. There are a number of side effects associated with their use.** These can range from minor (light-headed, headaches, and back pain) to troublesome (chest pain, vision, and hearing problems) to dangerous (increased risk of heart attacks and blood clots). Too much NO is the main cause of these side effects! Excessive Nitric Oxide is converted into a free radical called peroxynitrate, which causes circulatory and other systemic damage.
- 4. They are a temporary band-aid** that does nothing to improve NO production and/or blood flow.



***A better solution to sexual dysfunction is the restoration of healthful Nitric Oxide production. By taking the proper steps, your endothelial cells can naturally and consistently produce more NO!***

# Are your NO Levels Low?

## Take inventory of your current health status.

If you answer “yes” to two or more of the questions below, your NO levels are probably less than optimal.

Are you over the age of 40?

Do you eat very few green vegetables and/or red beets?

Do you lead a sedentary lifestyle?

Do you suffer from erectile dysfunction?

Are your testosterone levels low?

Do you have circulation problems and/or fluid retention issues?

Do you suffer from heart disease or high-blood pressure?

Are you hypoglycemic, diabetic, or pre-diabetic?

Do you suffer from memory lapses and/or mild cognition disorders?

Do you suffer from internal inflammation, abnormally high CRP, or an autoimmune dysfunction?

Do you suffer from frequent infections, viral, fungal, or bacterial?

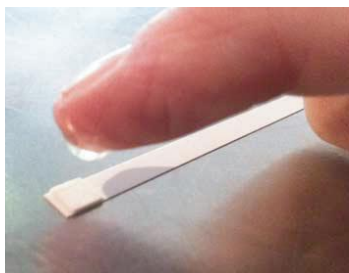
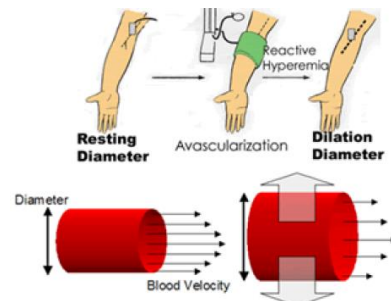
Do you suffer from hair loss?

Have you been diagnosed with asthma, bronchitis, or a lung disease?

Do you have any kidney problems?

## Find out for sure: Assess your Nitric Oxide level!

Until very recently, there was no way to easily assess your NO level. Testing required costly blood work or a complicated procedure called Flow Mediated Dilation, which indirectly predicted NO levels by measuring the rate of blood flow in the arm after the application of pressure.



Fortunately, recent advances in laboratory testing technology now make it possible for you to easily measure and regularly monitor your NO levels in the comfort and convenience of your own home with nothing but a simple test strip and a drop of saliva.



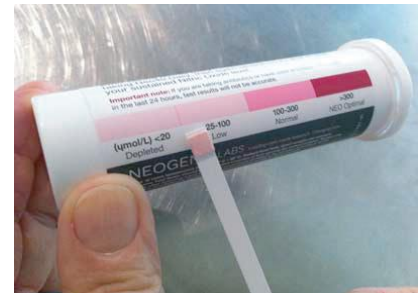
# Assessing your Salivary Nitric Oxide

Despite its deceptive simplicity, a salivary assessment is a powerful tool that will allow you to measure and monitor how your NO level change with your diet, lifestyle, training, stress, and the use of supportive supplements. By assessing your NO level the first thing in the morning, after consuming nitrate-rich foods and/or taking supportive supplements, Nitric Oxide assessment strips can be used to quantify your body's ability to produce and maintain an optimal amount of NO.

**Important:** While it is helpful to maintain an awareness of any improvements in your NO-related symptoms, the salivary test strips should be the objective foundation for determining improvements in your NO level.

## How do the NO strips work?

The reagent on the strip will react with the nitrates present in your saliva and change color based on its amount. This change is a very good indicator of your body's Nitric Oxide supply, derived from both the eNOS pathway (that which is created by the endothelium by NOS) and nitrate-NO pathway (that which comes from your dietary intake of nitrate rich foods).



## The NO assessment strips are easy to use.

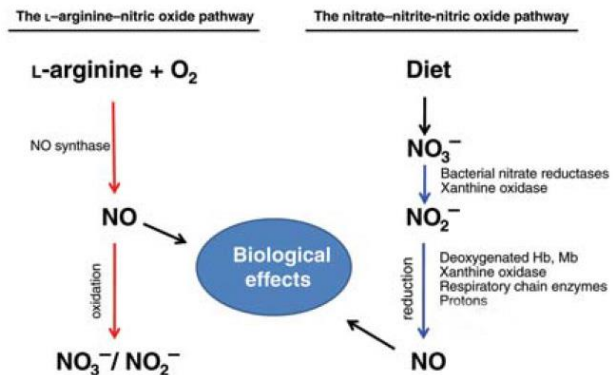
Simply place a drop of saliva on the end of the strip and compare the resulting color to the chart on the package. If the strip turns dark pink, your NO levels are strong. If the test strip only turns a pale pink or is entirely without color, you need more Nitric Oxide.

You should initially assess your NO level at least twice a week (the first thing in the morning) so that you will be able to note how fluctuations or definitive changes in your activity, lifestyle, and/or diet affect your results. Once a consistently-optimal Nitric Oxide level is achieved, you can assess your saliva every one to two weeks.

# Problems with your Nitric Oxide Pathways

As you have learned, a low NO assessment reading indicates a deficiency in your Nitric Oxide level. But it does not tell you whether the problem is caused by a faulty eNOS pathway problem, a nitrate-NO problem, or both.

Fortunately, by using some simple deduction and an assessment, you can determine where your problem lies.



**eNOS problems:** If you answered “yes” to a number of the questions on the NO health status (especially if you have cardiovascular, diabetes, high blood pressure, erectile or cognitive problems and/or are over 40 year old), you can be certain that—at a minimum—your eNOS pathway is not very productive.

**Nitrate-NO problems:** If you are under the age of 40 and have NO-related or GI issues, you almost certainly have a nitrate-NO problem.

**You can use these two simple challenges to assess your nitrate-NO pathway.**

If your nitrate-NO pathway is strong and healthy, you should see a significant darkening of color on the NO test strip. If it does not increase, then you most likely have a nitrate-NO pathway disturbance. On the next page, we will discuss the most common causes of this problem.

- 1:** Assess your NO level and then eat a meal of roasted beets and a kale salad with pomegranates. Wait 90 minutes, then re-assess your NO level. Do not drink for at least 30 minutes prior to performing this challenge.
- 2:** Wake up in the morning and assess your NO level. Then drink 16 ounces of beet juice. Re-assess your NO level again after waiting 90 minutes. Do not drink for at least 30 minutes prior to this challenge.

# Nitrate-NO Pathway Problems

As you now know, the nitrate-NO pathway produces the largest amount of NO found in your body. As such, a healthy nitrate-NO pathway is critical for optimal cellular health and functional, physical performance.

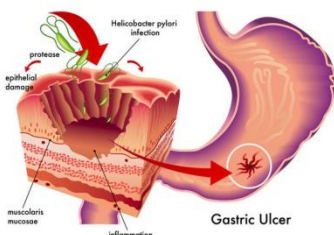
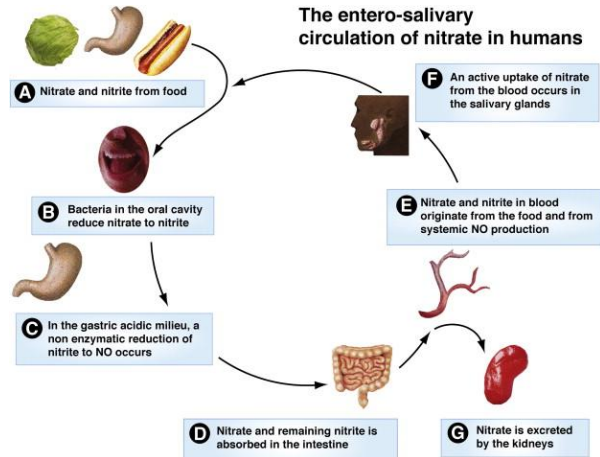
Even if you are satisfied with your current levels of health and fitness, and your endothelium is producing adequate amounts of Nitric Oxide, a low NO test strip result confirms that the nitrate-NOS pathway has been compromised due to an oral bacteria deficiency and/or a gastrointestinal imbalance.

This low reading should be taken as an early warning sign of an ineffective nitrate-NO pathway that will eventually result in inadequate NO reserves and subsequent health problems.

**Note:** This problem is particularly common among endurance athletes.

## There are seven main causes of nitrate-NO pathway defect:

1. Your diet is lacking in the nitrate-rich foods that fuel the nitrate-NO pathway.
2. Your levels of beneficial, oral bacteria are too low.
3. Your saliva levels are deficient.
4. Your stomach acid levels are low, or you have a bacterial infection of H-Pylori.
5. Your gut lining is unhealthy and interfering with your body's ability to absorb nitrates.
6. You suffer from high levels of oxidative stress and/or free radical activity.
7. Your body is struggling to recycle its eNOS-produced Nitric Oxide back into the saliva.



**Doctors have known for a decade that people with periodontal diseases, oral bacterial imbalances, and H-pylori infections carry a much greater risk of cardiovascular disease. With the new knowledge of the nitrate-NO pathway, we now understand the seemingly-unrelated connection.**

# Nitric Oxide Restoration Strategies

**Your male health and vitality require an adequate supply of NO.** By using a combination of strategies to optimize both the eNOS and nitrate-NO pathways, you can enjoy a youthful level of NO and all the benefits it provides—greater energy, improved athletic performance, increased endurance, a more enjoyable sex life, and a drastically-reduced risk of heart disease.

**Implement and adhere to the necessary lifestyle and dietary modifications.** In short, you must identify and eliminate any nitrate-NO roadblocks, regularly eat foods that are rich in NO-producing nitrates and nitrites (red beets and leafy greens), and adopt both a lifestyle and supplement regimen that will reduce the endothelial-damaging effects of internal inflammation.

You must also take steps to eliminate the consumption of inflammatory foods such as processed seed and vegetable oils, sugars and grains (especially wheat); adopt an NO-enhancing exercise regimen; and make lifestyle choices that preserve and promote the production of Nitric Oxide. That means getting enough sleep, minimizing your exposure to physical and emotional stress, and supporting your cells with supplemental amounts of micronutrients, antioxidants, vitamin D3 and omega 3 fatty acids.

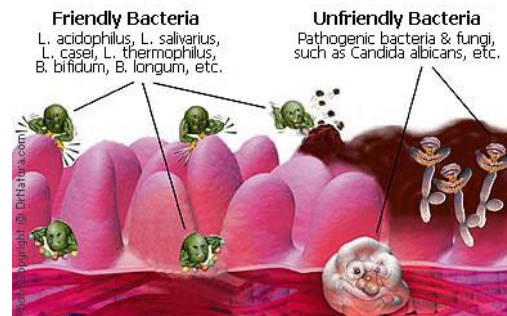
**Have patience.** While you should begin to notice immediate benefits in health and performance from the short-term elevation of your NO levels, the more long-term gains associated with the complete, systemic restoration of NO (that takes place throughout your body in the endothelial lining) can often take six to twelve months to achieve.

A more detailed overview of both the **eNOS** and **Nitrate-NO** pathways have been outlined below. It is important to note that BOTH are necessary and work **IN CONJUNCTION** to promote optimum cellular health and maximum male vitality.

## Nitrate-NO Restorative Strategies

### Restore your oral and gastrointestinal health.

Low NO readings, especially among those who are under the age of 40, are an indicator of poor oral and gastrointestinal health. In addition to taking basic steps toward improving your overall cellular health, there are some specific strategies that you can implement right away to restore your oral and gastrointestinal health—and improve the productivity of your nitrate-NO pathway:



- Avoid the use of antiseptic mouthwashes and antibiotics.
- Use good oral hygiene with regular water flossing; clean your teeth with baking soda.
- Use the ancient art of [oil pulling](#) to eliminate unhealthy oral bacteria.
- Stay hydrated to optimize your saliva levels. Drink enough filtered water daily so that your urine is light yellow. Find alternatives to medications that cause reduced saliva flow.
- Use a highly-effective probiotic supplement such as **ProbioMax DF** (which offers four, healthy bacterial strains including the extensively-studied HN019 of Bifidobacterium Lactis) or **Sustenex** (which contains the highly-effective Ganeden Bc30 strain).
- Eat fermented foods such as sauerkraut, kimchi, kefir, and kombucha every day.
- Eliminate the use of antacids and proton-pump inhibiting medications such as Pepcid. Instead, use natural formulas that contain digestive enzymes and Betaine HCL. Commit to completely eliminating processed sugars, grains, and dairy from your diet for at least 30 days.
- If problems persist, assess your GI health for the bacteria H-pylori, gluten sensitivity, and/or malabsorption due to a leaky gut. These assessments are available through specialty labs. They include **Metamatrix's** GI Effects Panel and **BioHealth Lab's** Intestinal Barrier Function and Secretory IgA/Gliadin IgA Screens.

**Eat five to seven servings of nitrate-rich vegetables daily.** Foods rich in dietary nitrate are converted into NO in your body. Make sure to chew your food well and consume liquids slowly in order to keep them in your mouth where healthy, naturally-occurring bacteria will activate the NO production process.



The foods highest in nitrate include beet roots and leafy greens such as kale, arugula, chard, and spinach. Others are parsley, Chinese cabbage, leeks, celery, radishes, and turnips. In order to increase your intake of these nitrate-rich vegetables, you can make vegetable juices, add steamed or roasted beets to a blended protein drink, or simply add a powdered fruit and vegetable concentrate to your daily supplement routine.

**Eat foods that are rich in polyphenols.** Foods rich in polyphenols and flavonoids activate the endothelial cells in your arteries to produce more NO. These foods include red wine, dark chocolate, berries, cherries, and pomegranates.

**Eat fresh foods that are rich in vitamins C and E.** Foods rich in naturally-occurring vitamin C and E can help preserve and maintain your NO level. These include citrus fruits, broccoli, blueberries, sunflower seeds, almonds, tomatoes, and green, leafy vegetables.

## e-NOS Restorative Strategies

**Get 20-30 minutes of some form of exercise daily.** Exercise boosts Nitric Oxide levels by increasing NO synthase. A high-intensity, low-duration workout is an easy way to get NO flowing throughout your blood stream. Many high-intensity interval training programs require just 10-20 minutes of activity per day.

But keep in mind that exercising regularly at a moderate level of intensity for more than 45 minutes will reduce your body's NO level. In longer, sustained endurance activities, Nitric Oxide becomes depleted because it is used to dilate the arteries and support tissue oxygenation.

**Get adequate rest and recovery.** Don't overlook the powerful, restorative effects of getting eight hours of sleep at night for healthy NO production and maintenance.



Take time out for yourself each day. Listen to calming music, watch a comedy show, read a book, go for a walk, play. If you're spiritual, dedicate a portion of each day to practicing your faith. Just five to ten minutes of silence a day can make you significantly more stress resistant.

**Optimize your omega 3 to omega 6 ratio.** Eat plenty of omega 3 essential fatty acids (found in wild, cold-water fish; grass-fed meats; macadamia nuts, pumpkin, hemp, and chia seeds) on a regular basis. Strictly avoid the inflammatory omega-6 fats found in soy, corn, safflower, canola, and sesame oils; and the artificial trans-fats found in margarines and other processed foods.

**Get at least 20 minutes of exposure to sunlight three to four times weekly.**

Sunlight also triggers production in the skin of vitamin D3, a key nutrient in the body which in turn stimulates eNOS and reduces cellular inflammation. It is important to assess your vitamin D3 level and supplement your diet accordingly in order to achieve a serum level of 45 to 60ng/dl. Because full-body sun exposure is often impractical due to time limitations and weather conditions, the use of a high-quality vitamin D3 supplement will be a necessity for at least a portion of the year.

**Optimize your testosterone level.** An adequate supply of testosterone will help to support your body's NO production capacity. If you have not already read the **Be All the Man You Can Be** Testosterone program, put it at the top of your "to do" list. This e-book will provide you with additional information on how to improve your cellular and hormonal health—both of which are necessary for strong NO production and utilization.

### Be All the Man You Can Be

*Regain your Youthful Sexual, Mental and Physical Vigor and Vitality*

Your Testosterone Health Handbook  
Hormone Primer  
Evaluate your Hormones  
Quick Start Guide  
Step by Step Program  
Resource Section



# The Hidden Power of Beets

Numerous research studies have proven that beet roots (red beets) are one of the best natural sources of NO support. In fact, the blood-red elixir of the beet was the hottest thing during the 2012 London Summer Olympics among athletes seeking an all-natural and perfectly-legal performance boost.

## Red beets improve blood flow to the brain.

Wake Forest University scientists not only proved that beets boosted NO, they documented significant and positive changes in the brains of their juice-drinking subjects.



After drinking a serving of beet juice in the morning, the researchers took blood samples and MRIs of their study participants' brains. They compared these results to those from a control group that did not drink any beet juice. The blood samples taken from beet juice drinkers were significantly higher in Nitric Oxide. And the MRI results showed that the brains of juice drinkers were being supplied with a healthy, generous supply of blood. Moreover, the specific areas of the brain most affected were those associated with poor (age-related) cognition.

## Red beets improve athletic performance in fit men and women.

In a double-blind, placebo-controlled study, 11 fit men and women were evaluated during two 5K treadmill time trials. 75 minutes prior to one trial, the subjects ingested 200 grams of roasted beet root with 500mg of nitrate. Prior to another trial, the subjects ingested cranberry relish as a placebo.

The investigators noted the mean running velocity during the 5K run to be faster after beet root consumption as compared to the placebo. During the last 1.1 miles of the timed trial, running velocity was five percent faster in the beet root trial with no change in velocity seen during the earlier portion of the trial. Subject feedback at 1.8K into the beet root trial also indicated a lower perceived rate of exertion as compared to the placebo.

## Red beets improve adaptation to altitude.

If you're planning a trip to a high altitude location, then it would be wise to consider upping your Nitric Oxide level. Studies prove that the consumption of red beets can ease the transition from low to high altitudes, preventing respiratory problems by improving lung function.

# Supplements that Boost Cell Health and NO

The three most important supplements for a NO-supportive regimen are an organic whole-food concentrate, an absorbable form of vitamin D3 and a high-quality, omega 3 fish oil.

**A powdered, whole-food concentrate blend.** If you're like most people, you simply may not be able to eat enough nitrate and antioxidant-rich foods. Supplementing your diet with 10 to 20 grams of a low-temperature-processed, concentrated, whole-food powder rich in greens, beet roots, and berries can be a simple, yet POWERFUL way to improve your cellular health. Most importantly, the use of a micronutrient and antioxidant-rich powder will supply your body with the nitrates it needs for stronger NO production and utilization.



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**A highly-absorbable form of vitamin D3:** Achieving and maintaining an optimal level of vitamin D3 is one of the most important things you can do to heighten your overall health and well-being. Vitamin D3 is a powerful activator of cellular health that controls more than 3,000 different physiological processes. Because full-body sun exposure is often impractical due to time limitations and weather conditions, the use of a high-quality vitamin D3 supplement will be a necessity for at least a portion of the year.

## VITAMIN D LEVELS 25 HYDROXY D

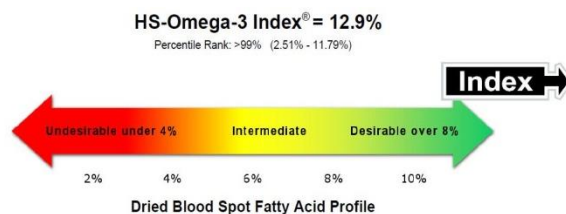
Deficient	Optimal	Treat Cancer and Heart Disease	Excess
< 50 ng/ml	50-70 ng/ml	70-100 ng/ml	> 100 ng/ml

*To insure that your body is properly absorbing a vitamin D3 supplement, you must assess your blood level, which can now be done easily and accurately at home. Your vitamin D3 level should be between 50 and 60 ng/ml.*

**A pure, high-quality fish oil:** Essential fatty acids provide the cardiovascular system with a variety of proven benefits. Perhaps most notably, optimal and balanced levels of omega 3 fats will reduce inflammation, which can seriously damage the endothelial lining of your blood vessels inhibiting the production of Nitric Oxide.



The most recent research confirms that an optimal omega 3 level will directly promote NO production. Our in-house research confirms that most adults will need to supplement their diets with 2400 mg of EPA/DHA from a pure fish oil source daily in order to achieve an optimal omega 3 level.



*To insure that your body is properly absorbing your omega 3 fatty acid supplement formula, you must assess your blood levels, which can now be done easily and accurately at home. Your omega 3 to omega 6 index should be between 10 and 13%.*



# Supplements that Directly Boost NO

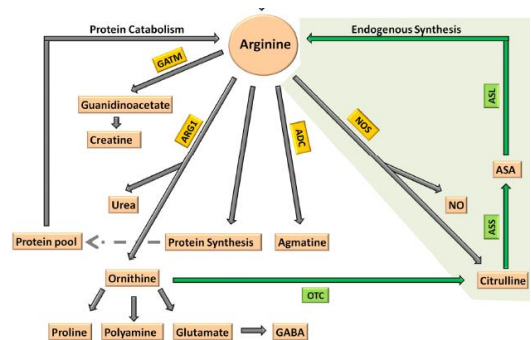
By following the NO restoration strategies and taking the supplements described above, many men will be able to restore their NO to an optimal level over a three to nine month period. But if you are over the age of 40 or would like to speed up your restorative process, you should consider taking nutritional supplements that directly support NO production.

As we previously discussed, there are two NO pathways in the body. One utilizes the eNOS enzyme and the amino acid L-arginine to produce NO in the endothelial lining. While the nitrate-NO pathway creates NO in our mouth and stomach from nitrates found in certain foods. There are supplement solutions that can be used to support both the eNOS and nitrate-NO pathways.

## The eNOS Pathway

Most NO supplements address this pathway and feature the amino acid L-arginine as their primary, active ingredient. L-arginine feeds the metabolic pathway in the body controlled by eNOS to enhance the production of NO.

**But L-arginine is not the complete solution.** The problem is that while L-arginine can be very effective when used by young adults with healthy endothelial function, it's less effective for aging men—and for those whose endothelial lining is already compromised. This is because the problems with the eNOS pathway are not due to insufficient amounts of L-arginine, but faulty L-arginine conversion.



Eight different pathways are needed in the endothelium to efficiently convert L-arginine to NO. If any one of these is defective, conversion rates will suffer. In addition, because of these conversion deficits, the use of large amounts of L-arginine (over a few grams daily) can result in an excess of L-arginine that is NOT converted into Nitric Oxide, but into tissue-damaging free radicals.

**A better answer.** eNOS conversion issues can be solved by using an **Arginine Cocktail** which includes a special form of L-arginine called A-AKG, the amino acid L-citrulline, Pycnogenol (pine bark extract) and pomegranate powder. This will greatly enhance the effectiveness of L-arginine conversion in the NOS pathway, and eliminate any associated free radical risks.

# Your e-NOS Cocktail is Served!

**Directions:** Scoop out the desired amount of each ingredient and put them into a large glass.



Add at least 8 ounces of water and stir vigorously. As the ingredients begin to blend, add the pomegranate powder or juice to taste. For best results, your NO Cocktail should consist of about 12 ounces of liquid.

Drink the Cocktail twice daily, beginning at the lower end of the dosage range. To insure optimal absorption, take the Cocktail on an empty stomach and wait at least 30 minutes before eating. Take one dose upon waking and a second dose later in the afternoon or at some point prior to bed.

## Arginine alpha-ketoglutarate (A-AKG): 1 to 3 grams



While many men experience positive benefits from the use of the base form of L-arginine in this cocktail, you should consider the use of a more bio-available form called arginine alpha-ketoglutarate (A-AKG). A-AKG has been shown to be faster acting with more extended effects and timed release results.

## L-citrulline: 1 to 3 grams



Many men can increase their L-arginine levels by using its precursor, L-citrulline. L-citrulline is more easily converted and absorbed than L-arginine when taken orally. In addition, the body's ability to convert L-citrulline into NO actually increases with age. Lastly, L-citrulline doesn't cause nausea, diarrhea, or digestive difficulties.

## Pycnogenol (or pine bark extract): 100 to 200 milligrams



Pycnogenol is a polyphenol derived from pine bark. It acts as a powerful antioxidant protecting the endothelial cells. It directly promotes the production of NO and literally helps to recycle L-arginine in the body. This last effect is critical as it helps to keep L-arginine working actively in the blood stream.

## Organic pomegranate powder (optional): 1 to 2 teaspoons



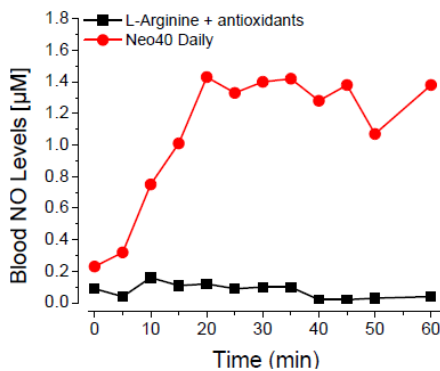
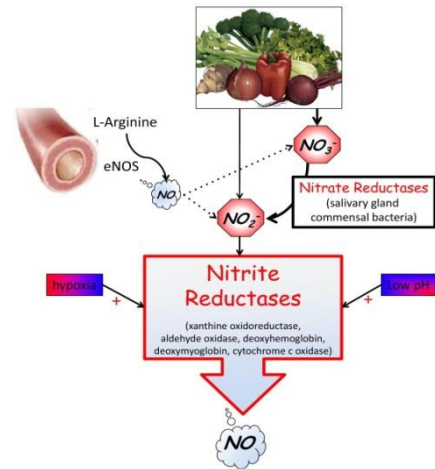
Like Pycnogenol, pomegranate is a polyphenol that protects the endothelial cells. Pomegranates are also an excellent source of nitrates that can be used in the nitrate-NO pathway to support NO production. Pomegranate powder, mixed with a few drops of liquid stevia or a few ounces of pomegranate juice, will also improve the flavor and taste of your NO Cocktail.

# The Nitrate-NO Lozenge

While the **eNOS-Arginine Cocktail** can be effective for many men, those over the age of 40, those who have a likely eNOS conversion defect (as evidenced by an erectile, hormonal, cardiovascular or cognitive problem) or those who simply want a more convenient restoration strategy should consider the use of an NO lozenge.

Each great-tasting NO lozenge contains a rich source of beet concentrates that will dissolve slowly in your mouth where saliva and beneficial bacteria will initiate the production of Nitric Oxide. In fact, these lozenges have been shown to **improve the uptake of nitrates in the body by as much as 10 times!**

The lozenge formula can also improve your body's ability to create NO from nitrates in vegetables. This means that once your NO level becomes optimized, you will be able to reduce your dosage over time. So while some men may require up to two lozenges daily for the first few months, dosing can be reduced over time to just one lozenge a few times weekly. In addition to being a fast and convenient source of NO support, the benefits received from the lozenges are not dependent upon age or endothelial health.

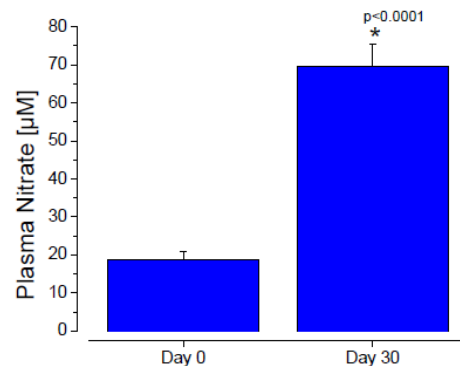


## NO lozenges are rapid-acting and very effective.

This graph compares the use of an NO lozenge to L-arginine supplementation. After just 60 minutes, there is a ten-fold increase in the amount of Nitric Oxide produced with the lozenge as compared to that from L-arginine.

**NO lozenges have been shown consistently effective at optimizing NO levels over a two to six month period.**

This graph shows the 30-day effect of the NO lozenge on plasma nitrate levels.



# Tracking Your Progress

**Use the NO test strips twice a week—first thing in the morning—to monitor your results.**

After six weeks of following your chosen NO supplement, your NO test strip should show some signs of improvement (significant darkening). If not, then increase your dose of either the NO troche or eNOS Cocktail by 50%.

If you have noticed some improvement (some darkening of the strip), maintain your new dose and continue to monitor your saliva NO for another six weeks, then re-evaluate. After 12 weeks, you should be seeing some obvious improvements in your NO test strip results.

**There is no magic solution.**

Regardless of quickly your test strip results begin to improve, the effects and benefits of a higher Nitric Oxide level will be greater when you also take steps to improve your body's basic, cellular health. If you have not done so already, adopt the previously-suggested lifestyle and dietary strategies. You should also be supplementing your diet with 2 grams of high-quality fish oil, 5000iu of vitamin D3, and at least 10 grams of a nitrate-rich, powdered food concentrate each and every day.

**Significant results can take 12 weeks or more.**

Be patient. The exact amount of time it will take your body to respond to the lifestyle, dietary and nutrient interventions you implement will depend on a number of factors including your age, endothelial health, and cellular nutrient status.

Even so you should be seeing some measurable and subjective signs of improvement by this time. If you have not seen visible progress after 12 weeks, you can consider combining the use of an NO troche with the eNOS Arginine Cocktail and make a more concerted effort to improve your dietary, lifestyle, and nutritional supplement strategies.

Please review the restorative strategies in this booklet as well as the **Be All the Man You Can Be Testosterone** program for additional information and details.

# Nitric Oxide Research

Since the Nobel Prize was awarded, there has been an explosion of research on Nitric Oxide and its effect on the myriad health problems associated with aging. To date, there have been more than a hundred thousand scientific studies published. The proven benefits of NO include the following:

## Improved Memory

Do you ever forget where you parked your car? Walk into a room and suddenly draw a blank as to why you're there? Forget someone's name right after you've met them? Or worse, run into an old friend and stammer as you try to remember his or her name? Well, here's some good news! Studies show that Nitric Oxide improves memory, slow response, and confused thinking in three ways:

1. It helps store memories as they are being created.
2. It helps retrieve memories at a later date.
3. It helps brain cells send and receive signals more quickly and efficiently.

Indeed, the brain-boosting effects of NO have been proven in before and after MRIs of the brain. [Researchers](#) at Wake Forest University studied volunteers over the age of 70, modifying their normal diets to include daily servings of beet juice and high-nitrate vegetables. The subjects were found to have increased blood flow to their brains, potentially protecting them against the harmful effects of dementia.

## Better Bone Health

In a study published in the *Journal of the American Medical Association*, it was shown that NO helps build strong bones. In the study, one group of women used a supplement to increase their NO levels. Another group took a placebo. At the end of the study, researchers compared before and after scans, which measured changes in bone density. They found that the women who boosted their NO increased their bone density significantly. In comparison, the women who took the placebo actually lost bone density in their hips.

## The Alleviation of Sleep Apnea

In Obstructive Sleep Apnea (OSA), you're aroused to semi-consciousness repeatedly during the night because sagging soft tissue at the back of the throat plugs your airway. Sleep Apnea afflicts an estimated 30 million Americans; many of them overweight men. And it dramatically increases the risk for heart disease and stroke. French researchers studied 62 people with OSA and found that many had reduced NO production and impaired endothelial function. They theorized that low NO might be the cause of the arterial disease so common in people with OSA.

## **More Restful Sleep**

Sleep quality declines with age. Studies show that more than 50 percent of all adults over the age of 60 having difficulty sleeping at least a few nights a week. Studies show that NO levels do not increase in the brain as we age thereby impairing the mechanism through which NO induces sleep.

## **Reduced Arthritic Pain**

In a study published by the *Clinical Journal of Pain*, researchers from the physical therapy program at the University of Colorado at Denver found that NO is a key factor in the reduction of arthritis pain. They hypothesized that NO is decreased in joints stressed by chronic, load-induced stress (such as knee arthritis in people who are overweight) and biochemical change-induced stress (such as the oxidative damage in bones caused by diets high in saturated fat and low in antioxidant-rich vegetables and fruits). Based on the fact that NO is decreased in arthritis, the researchers speculated that NO-based interventions may produce substantial pain relief by increasing circulation, decreasing nerve irritation, and decreasing inflammation in joints.

## **Healthier Skin**

“It has become clear that this extraordinary molecular messenger [NO] plays a vital role in the skin, orchestrating normal regulatory processes,” noted a team of French researchers in the medical journal *Nitric Oxide*. The researchers listed the many benefits NO provides to the skin including:

1. Its role strengthening and maintaining the “barrier function,” the all-important role of the skin in keeping out unwanted germs and toxins.
2. Its ability to protect the keratinocytes (external skin cells) from the damaging effects of the sun’s UV rays.

## **A Cure for Diabetes and Alzheimers?**

25 million North Americans suffer from Type 2 diabetes due to obesity and 57 million others have borderline diabetes. High blood sugar gradually destroys the circulatory system resulting in heart attack, stroke, kidney failure, blindness, and limb amputation. And it doubles the risk of Alzheimer’s disease. It’s believed that decreased amounts of NO may play a major role in the development of Type 2 diabetes. Low levels of NO result in insulin resistance, making it difficult for insulin to enter cells to maintain a normal blood sugar level. Italian researchers found that diabetes patients who also had kidney disease had NO levels 37 percent lower than those of healthy people.

**More technical information** on Nitric Oxide can be found [here](#) and [here](#).

## **NO REDUCES ISCHEMIC DAMAGE in Acute Stroke**

Research on hypertensive rats found that nitric oxide (NO) reduced ischemic damage during stroke resulting from blockage of the middle cerebral artery. The researchers concluded that NO may represent a new therapeutic strategy for reducing ischemic damage in acute stroke.

Zhang F, White JG, Iadecola C. Nitric Oxide Donors Increase Blood Flow and Reduce Brain Damage in Focal Ischemia: Evidence that Nitric Oxide is Beneficial in the Early Stages of Cerebral Ischemia. *Journal of Cerebral Blood Flow & Metabolism* 1994;14:217-226.

## **THE IMPORTANCE OF NITRIC OXIDE in Sleep Apnea**

Sleep apnea is associated with inadequate transport of nitric oxide (NO) to the lungs, resulting a lack of oxygen and the well-established cycle of frequent waking to 'kick start' breathing. NO also plays other roles in the thoracic musculature, underscoring the well-defined relationship between NO and sleep apnea.

Haight JB, Djupesland PG. Nitric oxide (NO) and obstructive sleep apnea (OSA). *Sleep Breath*. 2003;7(2):53-62.

## **NITRIC OXIDE HELPS Erectile Dysfunction**

Nitric oxide (NO) is believed to be the main neurovascular neurotransmitter and mediator of penile erection. Treatment of erectile dysfunction often utilizes medical therapies NO donors, which act on NO-dependent pathways.

Burnett AL. The role of nitric oxide in erectile dysfunction: Implications for medical therapy. *J Clin Hypertens (Greenwich)*. 2000;8(12 Suppl 4):53-62.

## **NITRIC OXIDE HELPS Facilitate Sleep**

Nitric oxide (NO) is made in the body from NO synthase (NOS) enzymes. In the brain NOS-containing neurons facilitate sleep (particularly rapid-eye-movement sleep).

Gautier-Sauvign  S, Colas D, Parnantier P, Clement P, Gharib A, Sarda N, Caspuglio R. Nitric oxide and sleep. *Sleep Med Rev*. 2005;9(2):101-13.

## **NITRIC OXIDE AND ANDROGENS The Effect on Blood Pressure**

Androgen hormones may play a role in making men more susceptible to increases in BP. This increase can be exacerbated when there is a lack of NO.

Vargas F, Morano JM, Wangensteen R, Rodriguez-G mez I, Garcia-Est n J. The endocrine system in chronic nitric oxide deficiency. *European Journal of Endocrinology*. 2007;150:1-12.

## **NO INCREASES MICROCIRCULATION IN Raynaud's Syndrome**

Patients suffering from Raynaud's syndrome experience abnormal vasoconstriction to the hands and feet, causing pain, discoloration and feelings of coldness or numbness. Research indicates that nitric-oxide can increase microcirculation in Raynaud's syndrome, which may help relieve symptoms.

Tucker AT, Pearson RM, Cooke ED, Benjamin N. Effect of nitric-oxide-generating system on microcirculatory blood flow in skin of patients with severe Raynaud's syndrome: a randomized trial. *Lancet*. 1999;354(9191):1670-1675.

## **NO IN THE TREATMENT OF Major Depression**

Nitric oxide modulates neurotransmitters involved in depression, as well as modulating antidepressants. Nitric oxide based antidepressants can be the future drugs of choice for major depression, particularly in the treatment of pharmacoresistant depression.

Dhir A, Kulkarni SK. Nitric oxide and major depression. *Nitric Oxide*. 2011;24(3):125-31.

## **NITRIC OXIDE PROMOTES Wound Healing**

Nitric oxide (NO) participating in the orchestration of wound healing. It does this via its critical influence on macrophage, fibroblast, and keratinocyte behavior during repair.

Frank S, K mpfer H, Weibler C, Pfaltzschiffer J. Nitric oxide drives skin repair: novel functions of an established mediator. *Kidney Int*. 2002;61(3):832-8.

## **NITRIC OXIDE IN THE TREATMENT of Glaucoma**

The distribution of nitric oxide synthase in the eye tissue of glaucoma patients suggests an important role of nitric oxide in the future therapies. Nitric oxide helps decrease intraocular pressure and provides neuroprotection.

Stefan C, Dumitrica DM, Ardeleanu C. [The future started: nitric oxide in glaucoma]. [Article in Romanian] *Oftalmologia*. 2007;51(4):89-94.

## **NITRIC OXIDE HELPS REGULATE Hair Follicle Activity**

Research has shown that dermal papilla cells derived from human hair follicles spontaneously produce nitric oxide (NO). The NO appears to be involved in the regulation of hair follicle activity.

Wolf R, Sch ntfelder G, Paul M, Blume-Peytavi U. Nitric oxide in the human hair follicle: constitutive and dihydrotestosterone-induced nitric oxide synthase expression and NO production in dermal papilla cells. *J Mol Med (Berl)*. 2003;81(2):110-7.

## **NITRIC OXIDE IMPROVES Exercise Performance**

In double blind research, a nitric oxide precursor (NOP) supplement increased nitric oxide levels during moderate- and severe-intensity exercise. NOP significantly improved VO2 during moderate intensity exercise, and significantly extended the time to exhaustion in severe-intensity exercise.

Balloy SJ, Winyard PG, Vanhatalo A, Blackwell JR, DiMarzio FJ, Wilkerson DP, Jonas AM. Acute L-arginine supplementation reduces the O2 cost of moderate-intensity exercise and enhances high-intensity exercise tolerance. *J Appl Physiol*. 2010;109(5):1394-403.

## **NITRIC OXIDE HELPS Prevent Gastroparesis**

Impairment of the nitric oxide (NO) system is one of the main factors responsible for gastroparesis (delayed stomach emptying with characteristic symptoms including abdominal discomfort, premature fullness after eating, nausea, vomiting, etc.). A reduction in an NO cofactor seen in female rats may explain the increase susceptibility to gastroparesis in females.

Gangula PR, Sekhar KR, Mukhopadhyay S. Gender bias in gastroparesis: Is nitric oxide the answer? *Dig Dis Sci*. 2011 Sep;56(9):2520-7

## **NITRIC OXIDE Modulates Pressure**

An NO signal from kidney cells is important for renin release, which plays a role in modulating blood pressure. Inhibition of the NO or reduced NO product can induce hypertension and result in cardio and kidney injury, as in the case of diabetes or atherosclerosis.

Vargas F, Morano JM, Wangensteen R, Rodriguez-G mez I, Garcia-Est n J. The endocrine system in chronic nitric oxide deficiency. *European Journal of Endocrinology*. 2007;150:1-12.

## **NITRIC OXIDE BUFFERS Prohypertensive Thyroid Hormone**

Hypothyroidism attenuates the prohypertensive and cardiotoxic effects of the NO inhibitor L-NAME (a non-selective inhibitor of nitric oxide synthase used experimentally to induce hypertension), whereas hyperthyroidism aggravates the effects of NO synthesis inhibition. Moreover, NO has been shown to play a major role in buffering prohypertensive actions of thyroid hormones.

Vargas F, Morano JM, Wangensteen R, Rodriguez-G mez I, Garcia-Est n J. The endocrine system in chronic nitric oxide deficiency. *European Journal of Endocrinology*. 2007;150:1-12.

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