THE NO SOLUTION: NITRIC OXIDE

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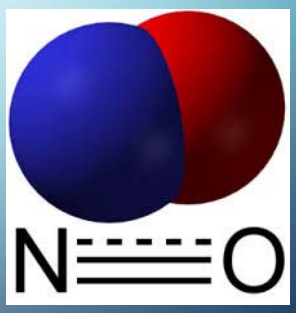
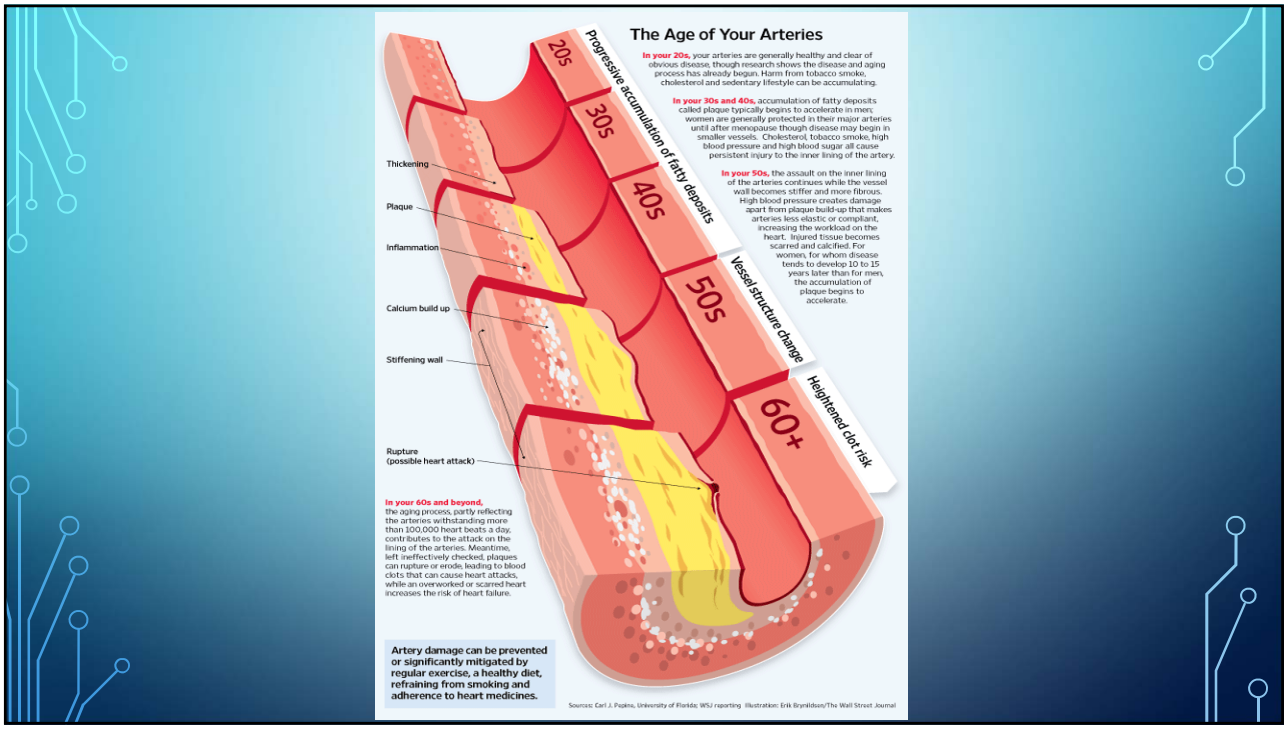


"A MAN IS AS OLD AS HIS ARTERIES."

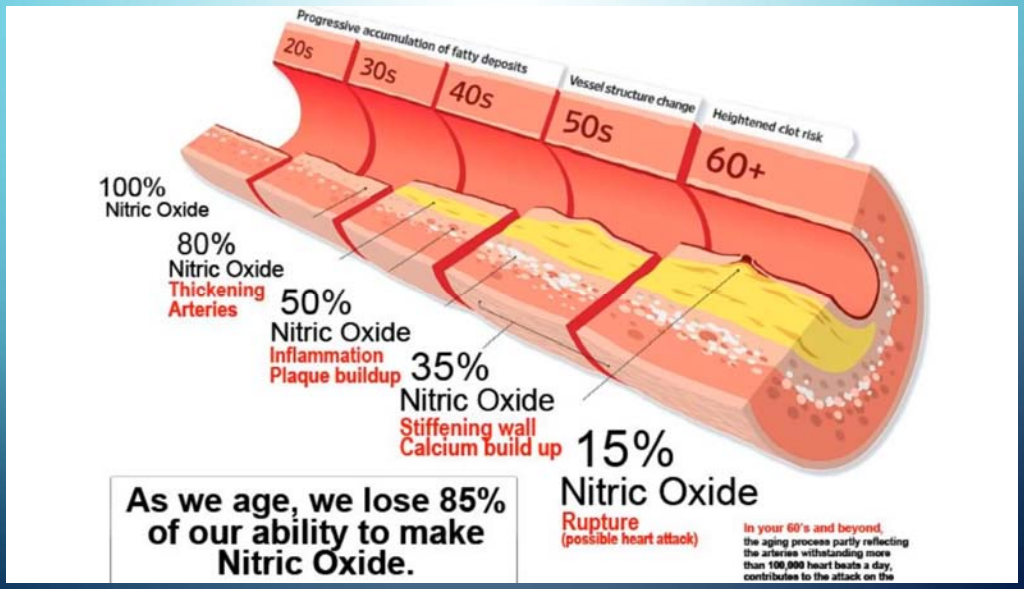
~ Thomas Sydenham, English physician, 1624-1689

"Women too! "

Susan Buckley, Dietitian, 195 (something) – Let's hope a long time from now!



Loss of NO is Associated with Atherosclerosis



WHAT IS NITRIC OXIDE?

- The nation's aging population is growing rapidly.
- By 2030, the number of adults age 65 and older will nearly double to 70 million.
- Americans are living longer and older adults can now live for many years with multiple chronic illnesses but with a substantial cost to health care.
- 20% of the Medicare population has at least five chronic conditions i.e., hypertension, diabetes, arthritis, etc.

WHAT IS NITRIC OXIDE?

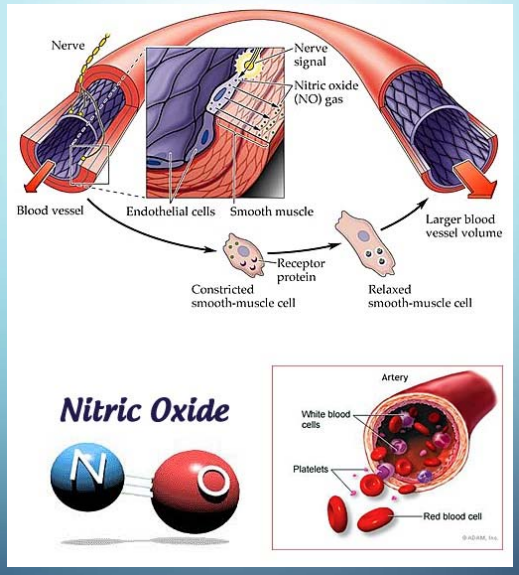
- As the body ages, nitric oxide (NO) production declines.
- Studies show that by age 40 the body makes about half or less Nitric Oxide than at age 20.
- By the age of 40, most men produce only about 50% of the NO in the body as they did in their teens and twenties

WHAT IS NITRIC OXIDE?

- **Women** fare worse.
- By age 50, their available NO levels are typically only about 35% of women in their twenties.

WAYS TO INCREASE NO

- As we age, our **blood vessels and nitric oxide system become less efficient** due to **free radical damage, inactivity, and poor diet**, causing our veins and arteries to deteriorate.
- Think of a fire hose as water rushes through it to put out a fire – it needs to expand enough to handle the pressure, still keeping enough force to put out the fire.
- Athletes and youth have the most optimal nitric oxide systems, reflecting their energy and resilience.



WHAT IS NITRIC OXIDE?

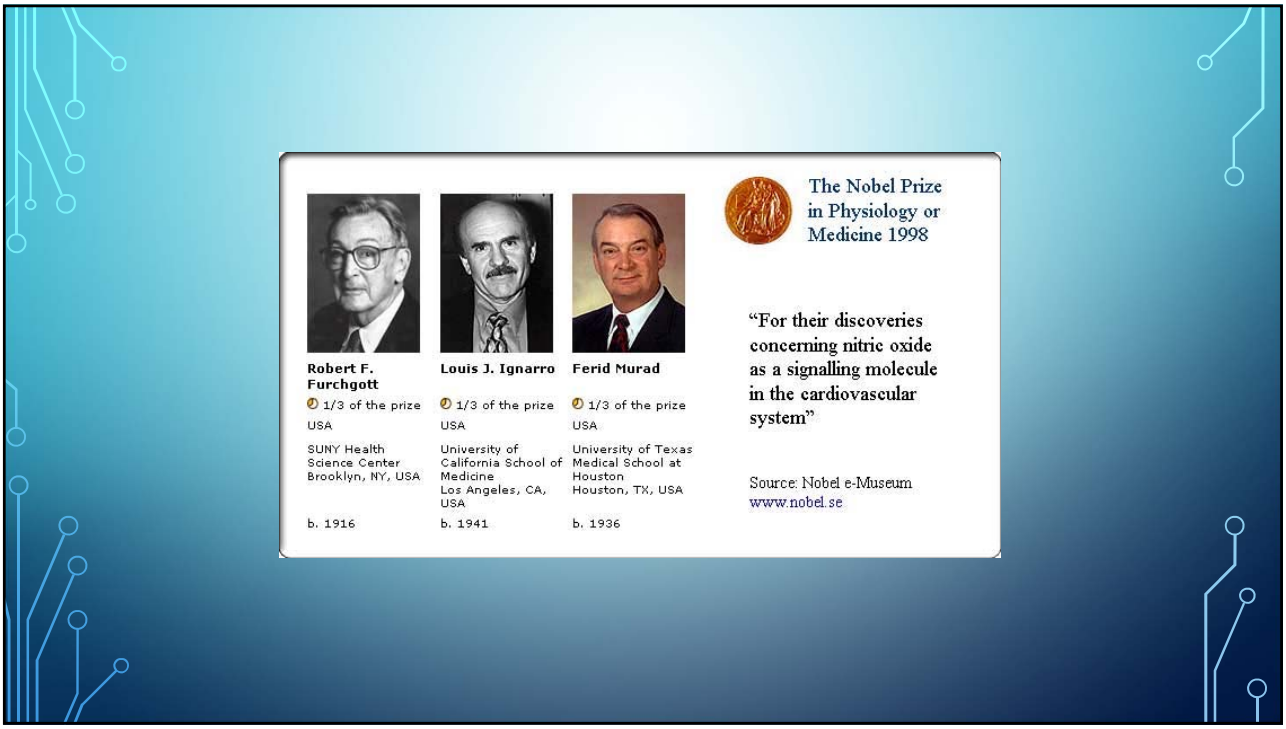
- Studies in experimental models and humans show that production of nitric oxide (NO) is **reduced with aging** and this may be relevant to a number of diseases that plague the aging population.
- NO is a **signaling molecule**, intricately involved with maintaining a host of physiological processes including the **regulation of blood vessel constriction** (artery and vein constriction) and is involved in **virtually every organ system**
- NO is one of the most important signaling molecules in our body, and loss of NO function is **one of the earliest indicators or markers of disease.**

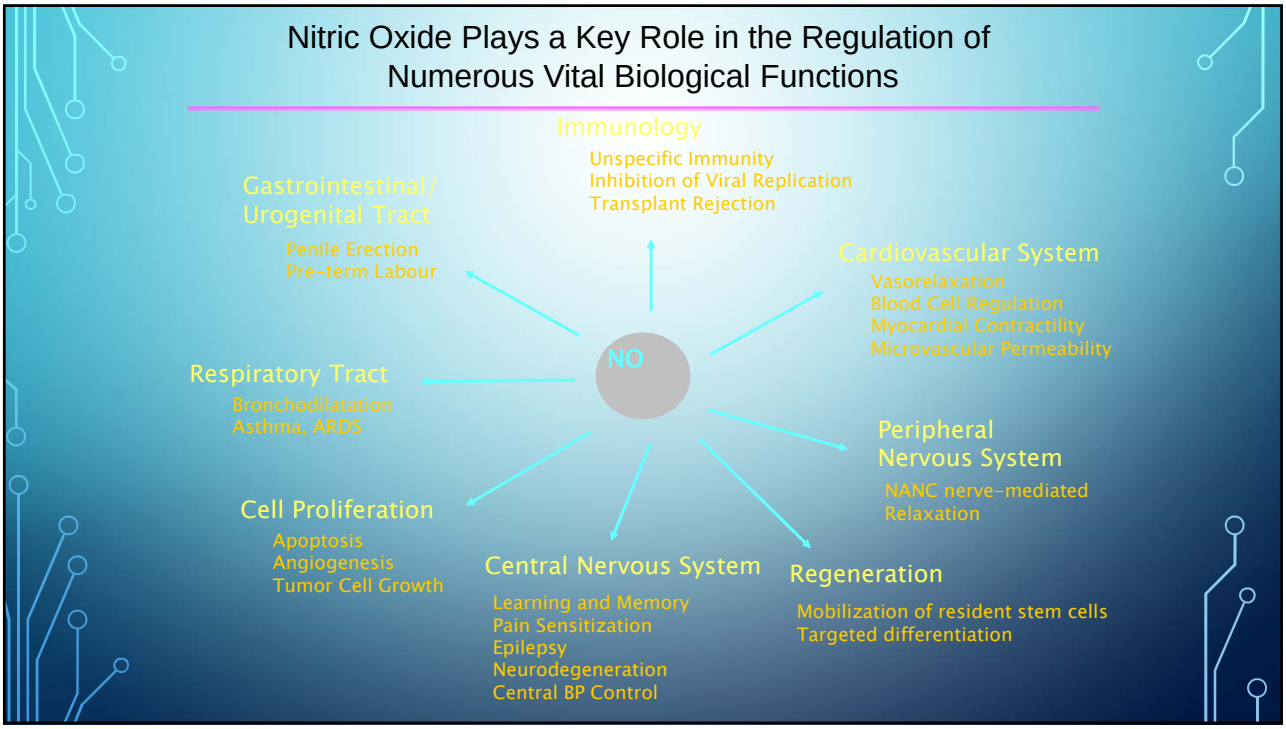
WHAT IS NITRIC OXIDE?

- Adequate NO production is the first step in a chain reaction that promotes **healthy cardiovascular function**, while insufficient NO triggers a cascade of destruction that **eventually results in heart disease.**
- **NO promotes healthy dilation of the veins and arteries** so blood can move throughout your body.
- Plus, it **prevents red blood cells from sticking together** to create dangerous clots and blockages.

What is Nitric Oxide?

- The chemical compound **nitric oxide** is a **gas** with chemical formula NO
- It is **one of the most important signaling molecules in the body of mammals** including humans, one of the few gaseous signaling molecules known.
- It is also a toxic air pollutant produced by automobile engines and power plants.
- NO should not be confused with nitrous oxide (N_2O), a general anesthetic, or with nitrogen dioxide(NO_2) which is another poisonous air pollutant.


The Nobel Prize in Physiology or Medicine 1998
"For their discoveries concerning nitric oxide as a signalling molecule in the cardiovascular system"
Source: Nobel e-Museum
www.nobel.se
Robert F. Furchgott
1/3 of the prize
USA
SUNY Health Science Center Brooklyn, NY, USA
b. 1916
Louis J. Ignarro
1/3 of the prize
USA
University of California School of Medicine Los Angeles, CA, USA
b. 1941
Ferid Murad
1/3 of the prize
USA
University of Texas Medical School at Houston Houston, TX, USA
b. 1936

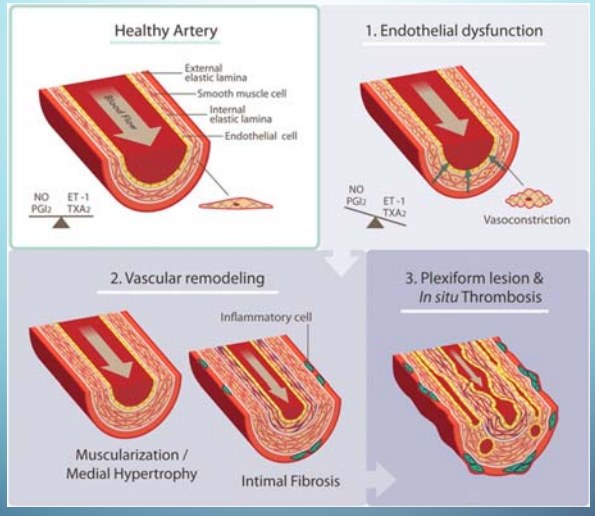

Nitric Oxide Plays a Key Role in the Regulation of Numerous Vital Biological Functions
Immunology
Unspecific Immunity
Inhibition of Viral Replication
Transplant Rejection
Gastrointestinal/ Urogenital Tract
Penile Erection
Pre-term Labour
Cardiovascular System
Vasorelaxation
Blood Cell Regulation
Myocardial Contractility
Microvascular Permeability
NO
Respiratory Tract
Bronchodilatation
Asthma, ARDS
Peripheral Nervous System
NANC nerve-mediated Relaxation
Cell Proliferation
Apoptosis
Angiogenesis
Tumor Cell Growth
Central Nervous System
Learning and Memory
Pain Sensitization
Epilepsy
Neurodegeneration
Central BP Control
Regeneration
Mobilization of resident stem cells
Targeted differentiation

"The discovery of NO and its function is one of the most important in the history of cardiovascular medicine."

Dr. Valentin Fuster
1998 President of American Heart Association

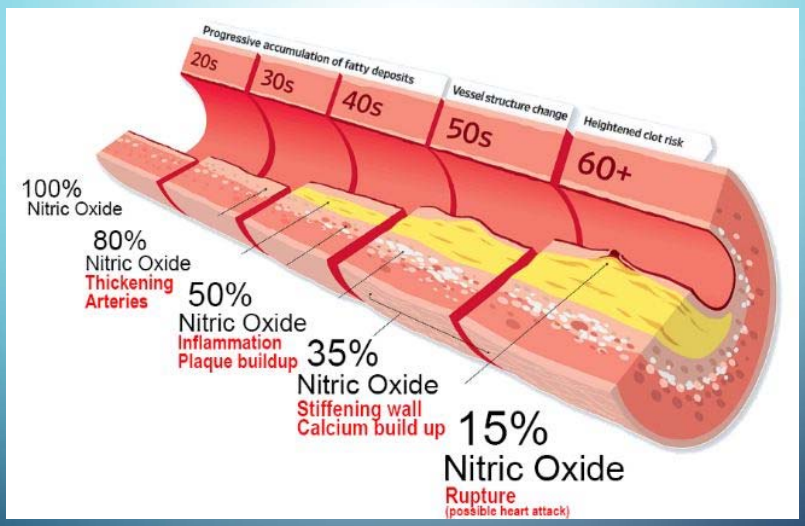
WHAT IS NITRIC OXIDE?

- NO is **produced by the endothelial cells lining the arteries**
- NO penetrates the underlying smooth muscles and acts as a potent vasodilator that **relaxes the arteries**.
- Therefore, nitric oxide plays a **critical role in blood pressure and overall circulation**.
- It also keeps the endothelium in shape by **curbing inflammation and oxidative stress.**



WHAT IS NITRIC OXIDE?

- Your body naturally generates NO in the endothelium that line the blood vessel walls.
- But, in the early stages of arterial disease, this lining is damaged—which **chokes off the production of NO**, making the vessels vulnerable to **inflammation** and other negative factors.



NITRIC OXIDE

- Clinical studies provide evidence that insufficient NO production is associated with all major cardiovascular risk factors, such as hyperlipidemia, diabetes, hypertension, smoking and severity of atherosclerosis, and also has a profound predictive value for disease progression including cardiovascular and Alzheimers disease.

- Nitric oxide is a molecule that our body produces to help its 50 trillion cells communicate with each other by transmitting signals throughout the entire body.
- Nitric oxide has been shown to be important in the following cellular activities:

  - Help memory and behavior by transmitting information between nerve cells in the brain
  - Assist the immune system at fighting off bacteria and defending against tumors
  - Regulate blood pressure by dilating arteries
  - Reduce inflammation
  - Improve sleep quality
  - Increase your recognition of sense (i.e. smell)
  - Increase endurance and strength
  - Assist in gastric motility

HEART DISEASE

- Nitric oxide has gotten the most attention due to its cardiovascular benefits.
- Alfred Nobel, the founder of the Nobel Prize, was prescribed nitroglycerin over 100 years ago by his doctor to help with his heart problems.
- He was skeptical, knowing nitroglycerin was used in dynamite, but this chemical helped with his heart condition.
- Little did he know nitroglycerin acts by releasing nitric oxide which relaxes narrowed blood vessels, increasing oxygen and blood flow.

HEART DISEASE

- Nitroglycerin is an effective therapy for angina.
- It triggers nitric oxide production, which dilates narrowed coronary arteries, improving circulation and delivering much-needed oxygen to the heart muscle.
- Restoring nitric oxide availability also lowers blood pressure and helps treat erectile dysfunction.
- In fact, the erectile dysfunction drugs Viagra, Cialis, and Levitra work on nitric oxide pathways to increase blood flow to the penis and substantially improve erections.

HEART DISEASE

- The interior surface (endothelium) of your arteries produce nitric oxide.
- When plaque builds up in your arteries, called atherosclerosis, you reduce your capacity to produce nitric oxide, which is why physicians prescribe nitroglycerin for heart and stroke patients.

HEART DISEASE

- Atherosclerosis, the underlying cause of heart disease and other vascular disorders, is characterized by endothelial dysfunction and a **limited capacity to produce nitric oxide**.
- It's a **vicious cycle**: diseased arteries can't generate enough protective nitric oxide, and low nitric oxide levels set the stage for further damage, hypertension, and increased risk of cardiac events.

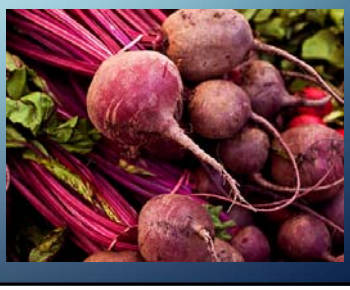
- Diet has a large impact on nitric oxide (N-O) production.
- That's because in addition to being produced in the endothelium (lining of the arteries), **it is also made in the mouth and the digestive tract … as long as the conditions are right.**
- When we're younger, the body easily converts the naturally occurring nitrates found in certain plant foods into NO.
- **Beets, spinach, and leafy greens are especially nitrate rich.**
- As these foods are chewed, helpful bacteria in the saliva converts the nitrates into nitrites. Once in the stomach, gastric juices act on nitrites and convert them to nitric oxide.
- The NO is then absorbed through the intestinal tract and back into the bloodstream.

NITRIC OXIDE

- As we age, though, this process becomes less efficient and the body does not produce as much nitric oxide.
- By the time you're 40, studies show you're only making about half or less of what you made when you were 20.

BEET ROOTS

- The key is to consume NO boosting foods regularly, in order to increase production of nitric oxide in your body, naturally.
- Beets rank on top as one of the most nitrate rich foods in nature, as it contains up to twenty times more nitrate than most other nitrate containing foods.



HEART FAILURE

- Kansas State University researchers found that the nitrate in beetroot concentrate **increases blood flow to skeletal muscles by as much as 38% during exercise**, according to research published in the journal *Physiology* in 2013
- In addition to improving athletic performance, the study also found that beetroot juice may **improve the quality of life of heart failure patients** because heart failure limits blood flow to particular tissues, especially working skeletal muscles.
- In heart failure patients the heart isn't pumping out as much blood – it is the gradual loss of pumping capacity
- When the heart is weak, **fatigue** and **shortness of breath** follow, making everyday activity difficult.
- When the **blood vessels can be dilated** a little bit further with beet root juice, then they're going to get **more of the oxygen rich blood**.

HEART FAILURE

- Researchers say improving a heart failure patient's blood flow by as little as 10% can mean the difference between them being wheelchair bound or getting around
- Heart failure is a disease where oxygen delivery to particular tissues, especially working skeletal muscles, is impaired, decreasing the capacity to move the arms or legs and be physically active," said Poole, one of head researchers.
- "The best therapy for these patients is getting up and moving around. However, that is often difficult. **Increasing the oxygen delivery to these muscles through beetroot can provide a therapeutic avenue** to improve the quality of life for these patients."

HEART FAILURE

- Working with a small group of patients, the research team gave each of them a beet juice treatment.
- The patients acted as their own control group; everyone received what appeared to be the same beet juice, the difference being that the nitrate content had been removed from some, making it a placebo beet juice.
- Between the trial sessions, there was a 1–2–week break.
- Neither those taking part in the trial nor the research team knew the order in which patients received the treatment beet juice and placebo beet juice.

HEART FAILURE

- **Two hours after drinking the juice, patients who consumed the beet juice containing nitrates showed a 13% increase in power in muscles that extend the knee, with the most benefit when they moved at greatest speed.**
- "One problem in aging is the muscles get weaker, slower and less powerful. Beyond a certain age, people lose about 1% per year of their muscle function," says Coggan, one of the researchers.
- "When we can boost muscle power like we did in this study, that could provide a significant benefit to older individuals."

BLOOD PRESSURE

- In a study in *Hypertension* in 2008, healthy volunteers who drank beet juice showed a drop in systolic (top number) and diastolic (bottom number) blood pressure of **10 and 8 points,** respectively, **after three hours**—an effect attributed to the nitrates in beets.
- Other research has found that drinking beet juice for two weeks has both immediate and longer-term effects on blood pressure.

Lowering blood pressure by 5 mmHg reduces risk of stroke by 34% and Ischemic heart disease by 21%

Health Technol Assess. 2003;7(31):1-94.
Lowering blood pressure to prevent myocardial infarction and stroke: a new preventive strategy.
Law M, Wald N, Morris J.

BLOOD PRESSURE

- Research conducted at Queen Mary University of London (QMUL) in the UK, and funded by the British Heart Foundation
- Recruited 64 patients aged 18–85.
- Half of the patients were taking prescribed medication for **high blood pressure** but were not managing to reach their target blood pressure, and the rest had been diagnosed with high blood pressure but were not yet taking medication for it.
- The patients were randomly assigned to one of two groups. One group consumed a daily glass (250 ml or around 8.5 oz) of beetroot juice, and the other group had the same except their beetroot juice was nitrate-free (the placebo).

BLOOD PRESSURE

- During the study, patients in the intervention group experienced an **improvement of around 20% in blood vessel dilation capacity** and around a **10% reduction in arterial stiffness**.
- These changes in blood vessel function have been shown, by other studies, to be associated with **substantial reductions in heart disease**.
- There were **no adverse side effects** from the daily dietary nitrate.
- In the two weeks after the study period, the blood pressure readings among patients in the intervention group returned to their previous high levels.
- There were no changes to blood pressure, blood vessel function or arterial stiffness among the placebo group during the study.

BLOOD PRESSURE

- Patients with high blood pressure who drank the daily 8.5 oz. glass of beetroot juice experienced an average decrease in blood pressure of about 8/4 mmHg (which for many patients brought their blood pressure levels back into the 'normal' range).
- Large-scale observational studies suggest that each 2mmHg increase in blood pressure increases the likelihood of death from heart disease by 7% and stroke by 10%.
- The average reduction in blood pressure through a single anti-hypertensive drug is 9/5 mmHg. Therefore, these findings suggest a role for dietary nitrate as an effective, easy and affordable treatment in managing blood pressure with similar results to drug treatment.

BRAIN HEALTH

- Nitric oxide is also generated in the brain, where it's involved in neurotransmission.
- That's why nitric oxide benefits also include protection against dementia and other neurodegenerative disorders
- NO activates the computational ability of the brain
- Studies show that NO may play a prominent role in the treatment of age-related degenerative disease such as AD.

BRAIN HEALTH

- In a study this year from Wake Forest University, older people who drank 16 ounces of beet juice a day for two days showed greater blood flow to the frontal lobe of the brain, an area associated with dementia and involved in skills such as planning and problem solving.
- Beet juice won't prevent or cure dementia, but perhaps future studies will determine whether beets can help improve mental function.

GI HEALTH

- In the gastrointestinal tract, it **relaxes smooth muscle cells** and helps **regulate intestinal peristalsis** and the secretion of mucus and gastric acid.
- Nitric oxide is also involved in insulin signaling, bone remodeling, respiratory function, ATP (energy) utilization, and mitochondrial biogenesis, or the creation of new cellular "energy factories"

ATHLETIC PERFORMANCE

- Research published in the journal *Physiology* in 2013 showed that the **nitrate found in beetroot concentrate increases blood flow to skeletal muscles during exercise**
- The journal *Physiology* is widely regarded as the world's premiere physiology journal
- Beet juice **increases muscle efficiency**, allowing the muscles to do the same work with less oxygen, allowing people to walk, run, or perform exercises with a lower "cost" in oxygen
- Consuming beet juice **creates a tolerance for higher-intensity exercise**.
- **Blood pressure stays lower during intense exercise**, putting less strain on the heart

ATHLETIC PERFORMANCE

- Another study, "Micovascular oxygen pressures in muscles comprised of different fiber types: Impact of dietary nitrate supplementation" published in the *Journal of Nitric Oxide, Biology and Chemistry*
- Beetroot juice consumption resulted in **38% higher blood flow** to the skeletal muscles during exercise

ATHLETIC PERFORMANCE

- Cermak et al reported in February 2012 that after 6 days of drinking a beet concentrate, equivalent to 2 cups a day of whole juice, the 12 riders in the double-blind clinical trial improved their 10-km time trial performance by approximately 12 seconds

IMMUNE HEALTH

- NO is **synthesized in the white blood cells** as well and is used as a weapon against bacteria, fungi, parasites, and aberrant cancer cells.
- Nitric Oxide authority, Dr. Jonathon S. Stamler, Professor of Medicine, Duke University Medical Center said this regarding NO, "It does everything, everywhere. You cannot name major cellular response or physiological effect in which Nitric Oxide is not implicated today. It's involved in complex **behavioral changes in the airway relaxation, beating of the heart, dilation of blood vessels, regulation of intestinal movement, function of blood cells, the immune system, even the way fingers and arms move."**

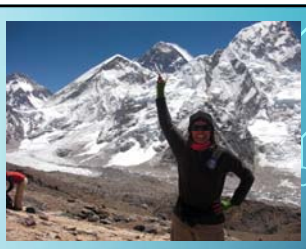
BONE HEALTH

- Nitric oxide is important in the regulation of bone formation and breakdown and is normally released by bone cells when mechanical stress is applied to the bones during weight-bearing activities.
- Nitric oxide supplementation can help to improve bone density by enhancing bone formation and reducing the extent of bone breakdown.
- The compound's effect on bones is improved when used in combination with supplements such as vitamin D.
- Nitric oxide is also key in fracture healing and acts to cue local bone cells to start the healing process as well as increasing blood flow to the area of injury.

JOINT PAIN

- Joint pain often causes major limitations in function in people who have osteoarthritis.
- Research published in 2008 in the journal "Arthritis Research and Therapy" shows that nitric oxide plays a role in perception of pain and can be used as a useful pain management tool while managing the symptoms of osteoarthritis
- Likely mechanisms of joint pain reduction by nitric oxide include increased blood flow, reduction of nerve irritation and reduction of inflammation in the joint space.
- Nitric oxide might also be useful in maintaining the health of existing cartilage cells in the joint space and could be a useful tool in joint protection and in minimizing further cartilage damage secondary to osteoarthritis.

ALTITUDE SICKNESS



- **Altitude sickness** — which affects about half of all travelers to elevations above 8,000 feet, regardless of fitness level — can seriously cramp your vacation style with several days of light-headedness, nausea, and other unpleasant symptoms.
- Your blood vessels, which deliver oxygen throughout your body, **depend on the oxygen** in the air to do their job
- It normally takes several days for your blood vessels to adjust to the decreased oxygen levels — a process called acclimatization — but researchers have found that **drinking beet juice can speed up the process.**

ALTITUDE SICKNESS

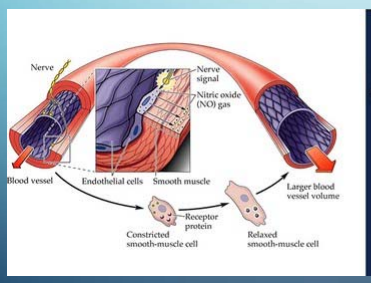
- One sign of successful acclimatization to altitude is that the blood vessels are able to deliver enough oxygen throughout the body.
- But normal blood vessel function depends on the body's ability to naturally produce a compound called nitric oxide.
- In healthy people at sea level, production of adequate amounts of NO is not a problem, but with the reduced oxygen availability at high altitude it is a challenge, simply because natural NO production requires oxygen.
- Drinking nitrate-rich beet juice helps improve blood vessel function at altitude by giving the body alternative building blocks to make nitric oxide.

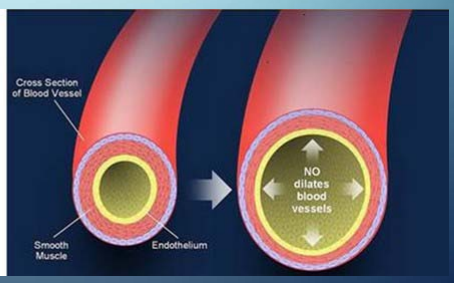
ALTITUDE SICKNESS

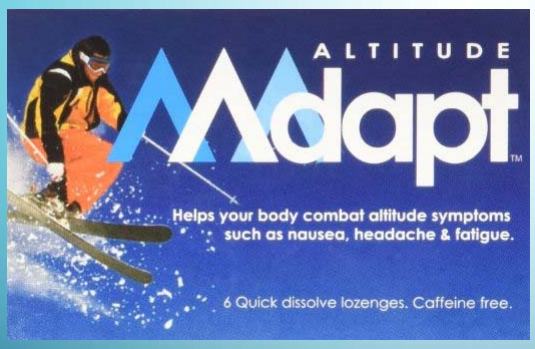
- A team of Norwegian and Swedish researchers decided to see how nitrate-rich beet juice might affect acclimatization on a 39-day expedition to Kathmandu and at 3700 meters in the Rolwaling Valley, Nepal.
- Previous research has shown that **blood vessels tend to contract at high altitude**, so researchers decided to see if they could improve blood vessel function at high altitude simply by having test subjects drink beet juice.
- They measured blood vessel function with a standard test of arterial endothelial function, a flow-mediated dilatation test (FMD) that uses ultrasound.
- In a study recently published in *Nitric Oxide: Biology and Chemistry*, the researchers showed that consumption of organic nitrate-rich beet juice **restored reduced blood vessel function at high altitude**.

ALTITUDE SICKNESS

- The study showed that beet juice with high amounts of nitrate **made the blood vessels relax and return to normal function**, while beet juice with no nitrate (the placebo) did not have any effect.







Supplement Facts

Serving Size: 1 Lozenge Servings Per Container: 6

	Amount Per Serving	% Daily Value
Vitamin C (as magnesium ascorbate and ascorbic acid)	100 mg	167%
Vitamin B12 (as methylcobalamin and cyanocobalamin)	1000 mcg	16,667%
Proprietary Nitric Oxide Blend for optimal Nitric Oxide activity† Beet Root Powder (root), Hawthorn Berry Extract (berry), L-citrulline, Sodium Nitrite	420 mg*	

*Daily Value not established.

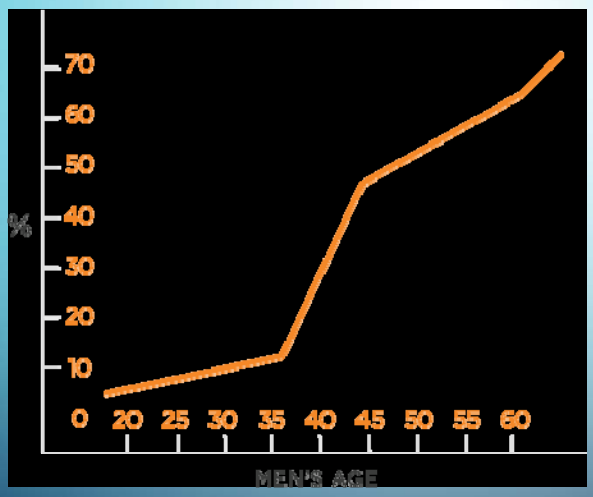
ERECTILE DYSFUNCTION

- Erectile dysfunction, or ED, is the inability to achieve or sustain an erection suitable for sexual intercourse.
- Causes include medications, chronic illnesses, poor blood flow to the penis, drinking too much alcohol, or being too tired.
- More than 18 million men in the United States over age 20 are affected by erectile dysfunction, according to a study by researchers from the Johns Hopkins Bloomberg School of Public Health.

ERECTILE DYSFUNCTION

- The prevalence of erectile dysfunction was strongly linked with age, cardiovascular disease, diabetes and a lack of physical activity.
- The findings also indicate that lifestyle changes, such as increased physical activity and measures to prevent cardiovascular disease and diabetes, may also prevent decreased erectile function.

Erectile Dysfunction with Age



20%UNDER 40
50%OVER 40
66%OVER 70

Erectile dysfunction is present in about 50% of men by age 40 with about a 10% increase for each decade thereafter.

Sexual Dysfunction linked to CVD in both men and women

- Atherosclerosis
- PAD
- Hypertension

Hatzimouratidis & Hatzichristiou J Sex Med 2007
Jackson G Int J Clin Pract 2009

Treatment of ED as purely a lifestyle disorder may severely **underestimate the seriousness of disorder**

Sexual Dysfunction is now considered an early marker/risk factor for cardiovascular disease and consequently a life-threatening condition

It is the canary in the coal mines!!!

BETTER SEX

- Did you know that Romans drank beet juice two hours before engaging in sex?
- It works by raising nitric oxide levels.
- The beet's ability to improve circulation has been documented in numerous studies.

HOW TO INCREASE NITRIC OXIDE

- Because nitric oxide is synthesized from the amino acid arginine, dietary recommendations for boosting nitric oxide often include protein-rich meat and poultry.
- But recent research suggests that vegetables may be your best bet.
- Plant foods, particularly beets and leafy greens like kale, Swiss chard, arugula, and spinach, are rich in dietary nitrates and nitrites—compounds that stimulate the production of nitric oxide in the body.
- Coupled with its abundance of protective potassium, it's not surprising that a plant-based diet is associated with lower blood pressure and reduced risk of stroke, heart attack, diabetes, and a variety of other health concerns.

- How can I increase nitric oxide – NO – for better health?

HOW TO INCREASE NITRIC OXIDE

- Your body uses two primary pathways to produce Nitric Oxide…
- The first is the classical eNOS pathway where oxide is produced from the amino acid, L-arginine (more animal foods), via an enzyme called endothelial Nitric Oxide Synthase (eNOS).
- Production of Nitric Oxide via the eNOS pathway **declines rapidly as you age or when the endothelial lining in your arteries becomes damaged.**
- This explains why **most older people are deficient in NO**.

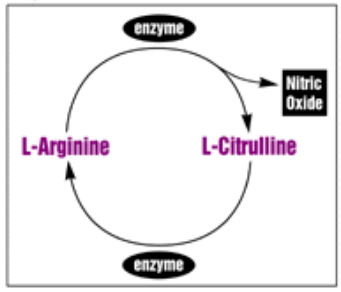
L-ARGININE PATHWAY

- For years, supplement makers have promoted L-arginine as a Nitric Oxide booster.
- Since endothelial NO is formed by the oxidation of L-arginine, it makes sense that ingesting more arginine would boost NO production, right?
- However **if you're middle-aged or older, L-arginine just doesn't work as well**
- Most of what you ingest will be diverted to other functions or eliminated as waste. Multiple studies show that even huge amounts of L-arginine won't make a difference

WAYS TO INCREASE NO

- One way to increase nitric oxide is through diet, most notably by consuming the amino acids L-arginine and L-citrulline.
- Arginine, which can be found in **nuts, fruits, meats and dairy,** directly creates nitric oxide and citrulline inside the cell
- Citrulline is then recycled back into arginine, making even more nitric oxide.

Diagram 1



WAYS TO INCREASE NO

- Enzymes that convert arginine to citrulline, and citrulline to arginine need to function optimally for efficient nitric oxide production.
- We can protect those enzymes and nitric oxide by consuming healthy foods and antioxidants, like fruit, garlic, soy, vitamins C and E, Co-Q10, and alpha lipoic acid, allowing you to produce more nitric oxide.
- Nitric oxide only lasts a few seconds in the body, so **the more antioxidant protection we provide, the more stable it will be and the longer it will last.** Doctors are utilizing this science by coating stents (mesh tubes that prop open arteries after surgery) with drugs that produce nitric oxide.

L-ARGININE TO NO

- When we are young and healthy, the endothelial production of NO through L-arginine is efficient and sufficient
- However, as we age **we lose our ability to synthesize endothelial derived NO.**

- For years, scientists and physicians have investigated L-arginine supplementation as a means to enhance NO production.
- This strategy has been shown to **work effectively in young healthy individuals with functional endothelium**
- Patients with endothelial dysfunction, however, by definition, are **unable to convert L-arginine to NO and, therefore, this strategy has failed in clinical trials.**
- Schulman *et al* found that L-arginine, when added to standard post heart attack therapies, **did not improve vascular stiffness** measurements or ejection fraction and was associated with higher post heart attack mortality

- Many NO-based products contain L-arginine or L-citrulline as their active ingredient.
- Simply giving more L-arginine to a patient with dysfunctional NO enzymes will likely not provide much benefit since the enzyme that converts L-arginine to N-O is the underlying problem.
- It's not possible to fuel a system that is broken.

HOW TO INCREASE NITRIC OXIDE

- But your body can produce Nitric Oxide another way that operates independently of eNOS and L-arginine…
- And this pathway uses the bacteria in your mouth to convert the nitrates found in certain foods into Nitric Oxide..
- And it can do this quite effectively.
- The key is to consume these NO boosting foods regularly, in order to increase production of nitric oxide in your body, naturally.

WAYS TO INCREASE NO

- Plant foods, particularly beets and leafy greens like kale, Swiss chard, arugula, and spinach, are rich in dietary nitrates and nitrites—compounds that stimulate the production of nitric oxide in the body
- Coupled with its abundance of protective potassium, it's not surprising that a plant-based diet is associated with lower blood pressure and reduced risk of stroke, heart attack, diabetes, and a variety of other health concerns.

Nitrate Content of Vegetables		
Vegetable	**Serving Size**	**Nitrate (mg)**
Rhubarb	**1 cup diced**	**343**
Butterleaf Lettuce	2 cups shredded	220
Agurula	**2 cups**	**192**
Salad mix, beet greens	2 cups leaves	135
Swiss Chard	**2 cups leaves**	**109**
Beets	.5 cup slices	94
Spinach	**2 cups leaves**	**47**
Cilantro	1 cup leaves	40
Basil	**.5 cup leaves**	**22**
Broccoli	1 cup chopped	18
Potato	**.5 cup diced**	**8**

SOURCES: The EFSA Journal (2008) 689, 1-79. Serving Size Information from USDA, 2011.

WAYS TO INCREASE NO

- For those looking to work dietary nitrate into their daily diets, the trick is <u>not to boil the vegetables</u> – as dietary nitrate is water soluble – but steaming, roasting or drinking in a juice all has a positive effect

HOW TO INCREASE NITRIC OXIDE

- Another way to up your intake of dietary nitrates is to **drink beet juice.**
- Studies have shown that two cups a day, which contain about six times the typical daily intake, can **lower blood pressure, increase stamina during exercise, and, in older people, boost blood flow to the brain.**
- Start with a daily cup of diluted beet juice, flavored with stevia or xylitol, if desired, and build up to two cups per day over time.

SIDE EFFECTS

- The dark carotenes of beet juice may give your urine and bowel movements a **red color**.
- This color change is harmless.
- Since beets are high in oxalates, people who tend to make oxalate kidney stones may want to avoid beet juice.

NITRIC OXIDE

- If you decide to juice the fresh fruits or vegetables, it's important that you drink the juice quickly as nitrate levels will decline rapidly if you let it sit too long.
- It's also very important that you **hold the juice in your mouth** for 10 seconds before swallowing because the bacteria in your mouth must act on the nitrates before they can be converted into nitric oxide.
- When you eat whole foods high in nitrates, chew them thoroughly to ensure that the **bacteria have plenty of time to do their job**, so that the nitric oxide conversion can take place.

NITRIC OXIDE

- If you have poor bacterial makeup in your mouth, your ability to convert nitrates into nitric oxide will be severely limited.
- So if you have gum disease, or poor dental health, these problem needs to be addressed, otherwise you'll convert very little of your dietary nitrate into nitric oxide.
- If you use **Listerine or any other antiseptic mouthwash** that destroys oral bacteria, best to drop the habit.
- A study recently published in the journal Free Radical Biology and Medicine, found that **using antiseptic mouthwash twice daily increases blood pressure and raises heart attack risk.**

NEO40

- Neo40® Professional was developed by researchers at the University of Texas School of Medicine in Houston.
- In the course of 15 years they developed the first natural, plant-based technology to effectively deliver NO directly to the body

NEO 40

NEO 40

NEO40® PROFESSIONAL

Suggested Use: Adults take once or twice daily (12 hours apart) or as directed by your healthcare professional. Place one lozenge in your mouth, dissolve or chew, and swallow. Do not place under tongue or swallow whole. Hydrate before and after taking to avoid mouth sensitivity. For best results, take on an empty stomach, approximately one hour before or two hours after eating. Do not exceed two lozenges in a 24-hour period. **Store in a cool dry place.**

Supplement Facts

Serving Size: 1 Lozenge		Servings Per Container: 60
Amount Per Serving		**% Daily Value**
Vitamin C (as magnesium ascorbate and ascorbic acid)	100 mg	167%
Vitamin B12 (as methylcobalamin)	1000 mcg	16,667%
Folate (as (6S)-5-Methyltetrahydrofolic acid, glucosamine salt)	400 mcg	100%
Proprietary Nitric Oxide Blend Beet Root Powder (root), Hawthorn Berry Extract (berry), L-Citrulline, Sodium Nitrite	425 mg	*

* Daily Value not established

Other Ingredients: mannitol, modified cellulose, xylitol, natural flavors, magnesium vegetable stearate, stevia, silica.

Manufactured for and distributed by:
Neogenis® Labs, Inc.
Austin, TX 78746

US Patent No's: 8,298,589 and 8,303,995

LOWERS TRIGLYCERIDES

- Research trial was conducted at the Houston Institute for Clinical Research in Houston, Texas
- Inclusion criteria for this double-blinded, placebo-controlled study were patients older than 40 years with 3 or more of the following cardiovascular risk factors: hypertension, obesity, hyperlipidemia, smoking, sedentary, family history of cardiovascular disease, and diabetes.
- Subjects were instructed to take either the NO dietary supplement called Neo40 Daily® or placebo twice daily on an empty stomach for 30 days.

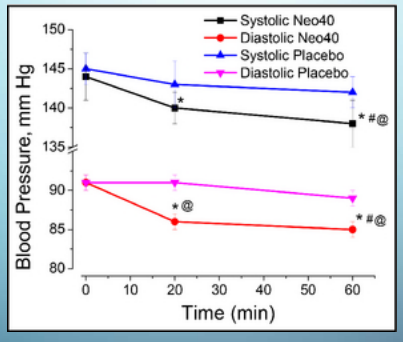
LOWERS TRIGLYCERIDES

- Patients taking the NO dietary supplement twice a day for 30 days led to a **significant increase in both plasma nitrite and nitrate**, indicating an increase in systemic NO availability.
- There was a statistically significant reduction in 72% of patients with elevated triglycerides (>150 mg/dL) after 30 days compared with their starting levels before taking the NO dietary supplement (168 ± 17 mg/dL vs 232 ± 19 mg/dL).
- Conclusion: the strategy of formulating a combination of natural products and botanicals chosen specifically for their NO activity shows promise in restoring NO homeostasis in human subjects at risk for cardiovascular disease for use as a dietary supplement.

NEO 40 LOWERS BLOOD PRESSURE

- The *Journal of Clinical Hypertension*
- Administration of a single dose of the nitric oxide (NO)–donating lozenge significantly reduces both systolic and diastolic blood pressure after 20 and 60 minutes compared with baseline in 30 patients
- Compared with placebo, the NO–donating lozenge led to a **significant reduction in diastolic blood pressure at 20 minutes and a significant reduction in systolic and diastolic blood pressure after 60 minutes**.
- Your doctor must order this product

ACUTE EFFECTS OF AN ORAL NITRIC OXIDE SUPPLEMENT ON BLOOD PRESSURE, ENDOTHELIAL FUNCTION, AND VASCULAR COMPLIANCE IN HYPERTENSIVE PATIENTS



The Journal of Clinical Hypertension
Volume 16, Issue 7, pages 524–529, 24 JUN 2014 DOI: 10.1111/jch.12352
http://onlinelibrary.wiley.com/doi/10.1111/jch.12352/full#jch12352-fig-0002

NEO 40 – FOR GENERAL PUBLIC

- https://www.neogenis.com – No folate, less Vitamin B 12

NEO 40 INDICATOR STRIPS

- Non-invasive salivary nitric oxide indicator strip for use in monitoring your nitric oxide restoration progress.
- Place a drop of saliva on the indicator strip, and compare the indicator strip with the accompanying color chart.
- Results are instant, and you can tell at a glance what your nitric oxide status is.

SODIUM NITRITE

- So what about nitrites in cured foods?
- The study that originally connected nitrates with cancer risk and caused the scare in the first place has since been discredited after being subjected to a peer review.
- There have been major reviews of the scientific literature that found **no link between nitrates or nitrites and human cancers**, or even evidence to suggest that they may be carcinogenic.

SODIUM NITRITE

- There is presently no research stating that sodium nitrite in food is not safe.
- However, research has found an **association** between processed meat intake, as a symptom of an overall dietary pattern, and various types of cancer, including prostate and colorectal.
- These studies however focus on how diet and lifestyle effect disease development — they in no way prove that eating any one type of food causes or prevents cancer.

NITRITES

- And if you think you can avoid nitrates and nitrites by eating so-called "nitrite- and nitrate-free" hot dogs and bacon, don't be fooled.
- These products use "natural" sources of the same chemical like celery and beet juice and sea salt, and are no more free from nitrates and nitrites than standard cured meats.
- In fact, they may even contain *more* nitrates and nitrites when cured using "natural" preservatives.

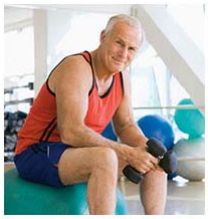
NITRITES VS NITRATES

- Beets, spinach and radishes all have naturally occurring ***nitrates***, which will **convert to nitrites during digestion in your body.**
- These naturally occurring versions are not harmful to the body and are very safe when they are eaten with the wonderful natural antioxidants that beets also provide.

HOW TO INCREASE NITRIC OXIDE

- Another way to increase nitric oxide is through **exercise.**
- When you run or lift weights, your muscles need more oxygen which is supplied by the blood.
- As the heart pumps with more pressure to supply the muscles with blood, the **lining in your arteries releases nitric oxide into the blood**, which relaxes and widens the vessel wall, allowing for more blood to pass though.

HOW TO INCREASE NITRIC OXIDE



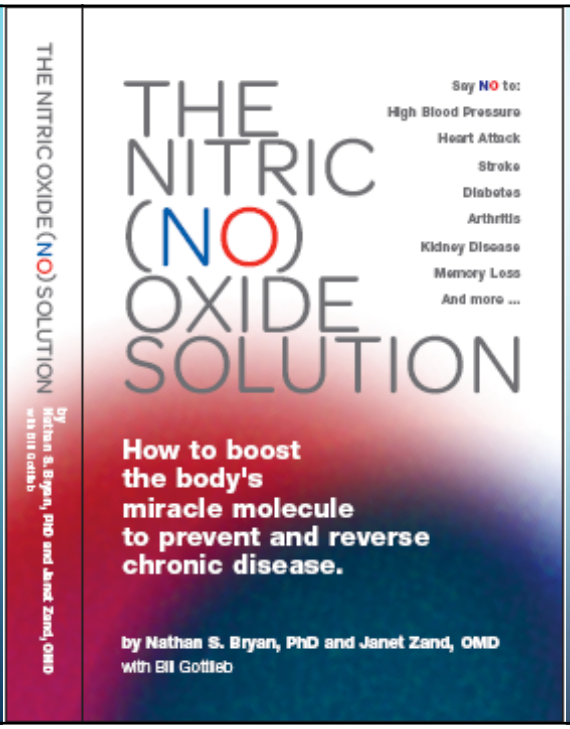
- Exercising muscles require extra oxygen and nutrients, and this prompts endothelial nitric oxide release, which relaxes the arteries and increases blood flow.
- Habitual physical activity keeps these mechanisms in shape and **protects against disease and aging of the vascular system**.

INHIBITORS OF NO

- High-fat, high-carb diets tend to increase blood levels of asymmetric dimethyl-arginine (ADMA), a naturally occurring **inhibitor of nitric oxide production**, so go easy on fatty foods and high-glycemic carbohydrates.

PRECAUTIONS

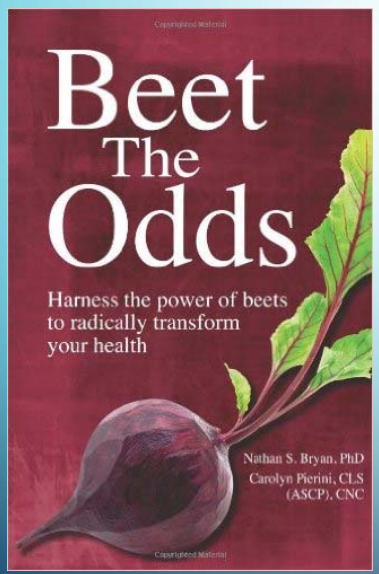
- Certain medications **may adversely interact** with a high-nitrate diet, including organic nitrate or nitrite drugs used for angina and PDE-5 inhibitors such as
- sildenafil citrate,
- tadalafil,
- Vardenafil
- Best to consult your doctor

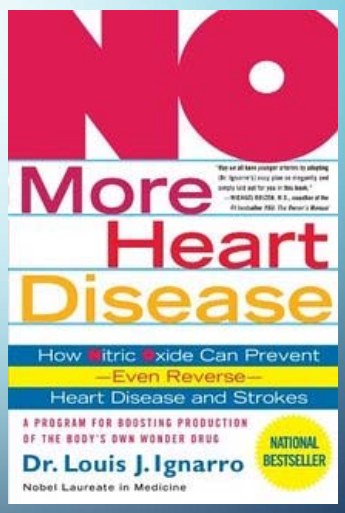


Book Highlights:

Restoring nitric oxide production in the body thereby combating:

- High blood pressure
- Heart attack
- Stroke
- Diabetes
- Arthritis
- Kidney disease
- Memory loss
- Osteoporosis





Let's Get Cooking!