Nitric Oxide for the Prevention and Treatment of Cardiovascular Disease with a Splash of Covid 19

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CONFLICTS OF INTEREST

- Co-founder and Shareholder – HumanN, Inc.
- Founder and CEO – Nitric Oxide Innovations, LLC
- Founder and CEO – Pneuma Nitric Oxide, LLC
- Founder and CEO – Bryan Nitriceuticals, LLC
- Shareholder – SAJE Pharma
- Shareholder – DermaShower, LLC
- Consultant – Berkeley Life
- Receives royalties from issued patents from the University of Texas Health Science Center Houston

LEARNING OBJECTIVES:

1. Learn nitric oxide signaling in the human body

2. What goes wrong in people that cannot make nitric oxide and how this contributes to chronic disease

3. Instruct on how to improve nitric oxide in your patients based on real science

“Research is to see what everybody else has seen, and to think what nobody else has thought.”

Albert Szent-Gyorgyi
1937 Nobel Prize for Medicine

SIMPLIFIED THEORY OF DISEASE

All disease is caused by only 2 things:

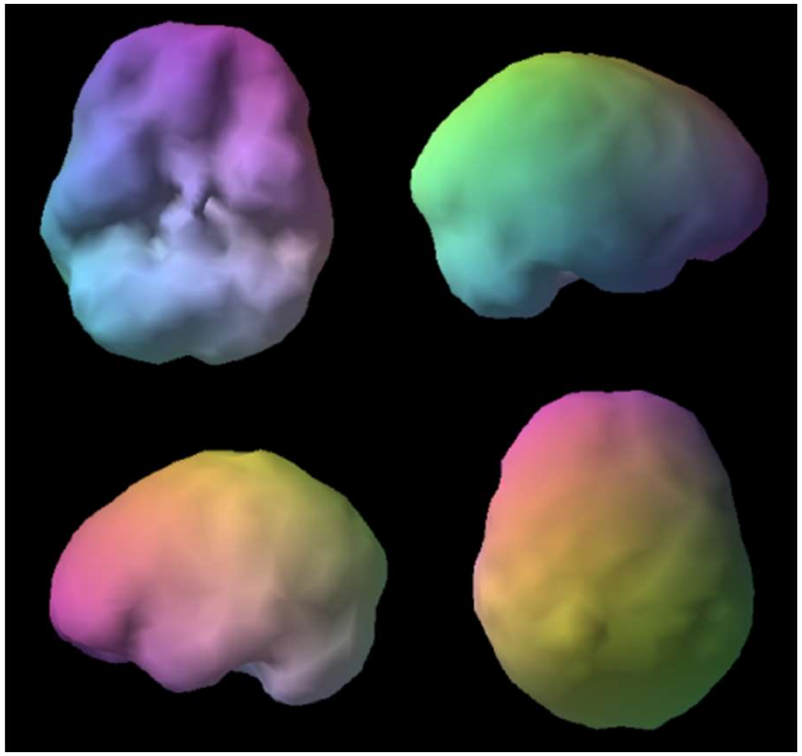
- Body is exposed to a toxin that interrupts normal cellular function
- Body is missing an essential nutrient that disrupts normal cellular function

One of the end results is disruption of N.O. production, decreased circulation, increased Inflammation, oxidative stress and immune dysfunction

SPECT SCANS OF BRAINS

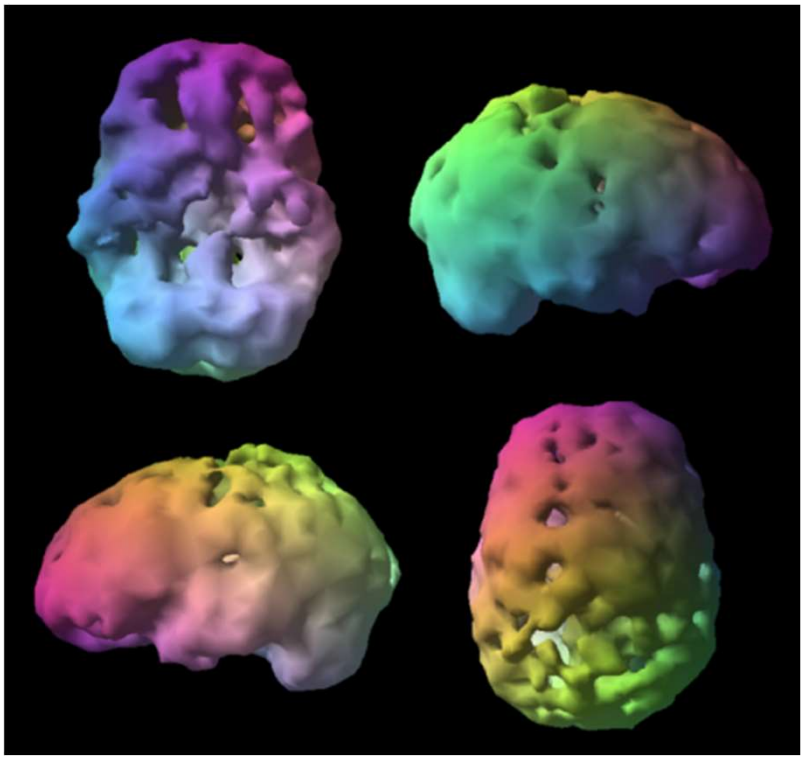
SPECT stands for Single Photon Emission Computed Tomography. It is a nuclear medicine procedure widely used to study heart, liver, thyroid, bone and brain problems. Brain SPECT imaging is a proven, reliable measure of cerebral blood flow. Because brain activity is directly related to blood flow, SPECT effectively shows us the patterns of activity in the brain. SPECT allows physicians to look deep inside the brain to observe three things: areas of the brain that work well, areas of the brain that work too hard and areas of the brain that do not work hard enough.

www.amenclinics.com



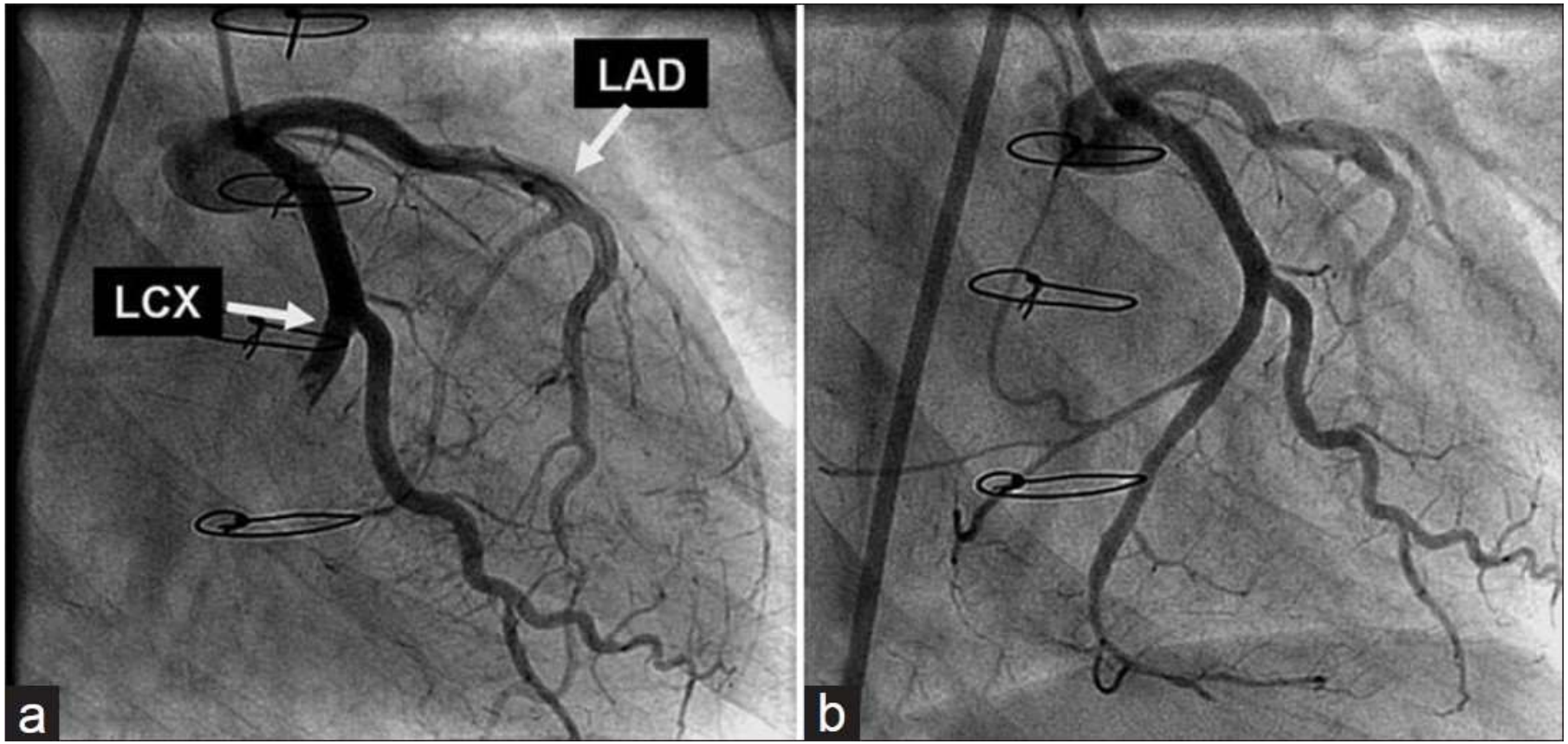
A HEALTHY BRAIN

On SPECT, the surface of a healthy brain looks smooth with full and symmetrical blood flow and activity. This tells us that the brain is working the way it is supposed to.



AN UNHEALTHY BRAIN

This SPECT image of an unhealthy brain reveals many “holes” on the surface, which represent areas of low blood flow and poor activity because of damage from substance and alcohol abuse



Invasive coronary angiography that demonstrates total occlusion of the left circumflex coronary artery with filling defect suggestive of thrombus

TIMI 3 flow was restored after repeated aspirations of the thrombus

Alsaileek A, et al Heart Views 2012;13:111-3

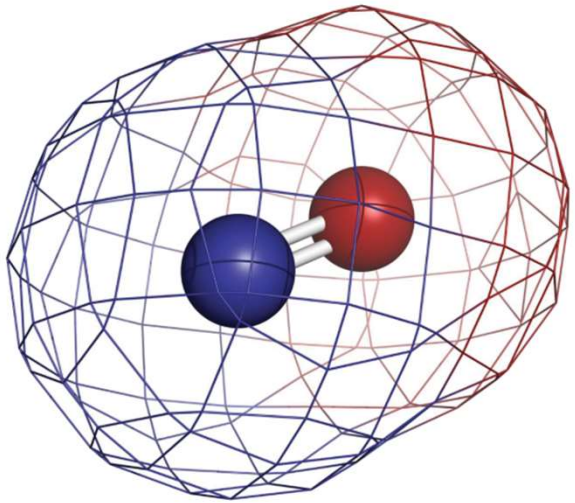
Nitric Oxide Deficiency Causes **Chronic Disease** and **Increases Sickness** and **Mortality** from **Viral Infection**

The most important thing you can do is enhance your body's ability to make **nitric oxide**

Every single **chronic disease** is characterized by **decreased blood flow** to the affected organ/tissue.

If you can restore blood flow and perfusion to every organ, tissue and cell in the body, you can **correct most if not all chronic diseases.**

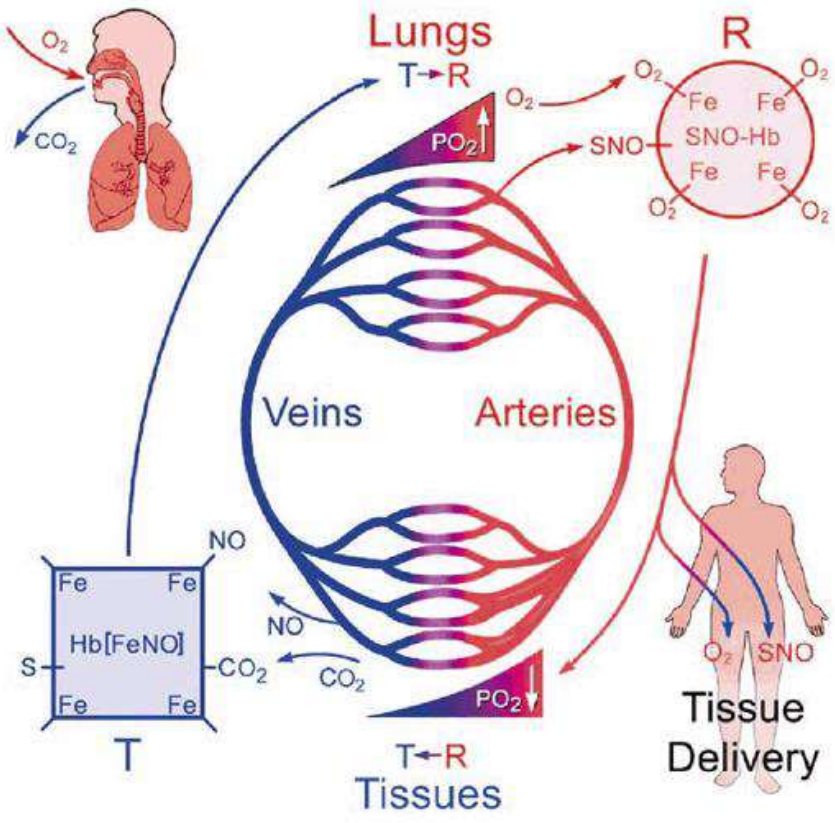
How do we restore blood flow and perfusion to the specific organs and tissue?



NITRIC OXIDE

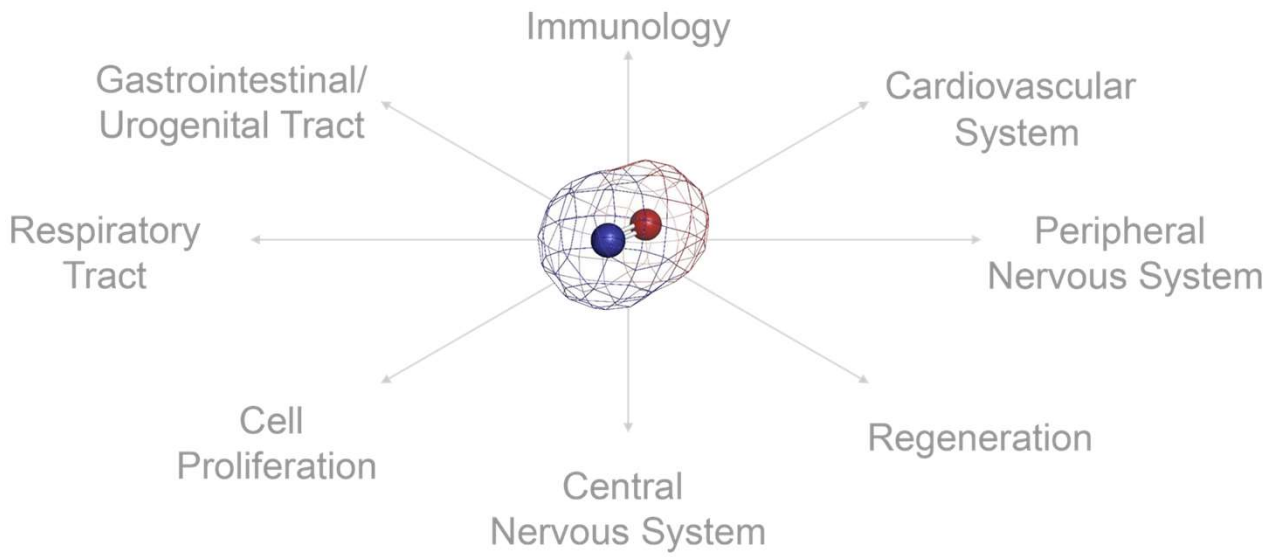
Nitric oxide is required for red blood cell delivery of oxygen from the lungs to tissue.

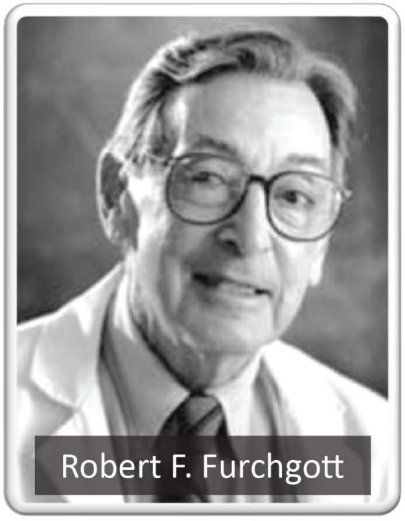
Prof. Stamler says "blood flow to tissues is actually more important in most circumstances than how much oxygen is carried by hemoglobin. The respiratory cycle is actually a three-gas system."



Zhang et al Proc Natl Acad Sci U S A. 2015 May 19;112(20):6425-30

Nitric Oxide Plays a Key Role in the Regulation of Numerous **Vital Biological Functions**



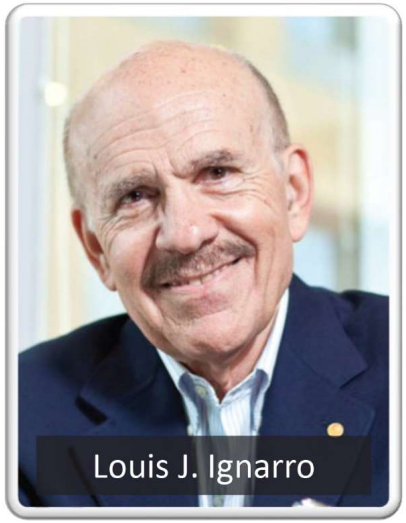


Robert F. Furchgott

1/3 of the prize

USA
SUNY Health Science Center
Brooklyn, NY, USA

Born: 1916



Louis J. Ignarro

1/3 of the prize

USA
University of California School of Medicine - Los Angeles, CA

Born: 1941

Ferid Murad

1/3 of the prize

USA
University of Texas Medical School at Houston, TX, USA

Born: 1936

The Nobel Prize in Physiology 1998

"For their discoveries concerning nitric oxide as a signaling molecule in the cardiovascular system."

Source: Nobel e-Museum
www.nobel.se

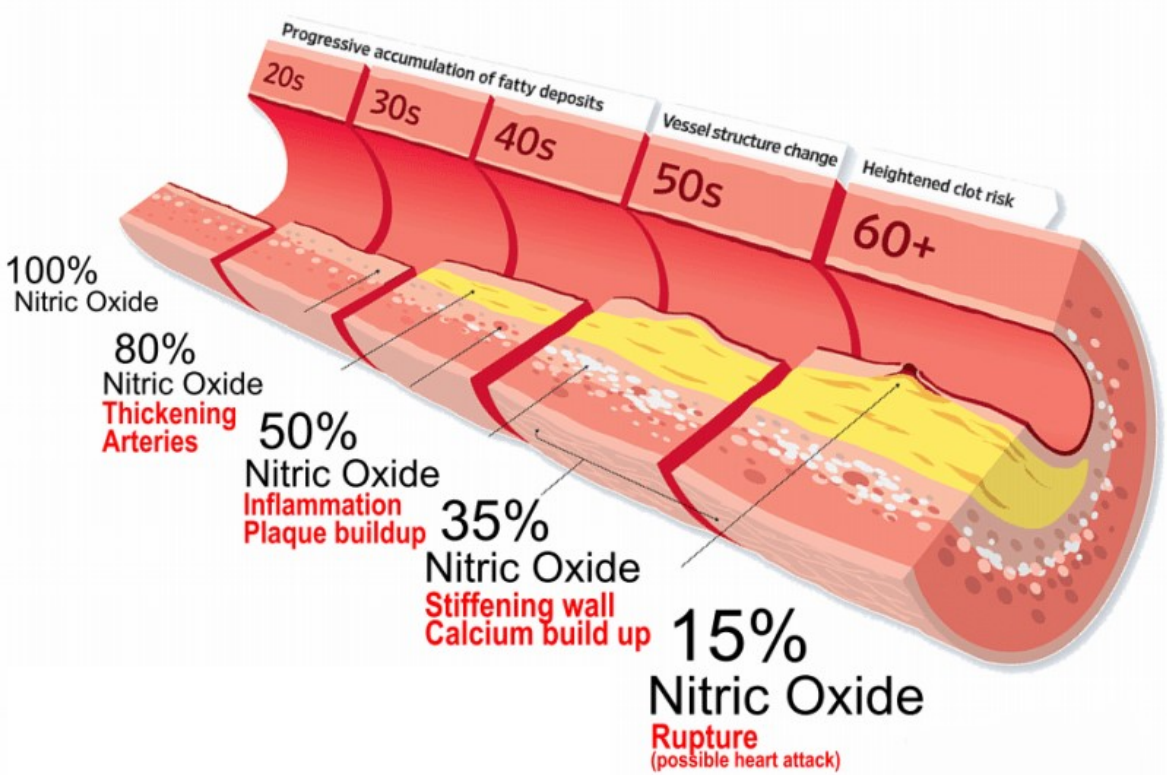
Clinical Consequences of Insufficient **Nitric Oxide Production**

Hypertension
Erectile Dysfunction
Vascular Dementia – Alzheimers
Diabetes
PAD
Small vessel disease
Atherosclerosis
Coagulation Disorders
ARDS
Heart Failure
Acute Kidney Injury – Renal Failure
Immune Dysfunction

Risk factors for COVID, Influenza, etc.

“A man is as old as his arteries”

Thomas Sydenham,
English Physician,
1624-1689



Loss of N.O. is Associated with **Atherosclerosis.**

As we age, we lose 85% of our ability to make nitric oxide.

Bryan NS Curr Atheroscler Rep. 2018 Mar 17;20(5):21

Diabetes by the **Numbers**

34.2 million Americans have diabetes (10.5% of the US population)

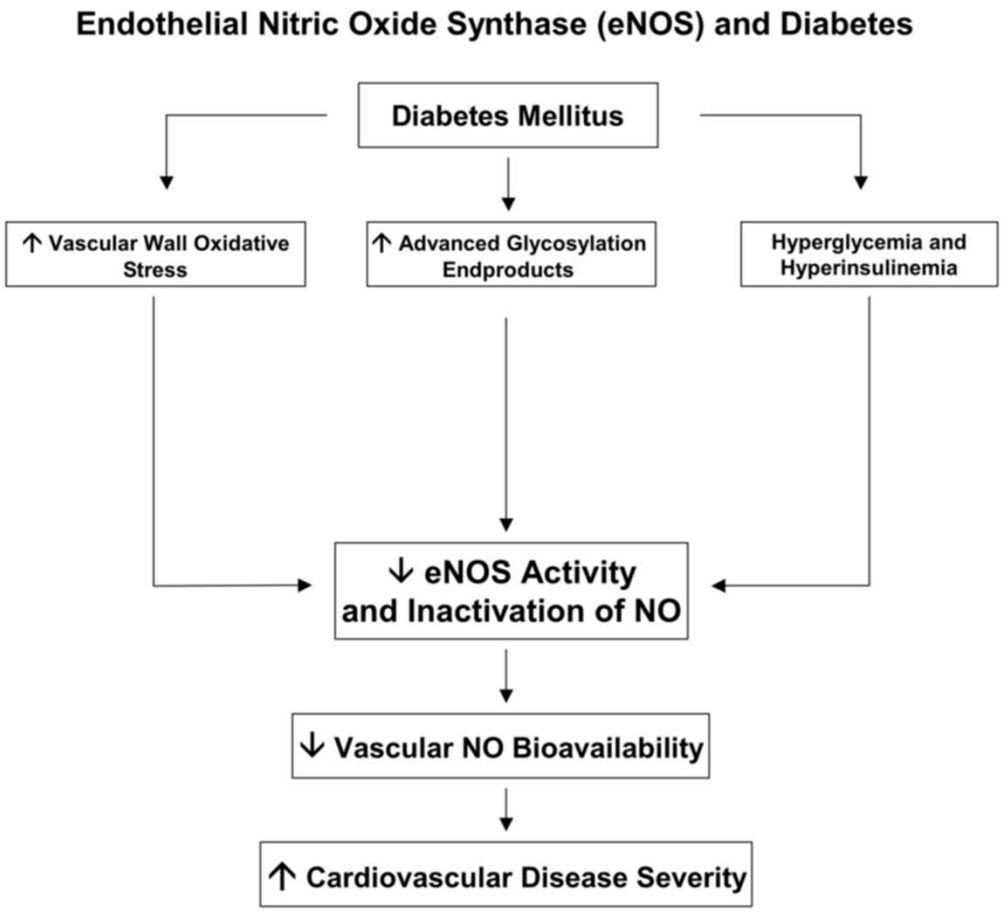
Diagnosed: 26.9 million people, including 26.8 million adults
Undiagnosed: 7.3 million people (21.4% are undiagnosed)

Prediabetes
88 million Americans aged 18 years or older have prediabetes
(34.5% of US)

24.2 million Americans aged 65 years or older have prediabetes

$327 billion: Total cost of diagnosed diabetes in the United States in 2017

Diabetes Leads to Insufficient N.O. Production



Rogers et al Clin Transplant. 2004;18 Suppl 12:7-11

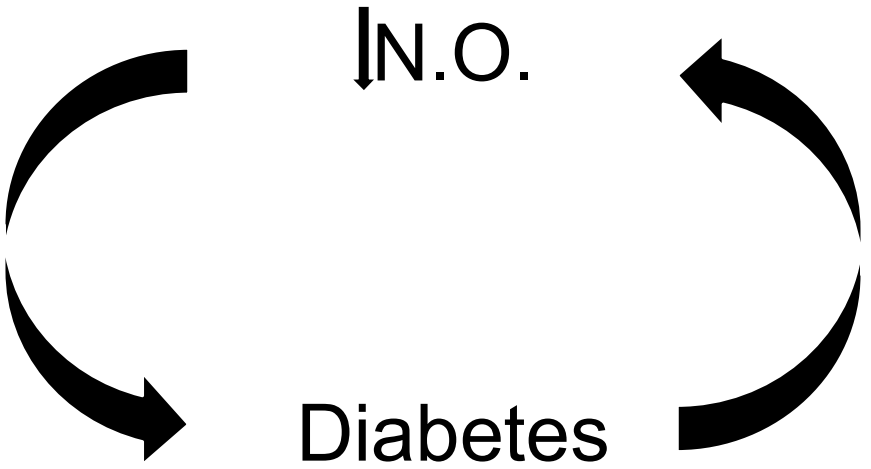
Insufficient N.O. Production
Leads to Diabetes

- eNOS$^{-/-}$ mice display a disturbed blood-glucose concentration curve
- eNOS-/- mice have high proinsulin/insulin ratios
- eNOS-/- mice have higher visceral fat

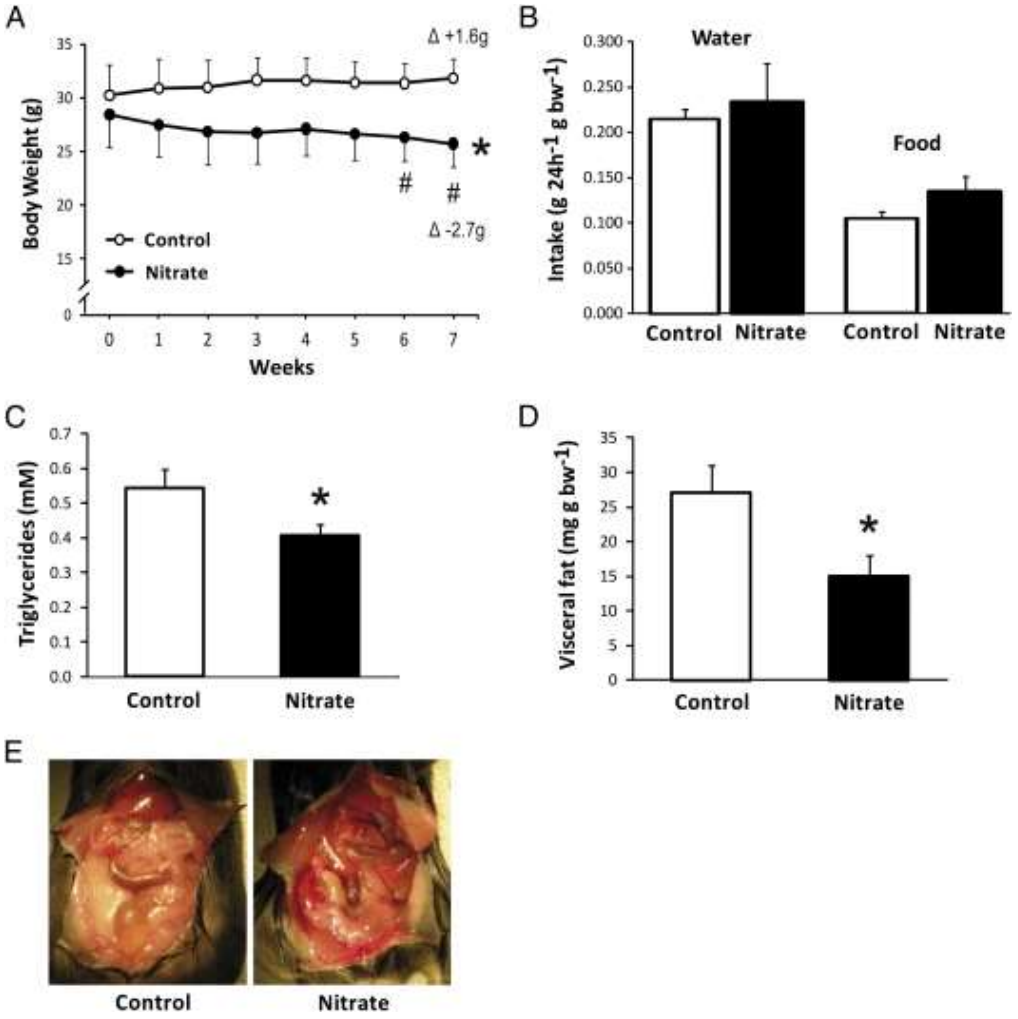
Diabetic patients suffer from higher incidence of hypertension, heart disease and stroke, high blood pressure, blindness, kidney disease, nervous system disease, amputation, and complications of pregnancy and surgery – all conditions associated with insufficient N.O. production.

Hwang et al Nature volume 377, pages239–242 (1995)

Perpetual Cycle of N.O. and Diabetes

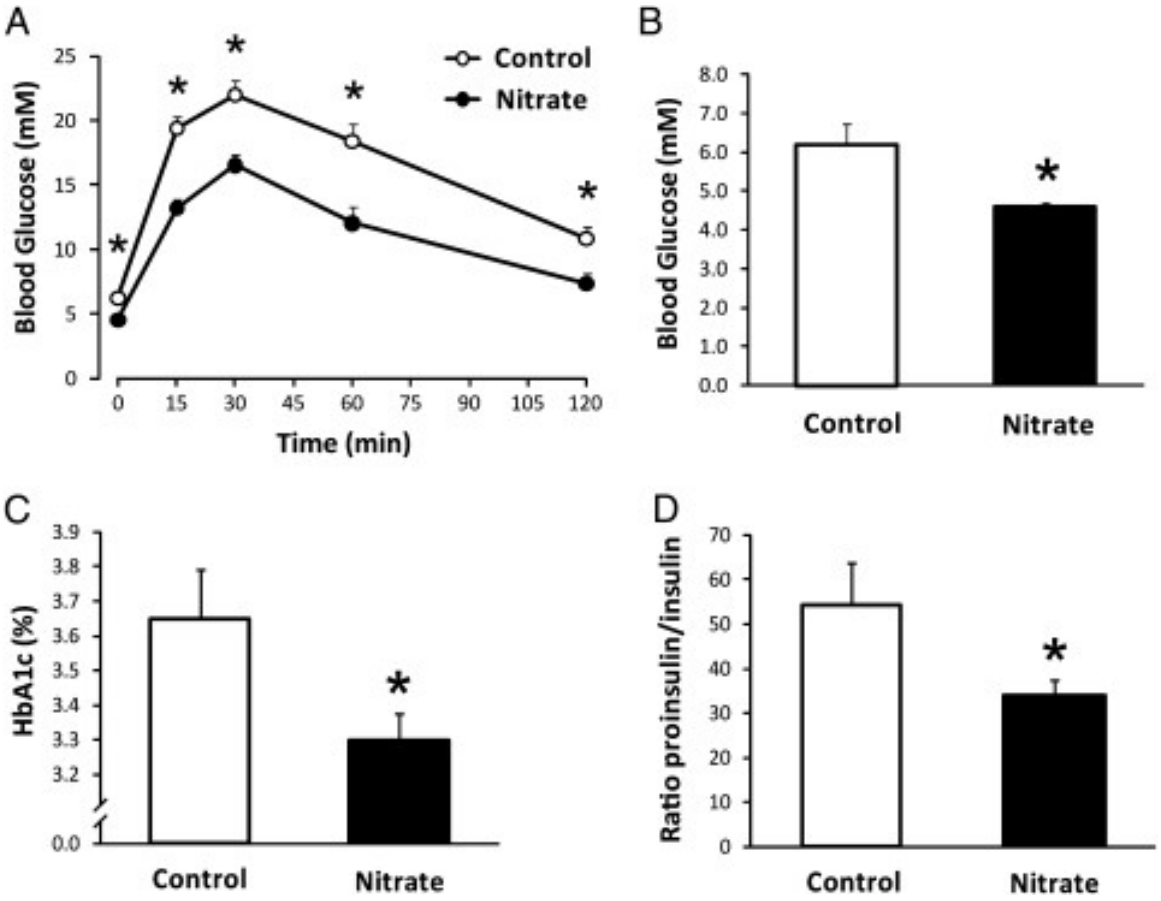


Dietary nitrate **reduces body weight** and **decreases** the amounts of **visceral fat** and circulating triglycerides in eNOS-deficient mice



Carlstrom et al, Proc Natl Acad Sci U S A. 2010 October 12; 107(41): 17716–17720.

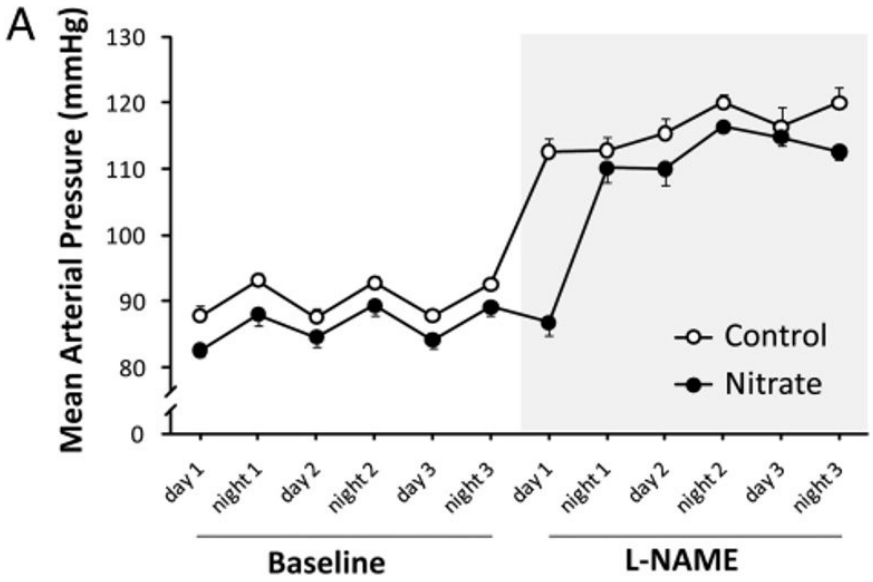
Dietary nitrate **improves glucose tolerance** and **reduces fasting blood glucose** in eNOS-deficient mice.

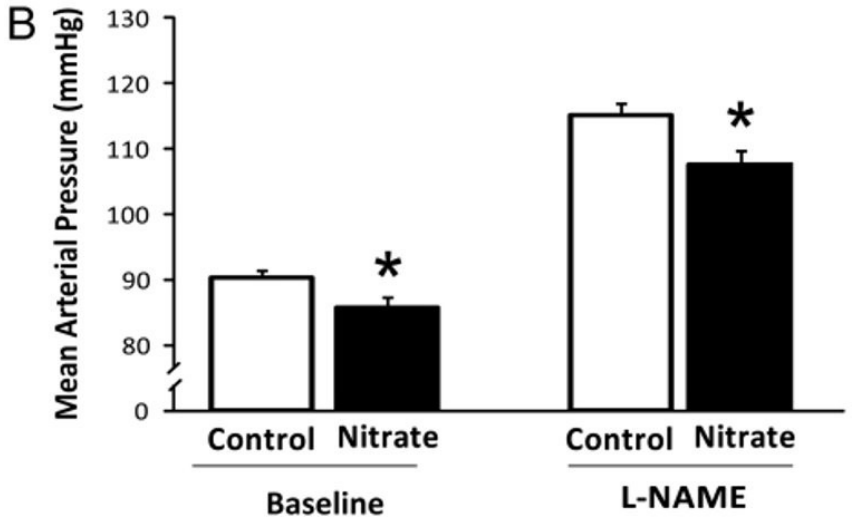


Carlstrom et al, Proc Natl Acad Sci U S A. 2010 October 12; 107(41): 17716–17720.

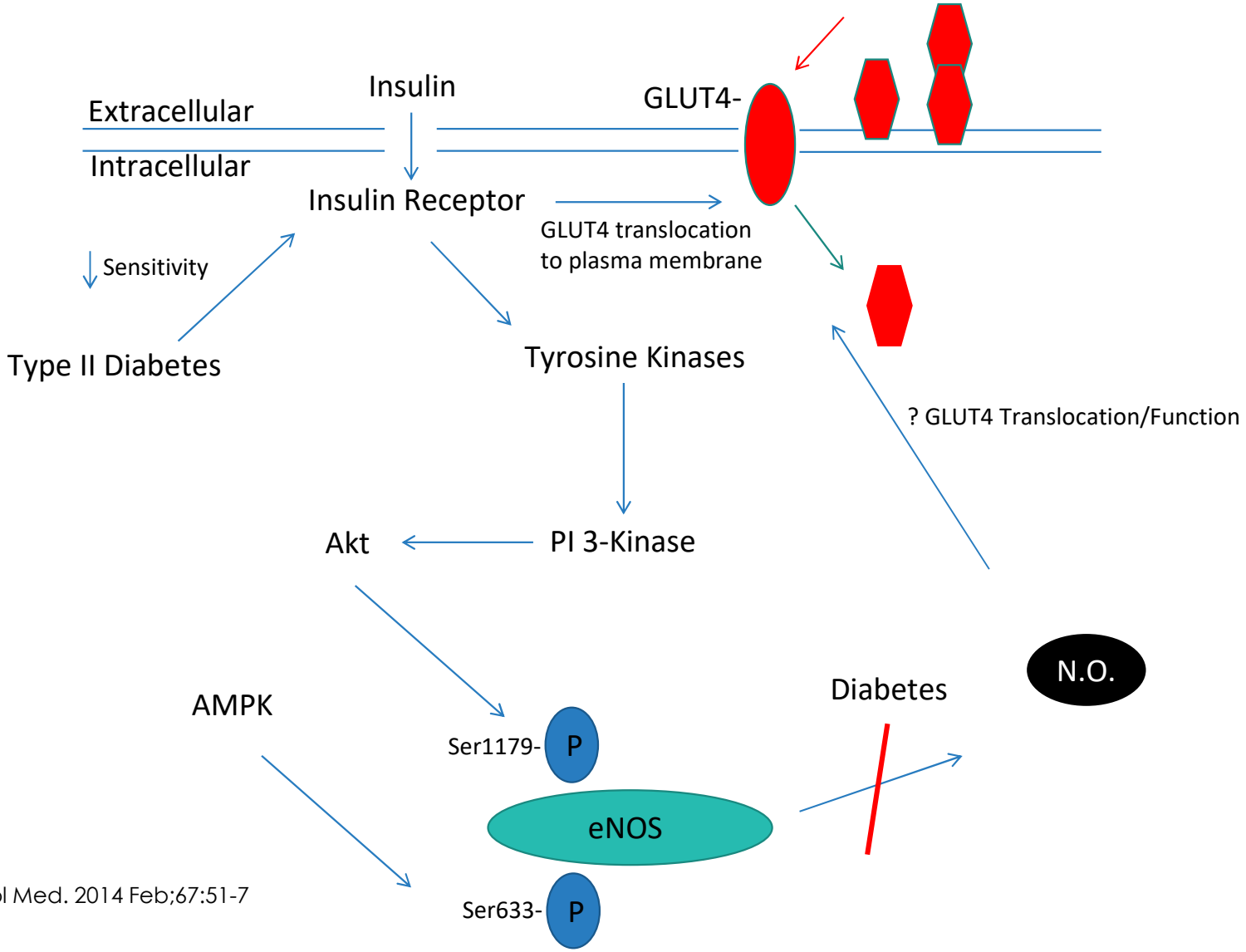
Effects of dietary nitrate on **blood pressure**.

water (control) or water supplemented with sodium nitrate (0.1 mmol·kg−1·d−1) for 8 wk.

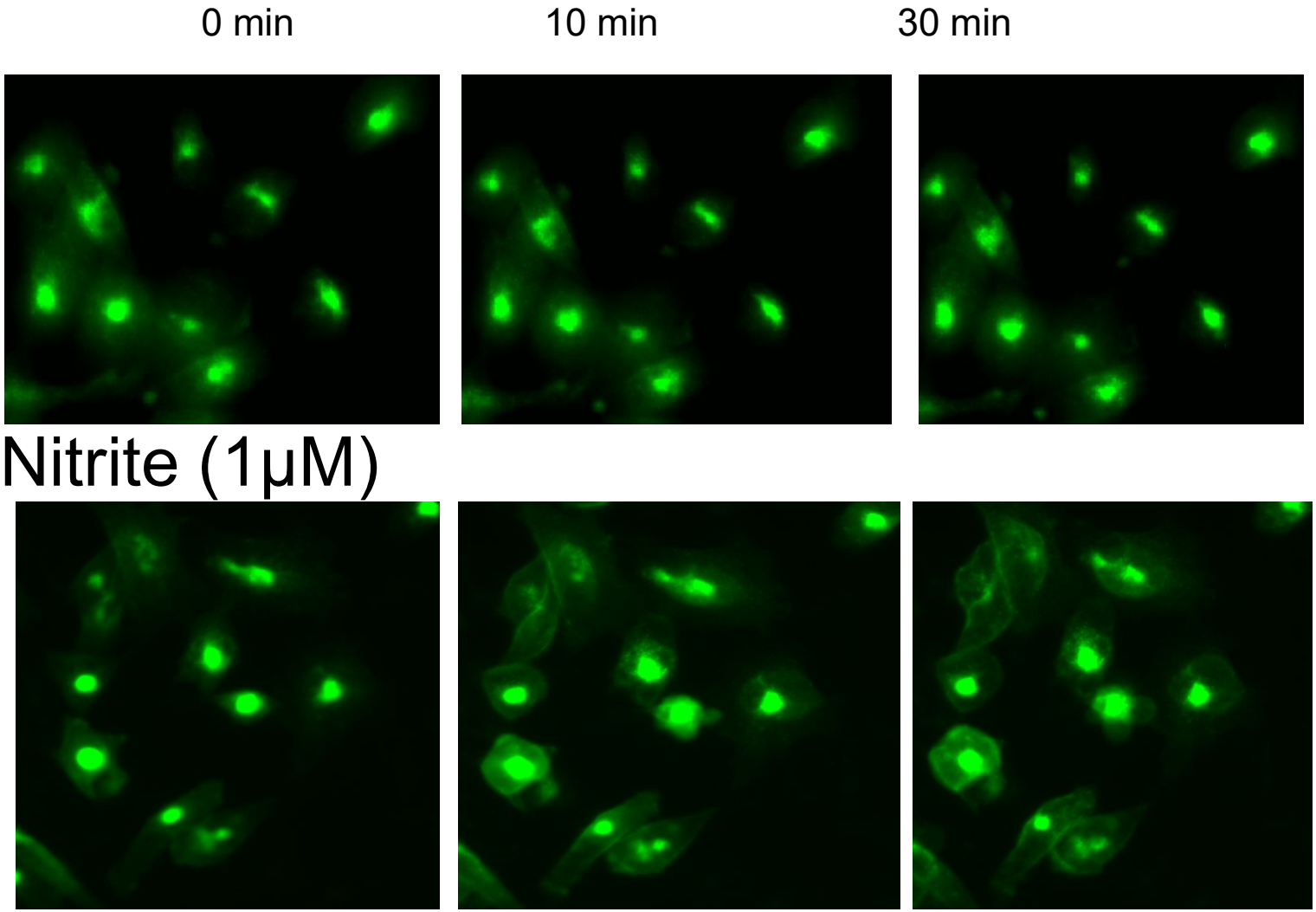




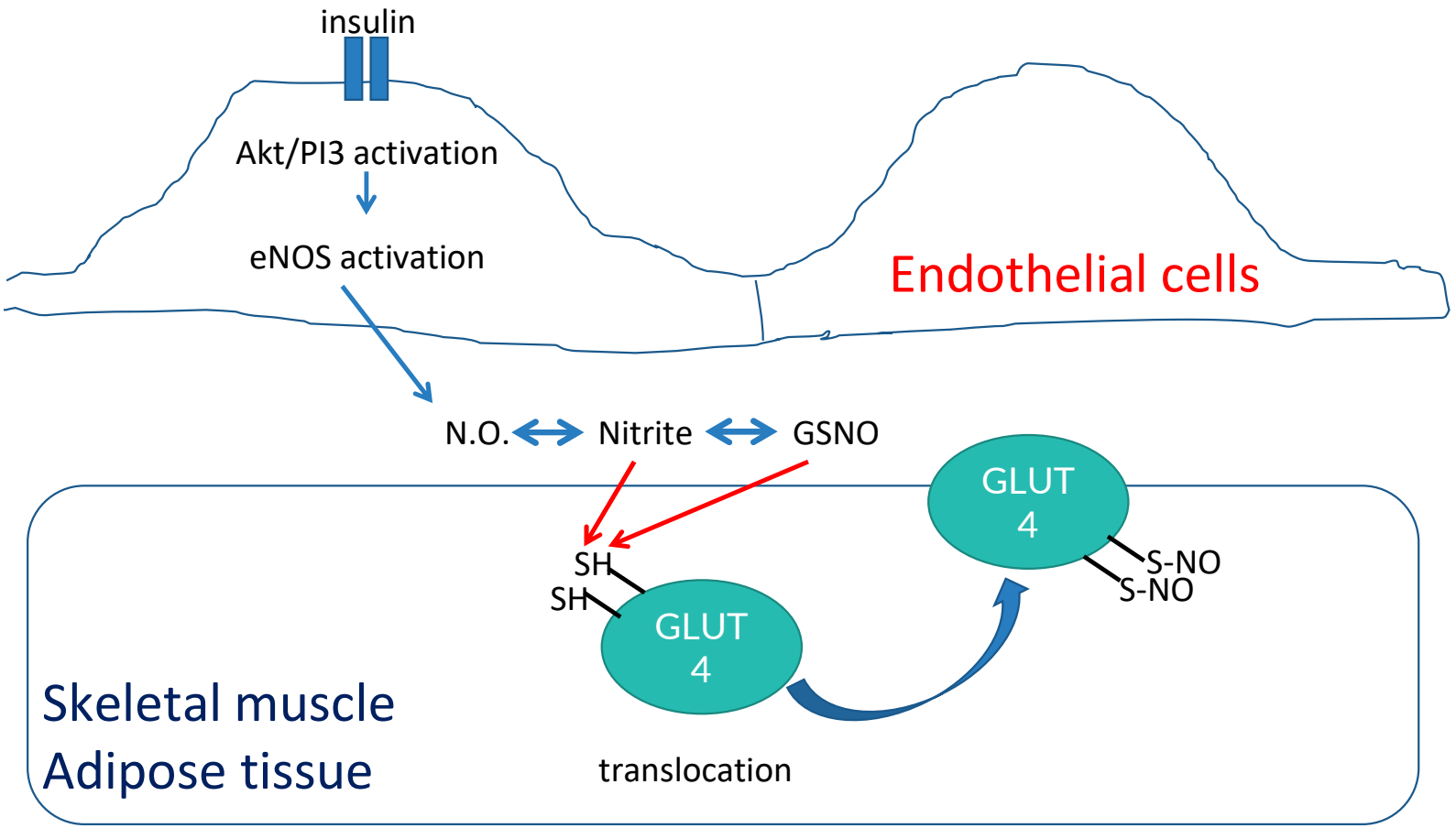
Carlstrom et al, Proc Natl Acad Sci U S A. 2010 October 12; 107(41): 17716–17720.



Jiang et al Free Radic Biol Med. 2014 Feb;67:51-7



Jiang et al Free Radic Biol Med. 2014 Feb;67:51-7



Jiang et al Free Radic Biol Med. 2014 Feb;67:51-7

Nitric oxide synthase-derived plasma nitrite predicts exercise capacity

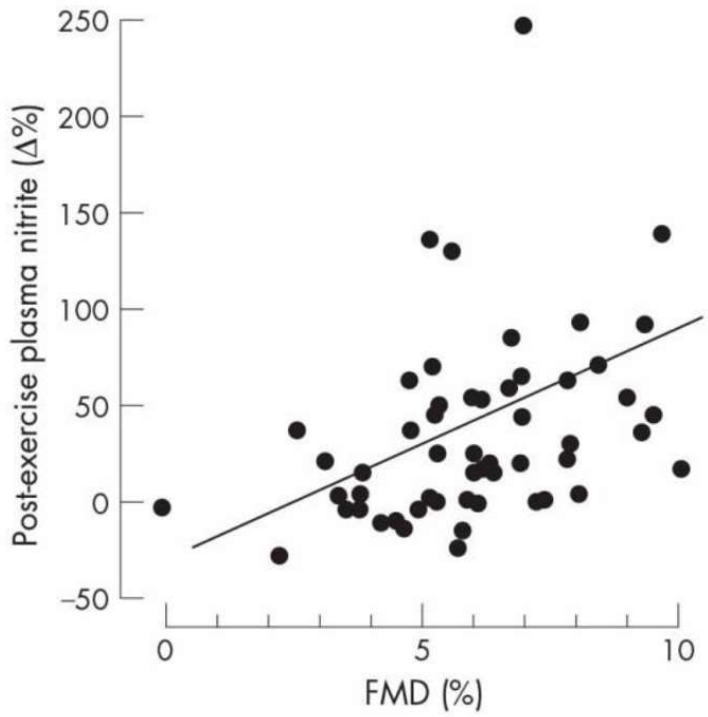


Figure 1 Correlation of percentage increases in plasma nitrite after ergometric exercise with flow-mediated dilation (FMD) ($r = 0.36$; $p = 0.01$).

Rassaf T, et al
Br J Sports Med 2007;41:669–673

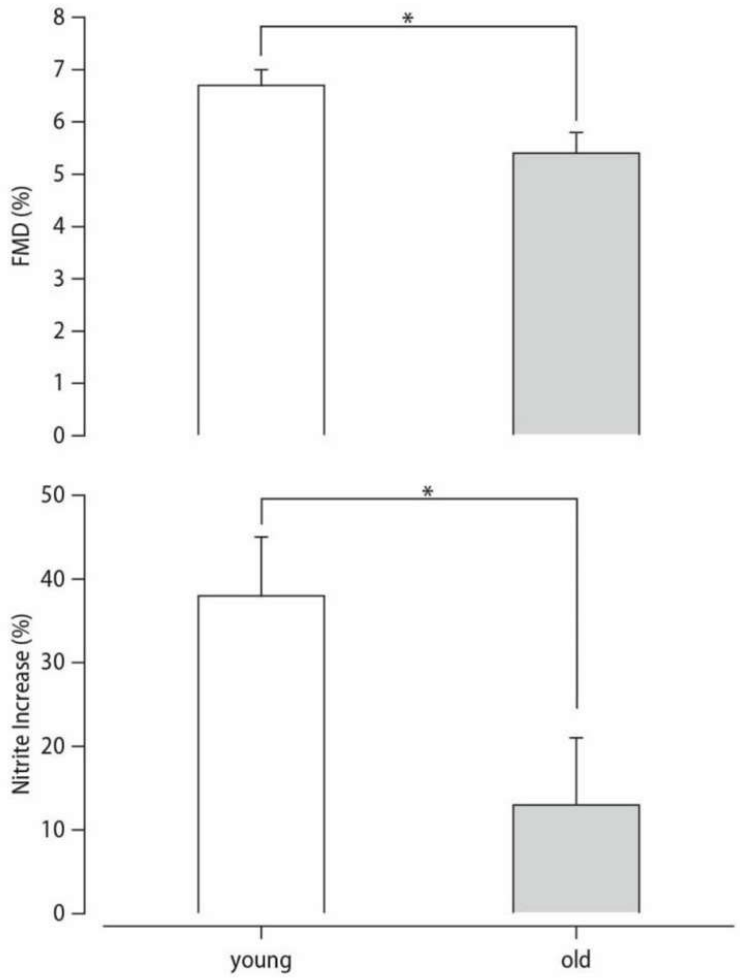


Fig. 1 Brachial artery flow mediated dilation (FMD) at baseline (*upper panel*) and changes in plasma nitrite after exercise (*lower panel*) in young and old subjects. *Asterisks* indicate significantly different at the $P < 0.05$ level

Age-dependent endothelial dysfunction is associated with failure to increase plasma nitrite in response to exercise

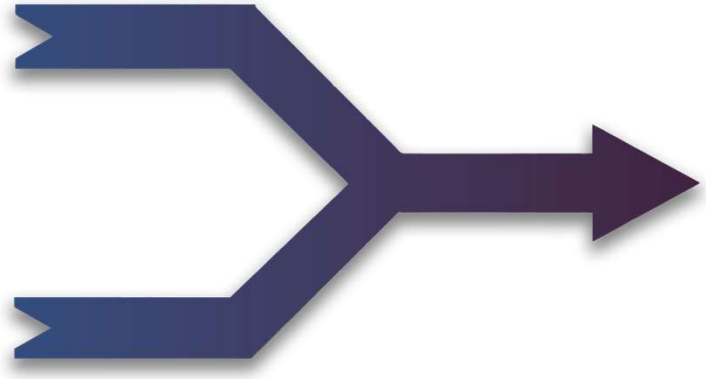
Lauer et al

Basic Res Cardiol 103:291–297 (2008)

How do we **control** and **regulate** **Nitric Oxide** production?

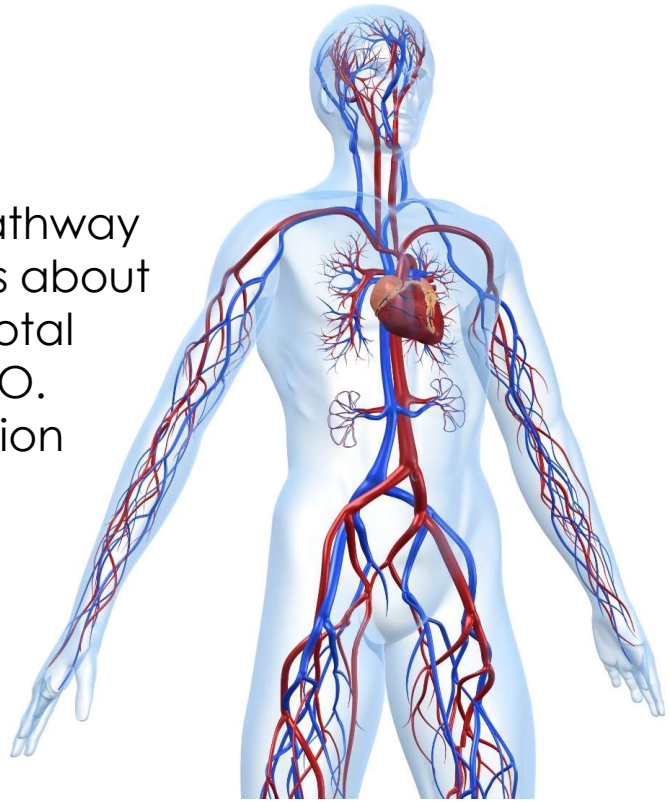
TWO NITRIC OXIDE PATHWAYS

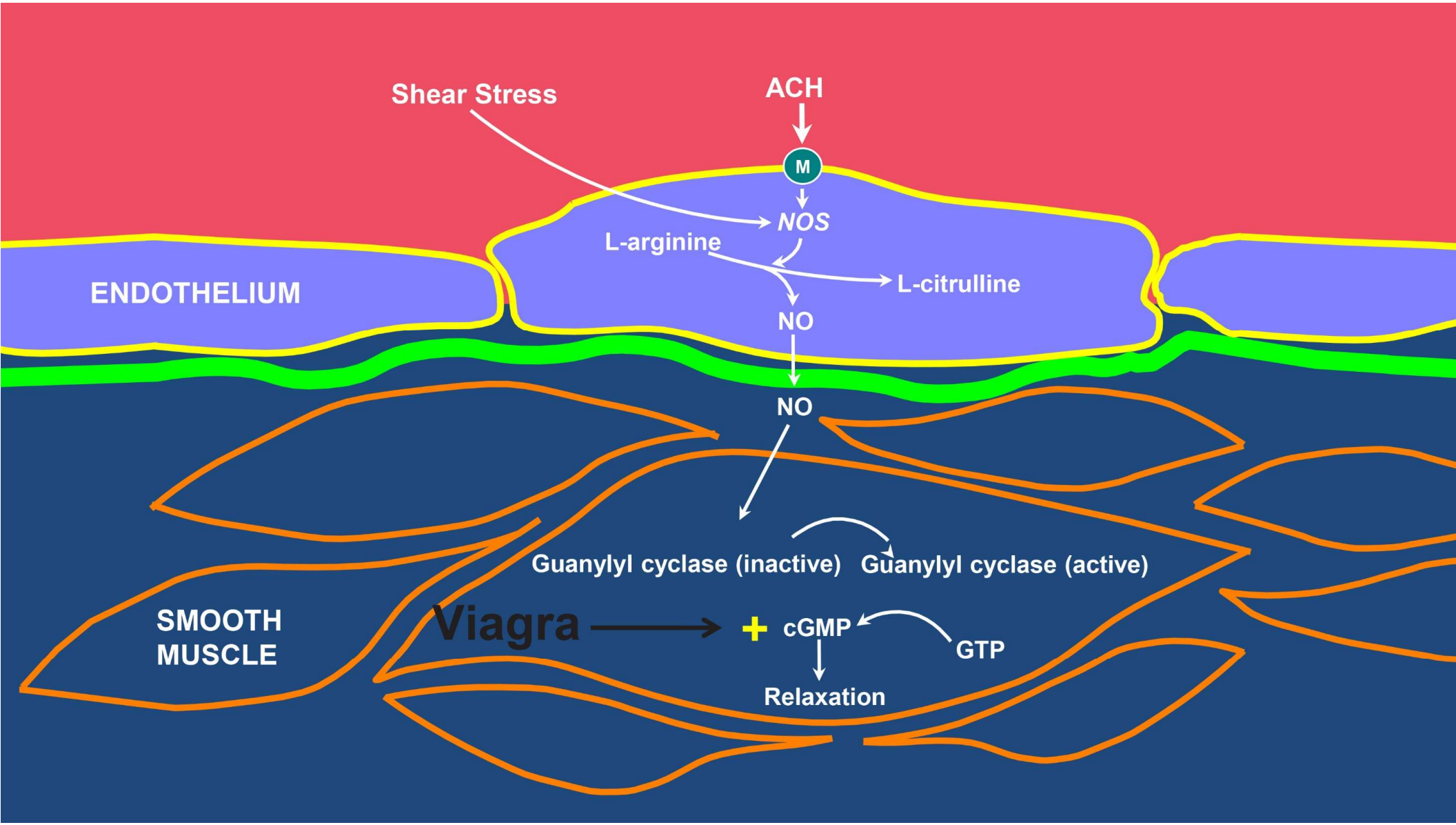
1. Oxidation of L-arginine (NOS)



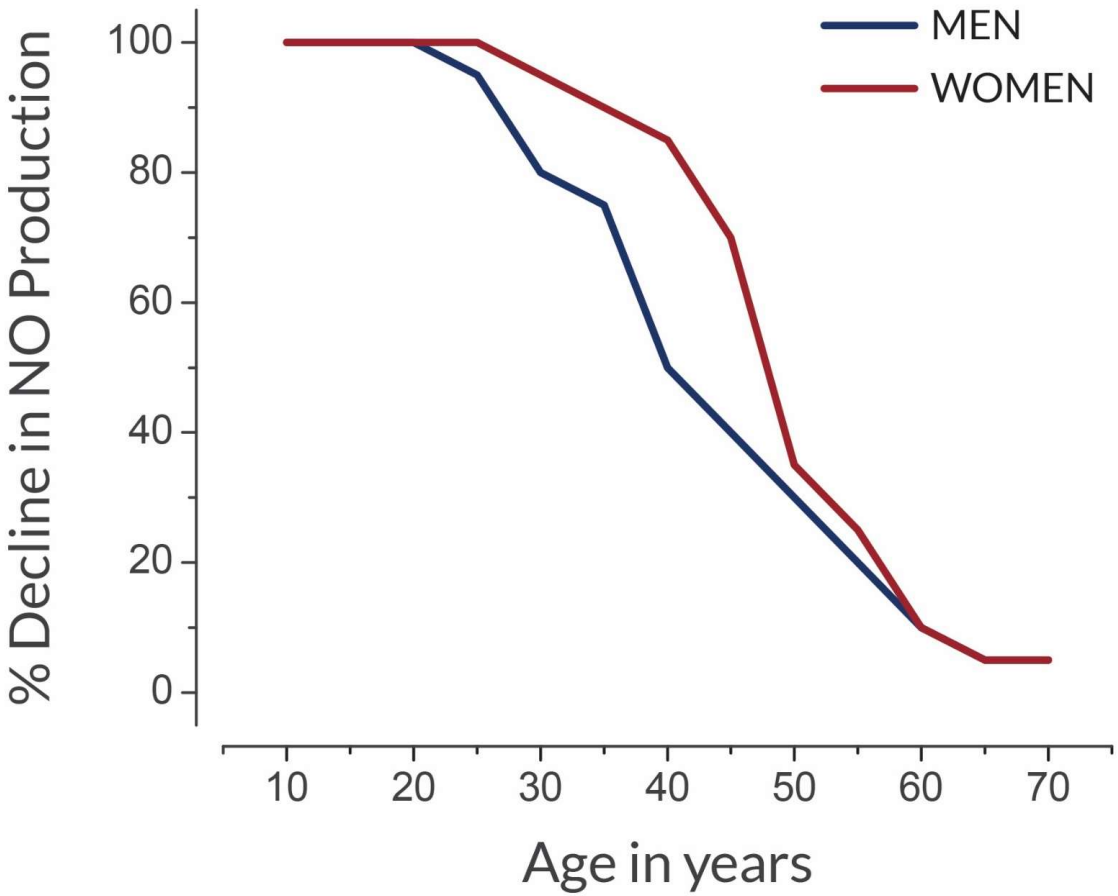
2. Nitrate-Nitrite-Nitric Oxide

Each pathway provides about 50% of total body N.O. production




Shear Stress
ACH
M
NOS
L-arginine
L-citrulline
ENDOTHELIUM
NO
NO
Guanylyl cyclase (inactive)
Guanylyl cyclase (active)
SMOOTH
MUSCLE
Viagra
+
cGMP
GTP
Relaxation

Endothelial Production of N.O. Declines with Age



Gerhard et al Hypertension 1996

Celermajer et al JACC 1994

Taddei et al Hypertension 2001

Egashira et al Circulation 1993

Can proper nutrition, food or Supplements provide N.O. support?

Atmospheric Nitrogen Cycle

The store of nitrogen found in the atmosphere, where it exists as a gas (mainly N2), plays an important role for life. Most plants can only take up nitrogen in two solid forms: ammonium ion (NH4+) and the nitrate ion (NO3-). Most plants obtain the nitrogen they need as nitrate from the soil. When released, most of the ammonium is often chemically altered by a specific type of bacteria (genus Nitrosomonas) into nitrite (NO2-). Further modification by another type of bacteria (genus Nitrobacter) converts the nitrite to nitrate. All nitrogen obtained by animals can be traced back to the eating of plants at some stage of the food chain.

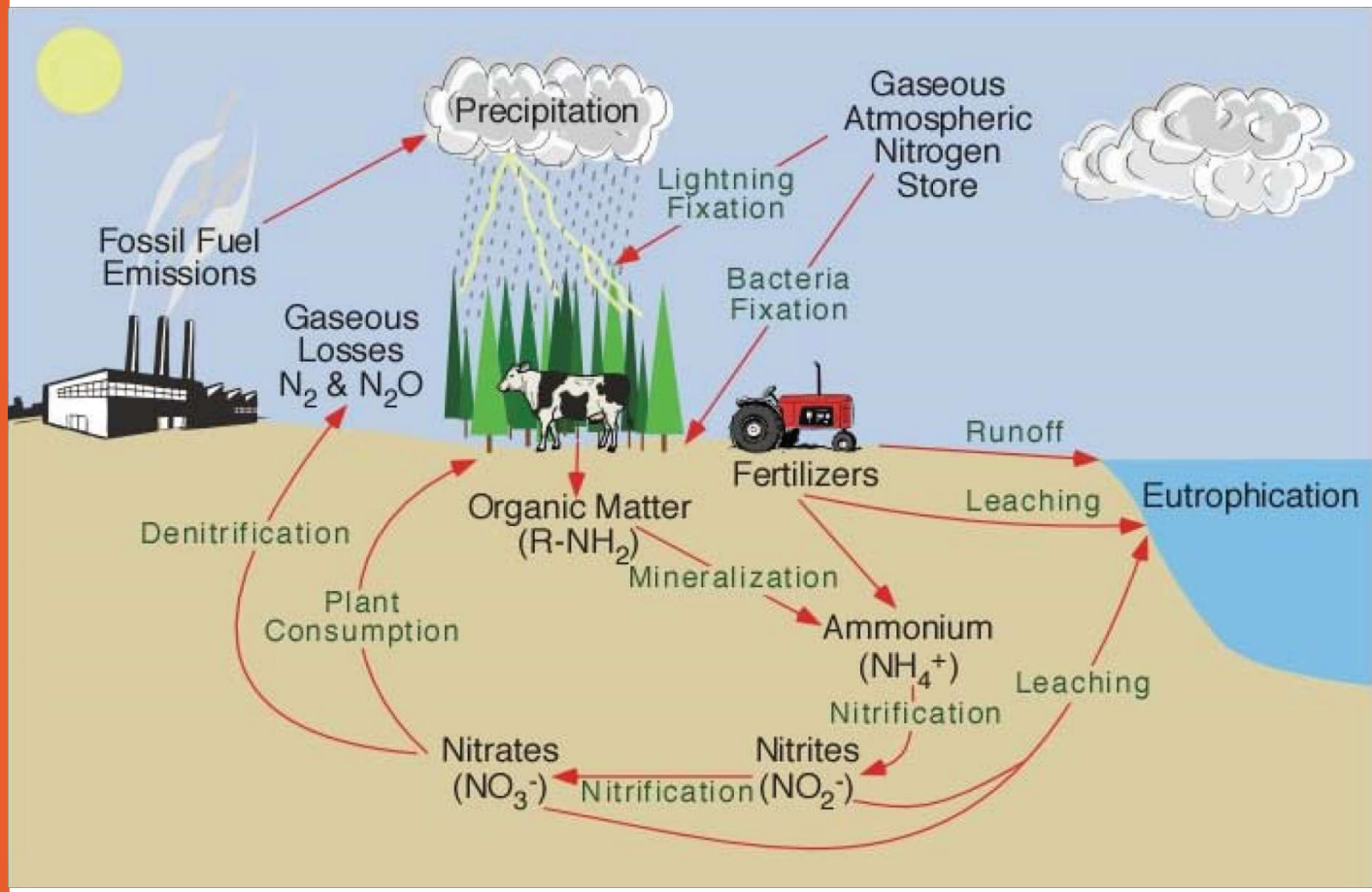
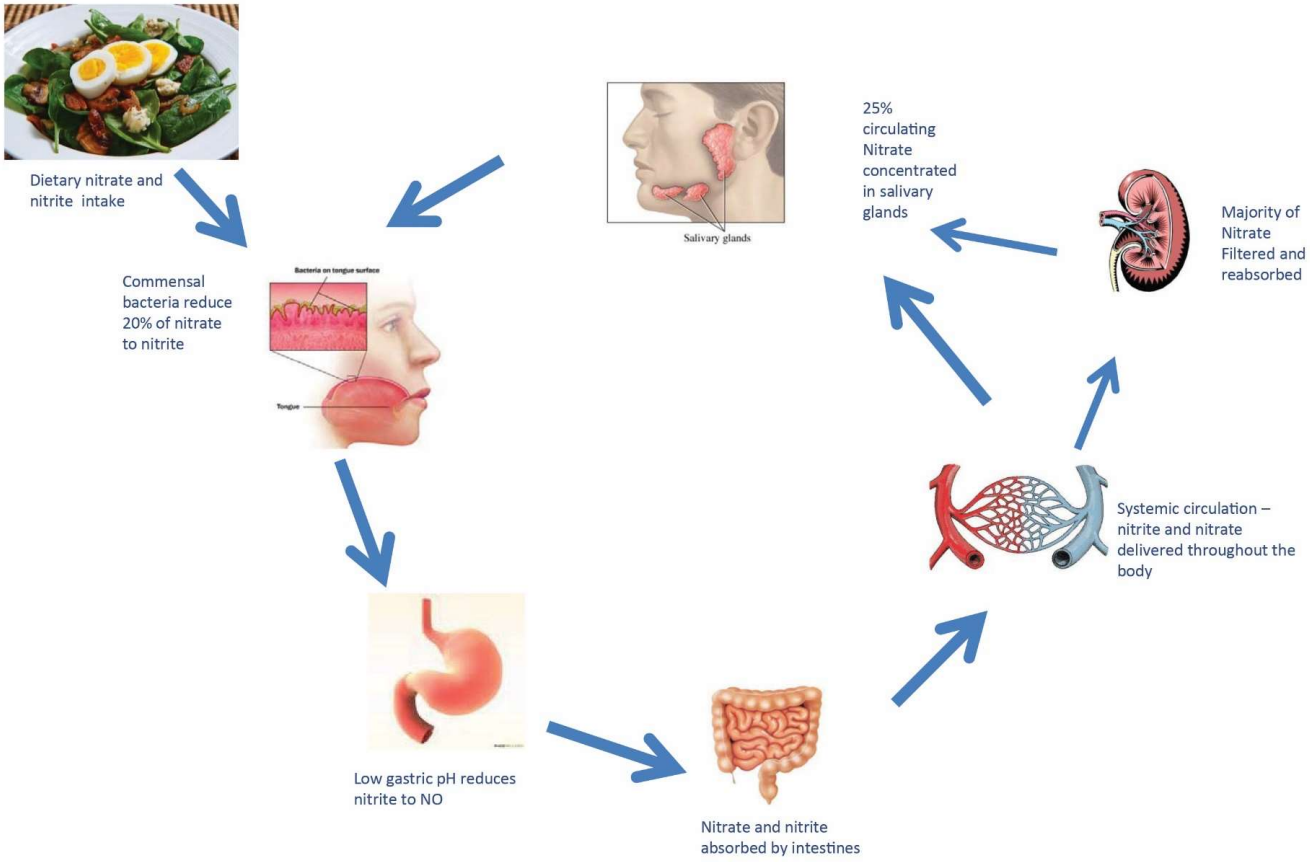


Image from wikipedia.com

New Paradigm - **Human Nitrogen Cycle**



How Much **Nitrate** Do We Need?

300-400 mg nitrate necessary to see changes in blood pressure or improvement in exercise capacity

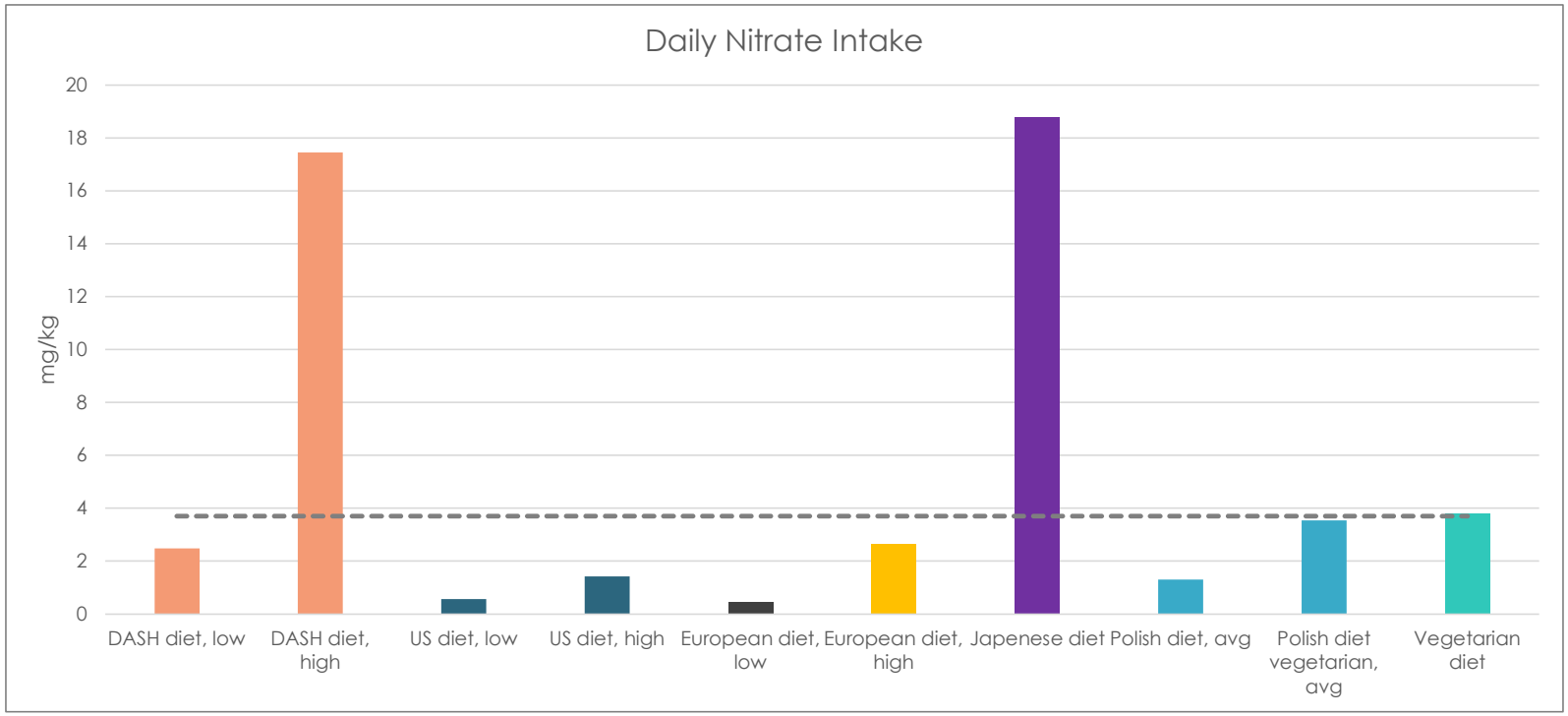
Estimated that US population consumes ~150 mg nitrate per day (over 2-3 meals)

• • •

We are a Nitrate Deficient Population

Bryan NS Nutr Res. 2015 Aug;35(8):643-54

Comparison of Daily Nitrate Intake Values



The data presented above was collected from published literature as follows: DASH, US, and European diets as cited in Hord et al, 2009; Japanese diet as presented in Sobko, et al 2010; Polish diets as presented and cited in Mitek et al 2013; and Vegetarian diet as cited in Lidder and Webb, 2012.

A Survey of **Nitrate and Nitrite Concentrations** in Conventional and Organic-Labeled Raw Vegetables at Retail

Regional and Category Differences In **Conventional Vegetable Nitrate Values**

Table 2. Mean nitrate (NO_3?) concentrations[a] (ppm)[b] of raw vegetables classified as conventional from each city

Product category	Chicago	Dallas	Los Angeles	New York	Raleigh
Broccoli	271 ± 89 (61-822)	357 ± 50 (165-664)	512 ± 85 (164-1140)	279 ± 80 (29-1009)	553 ± 28 (374-680)
Cabbage	475 ± 46 (256-670)	256 ± 33 (63-434)	800 ± 142 (275-1831)	193 ± 28 (37-283)	364 ± 79 (72-882)
Celery	230 ± 19 (147-359)	2052 ± 156 (918-2973)	2651 ± 339 (608-4269)	88 ± 17 (20-157)	2201 ± 112 (1397-2727)
Lettuce	207 ± 32 (79-425)	1370 ± 93 (870-1909)	1051 ± 122 (422-1495)	568 ± 93 (321-970)	986 ± 185 (450-2171)
Spinach	647 ± 69 (162-875)	4923 ± 327 (2377-6473)	4138 ± 451 (2141-8000)	564 ± 174 (65-1545)	3155 ± 145 (2478-4168)

[a]Mean value with standard error; minimum and maximum nitrate values in parentheses.
[b]mg/ kg of fresh weight.

Nunez de Gonzales et al J Food Sci. 2015 May;80(5):C942-9

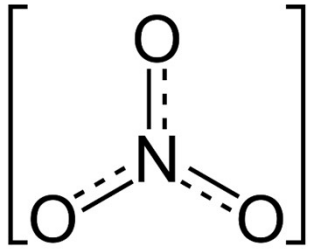
Regional and Category Differences In **Organic Vegetable Nitrate Values**

Product category	Chicago	Dallas	Los Angeles	New York	Raleigh
Broccoli	212 ± 35 (84-417)	430 ± 40 (225-683)	196 ± 47 (44-501)	167 ± 53 (11-502)	8 ± 2 (3-22)
Cabbage	53 ± 12 (2-107)	989 ± 166 (71-1472)	612 ± 85 (335-1365)	898 ± 191 (3-2114)	167 ± 18 (94-271)
Celery	310 ± 58 (26-597)	390 ± 139 (0.7-1453)	2022 ± 208 (1196-3589)	807 ± 208 (11-2053)	1023 ± 69 (598-1461)
Lettuce	100 ± 8 (58-159)	1367 ± 99 (989-2013)	1277 ± 73 (1029-1702)	780 ± 111 (347-1595)	692 ± 28 (567-869)
Spinach	459 ± 48 (238-744)	1610 ± 209 (488-2941)	2199 ± 237 (1075-3820)	1566 ± 384 (16-4089)	755 ± 101 (399-1362)

Nunez de Gonzales et al J Food Sci. 2015 May;80(5):C942-9

Nitrate is inert in Humans.

Nitrate must be reduced to nitrite by commensal bacteria.



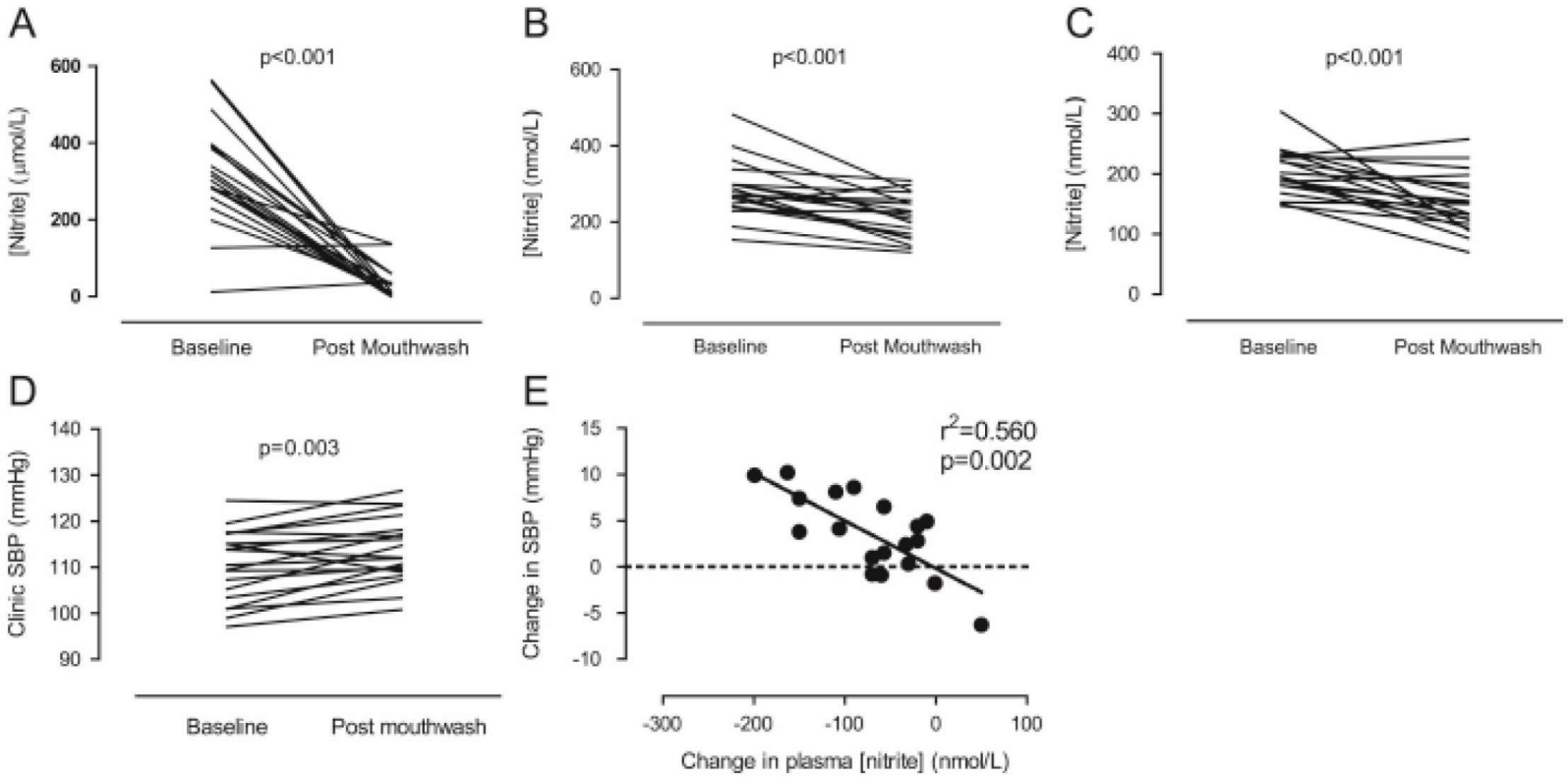
200 million Americans use mouthwash daily

200 million Americans use antacids daily

200 million prescriptions for antibiotics every year

Bryan NS Pharmacol Res. 2012 Dec;66(6):448-56

Physiological Role for Nitrate-Reducing Oral Bacteria in **Blood Pressure Control**



Kapil et al Free Radic Biol Med. 2013 Feb;55:93-100

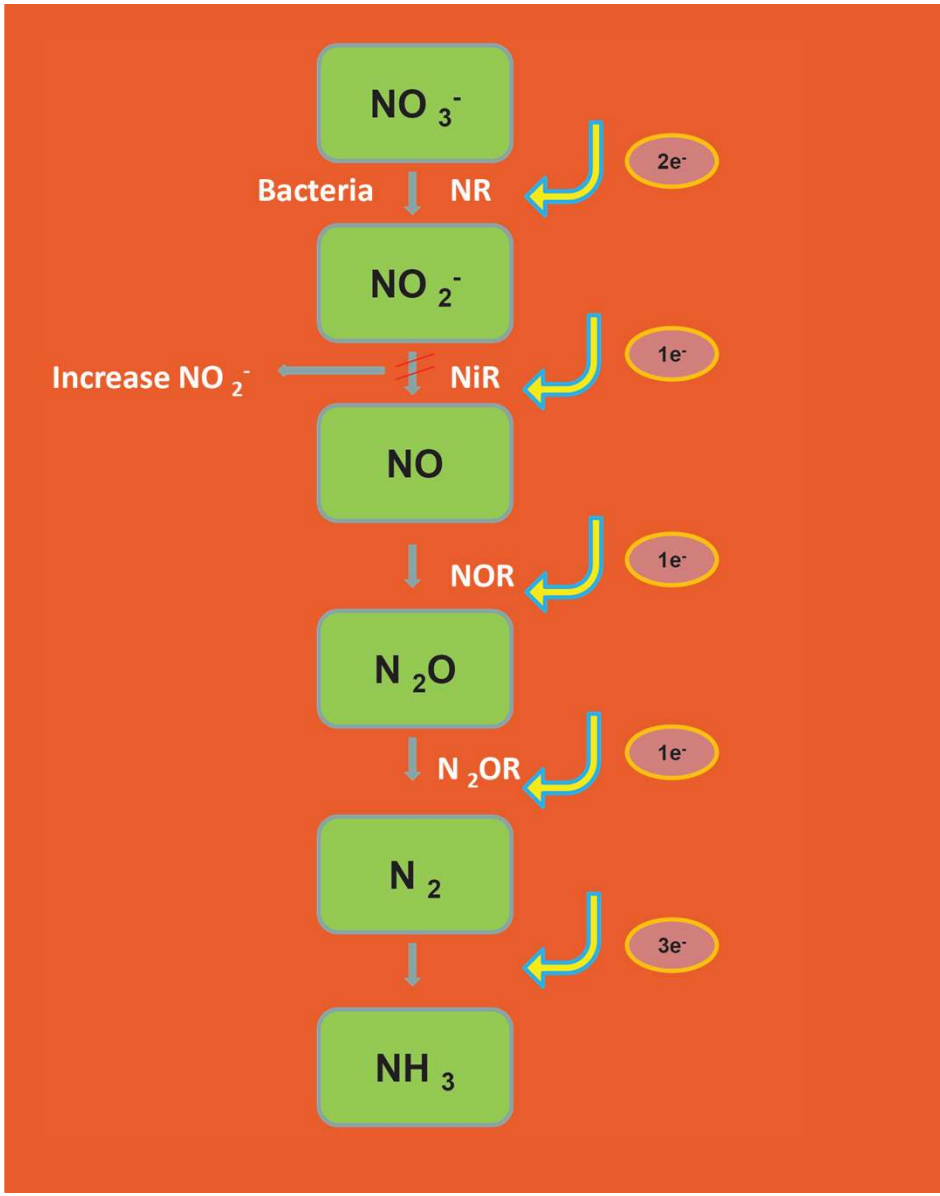
Genetic Diversity

23,000 genes

3,000,000 genes

Ideal Community:

- Higher Nitrate reduction efficacy
- No NiR enzyme; Nitrite can accumulate, enrich saliva to form N.O. when swallowed.



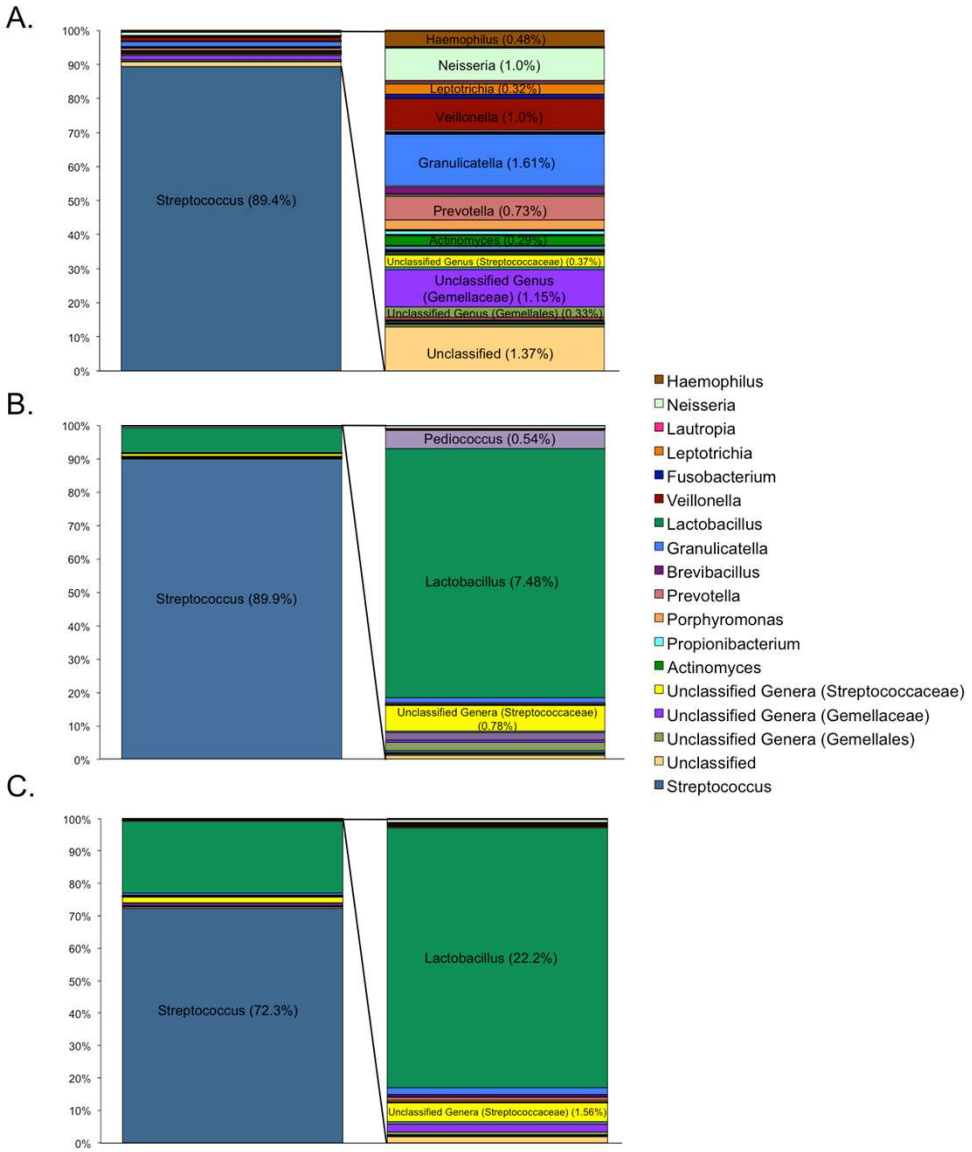
Hyde et al PLoS One (2014)

Best

Intermediate

Worst

Hyde et al PLoS One (2014)

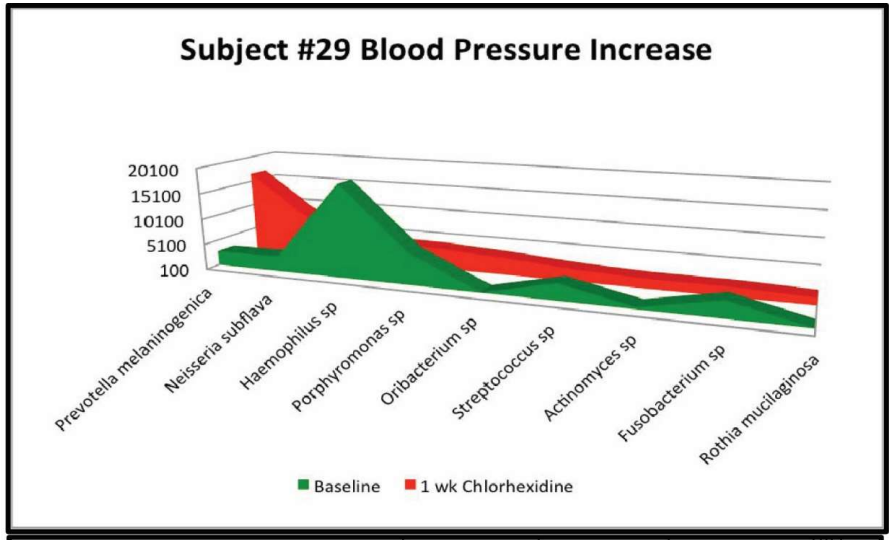


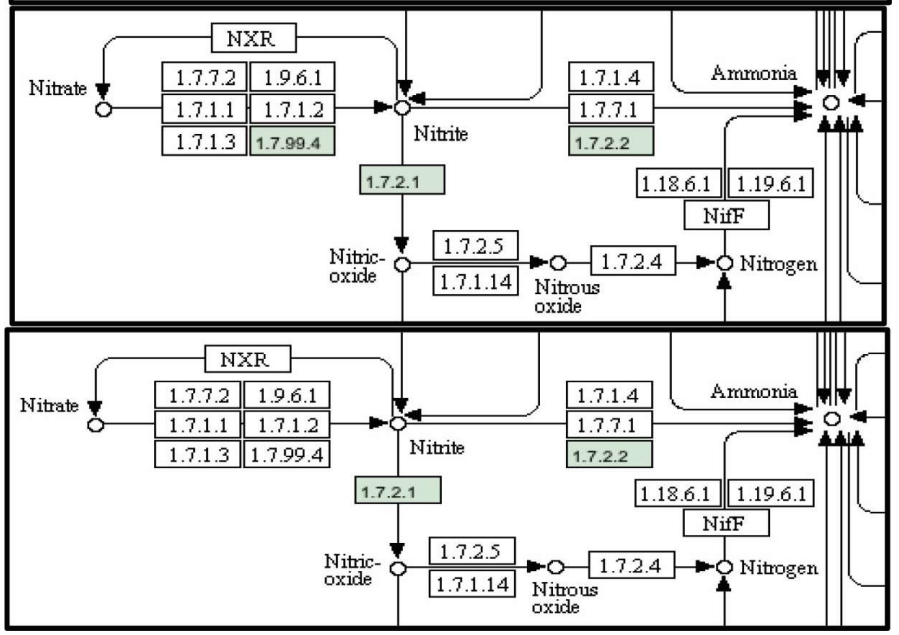
How Does **Chlorhexidine Treatment** Affect Diversity of **Oral Microbiome** And **Nitrate Reduction** in Healthy Subjects and what Effect Does this have on **Systemic Blood Pressure**?

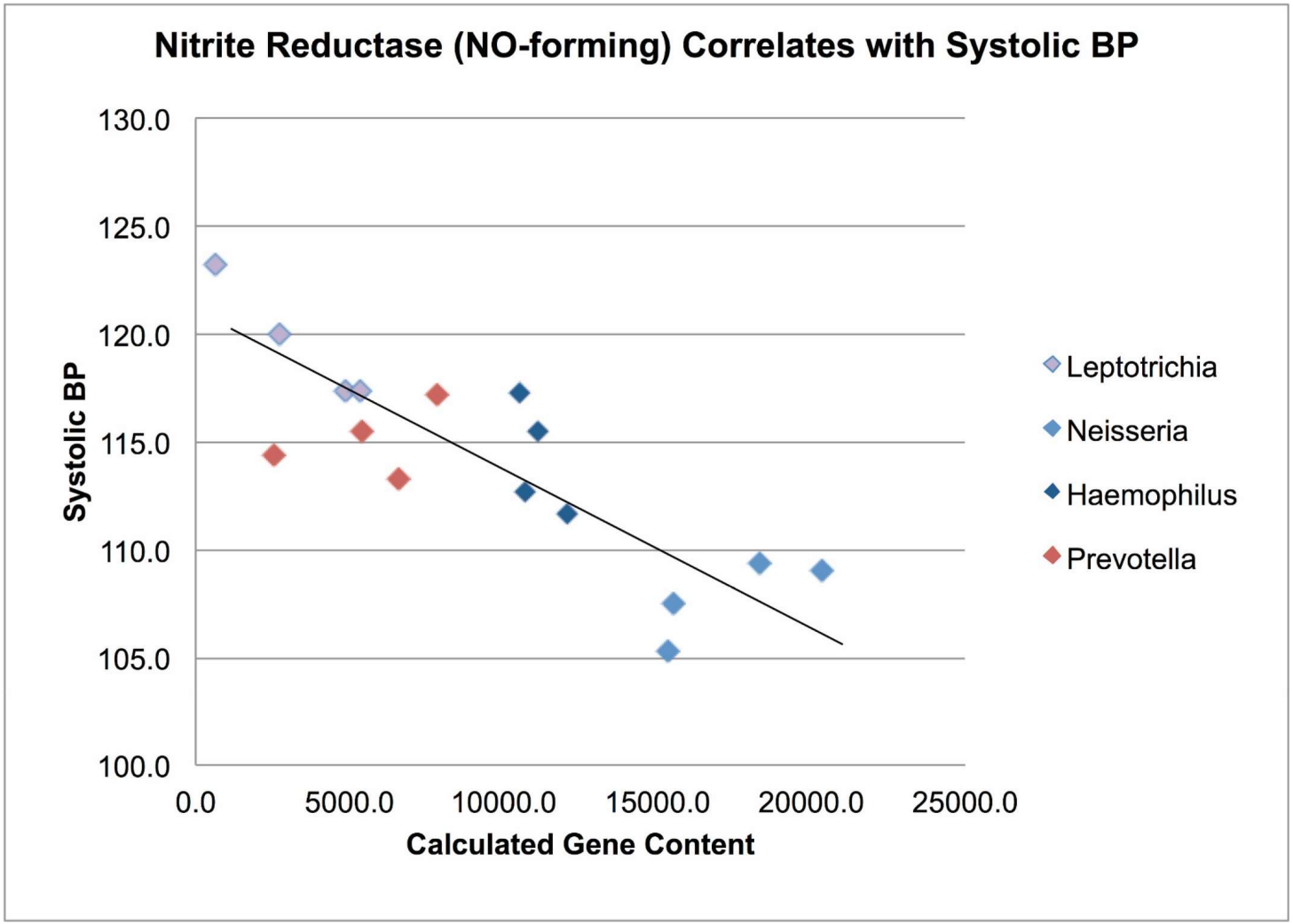
One week Chlorhexidine treatment caused 26 mmHg increase in systemic blood pressure.

This was associated with change in bacterial communities that disrupted nitrate reduction and N.O. production.

Tribble et al Front Cell Infect Microbiol. 2019 Mar 1;9:39.



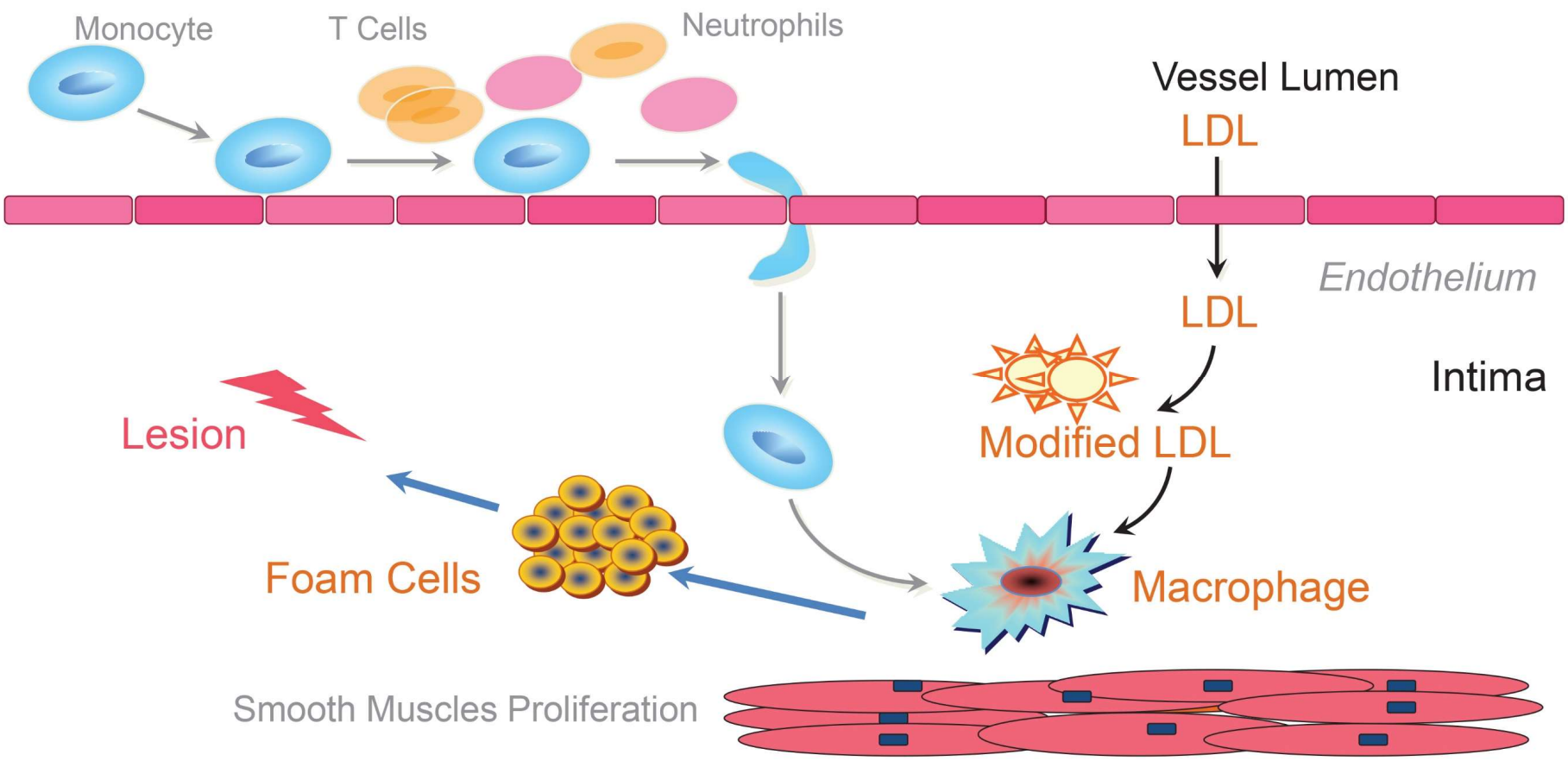




Tribble et al Front Cell Infect Microbiol. 2019 Mar 1;9:39.

Can we **overcome variability** in nitrate reduction based on differences in **oral bacteria**?

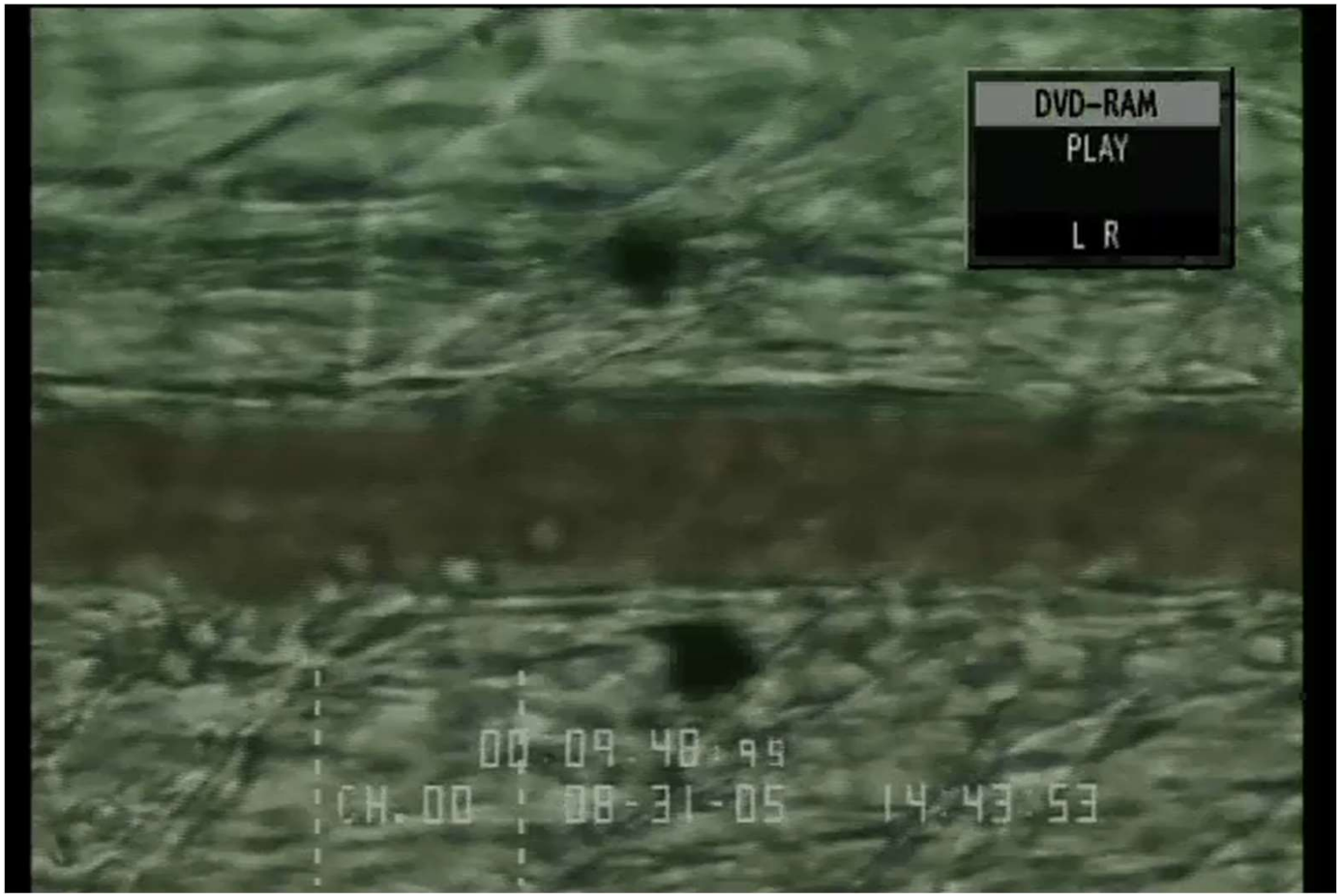
Atherogenesis



Atherogenic Diet

Stokes et alAm J Physiol Heart Circ Physiol 2009 May;296(5):H1281-8

Atherogenic Diet + N.O.



Stokes et alAm J Physiol Heart Circ Physiol 2009 May;296(5):H1281-8

Facts.

Cardiovascular disease (CVD) is the number one killer of both men and women in the U.S. Close to 1 million people die each year and more than 6 million are hospitalized due to CVD. The cost of CVD, in terms of health care and lost productivity, is over $270 billion and increasing as the baby boom population ages.

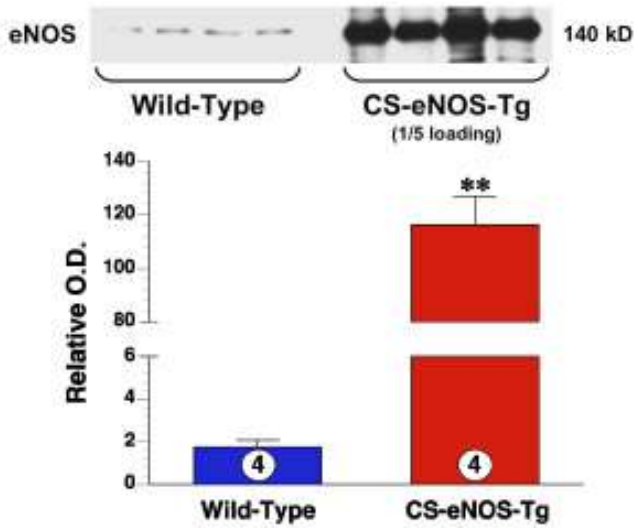
Ischemic heart disease, including myocardial infarction, remains the leading cause of morbidity and mortality in all industrialized nations

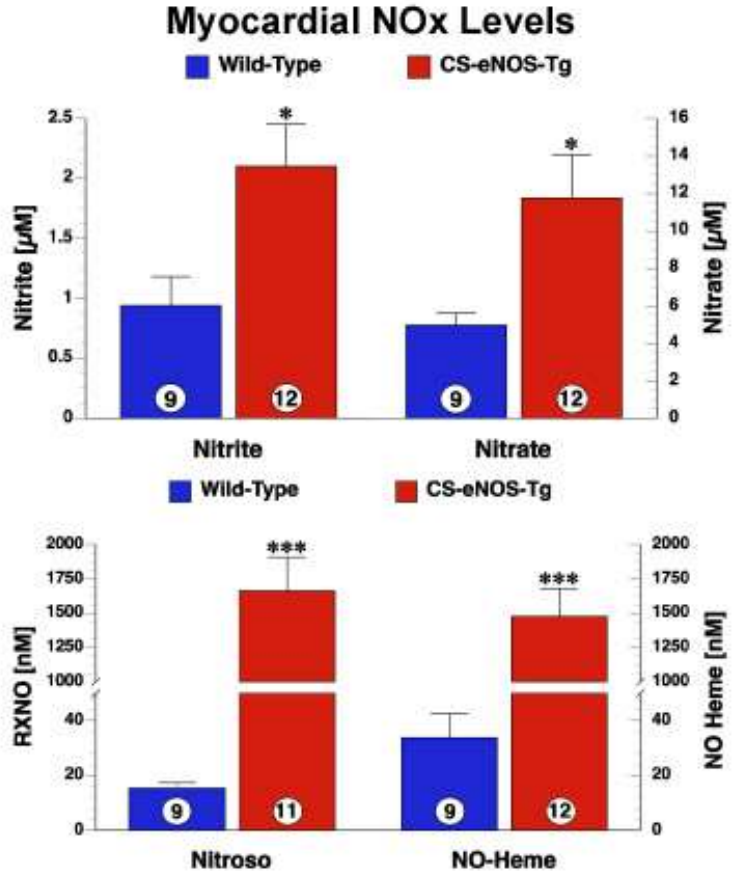
What is the physiological consequence of enhanced N.O. production in Ischemia-reperfusion injury?

Can we trace the phenotype biochemically?

https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

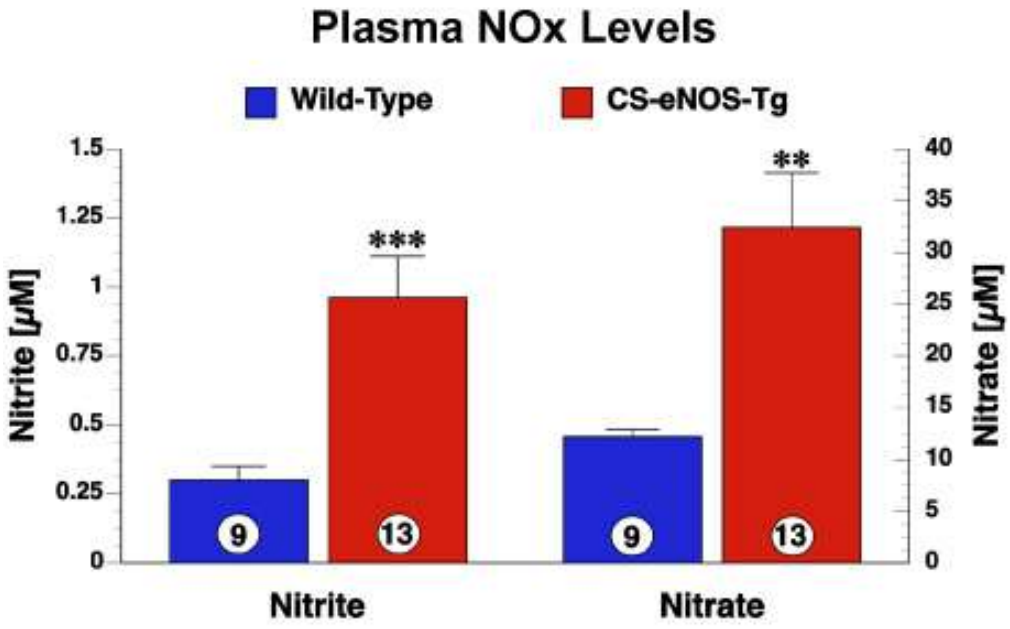
Cardiac Specific Overexpression of eNOS results in Increased Cardiac N.O. Production and Protects from I/R Injury





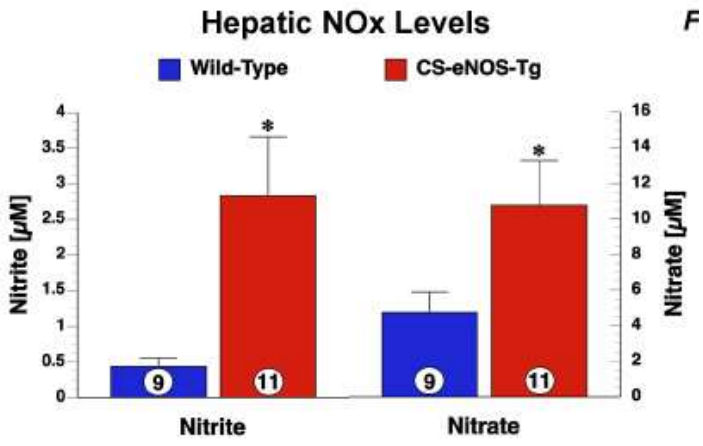
Elrod et al ATVB 2006

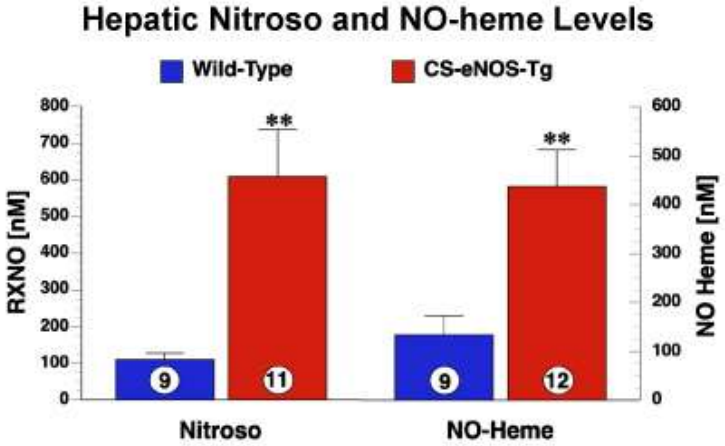
Increased Cardiac N.O. Production Results in Increased Circulating Nitrite and Nitrate

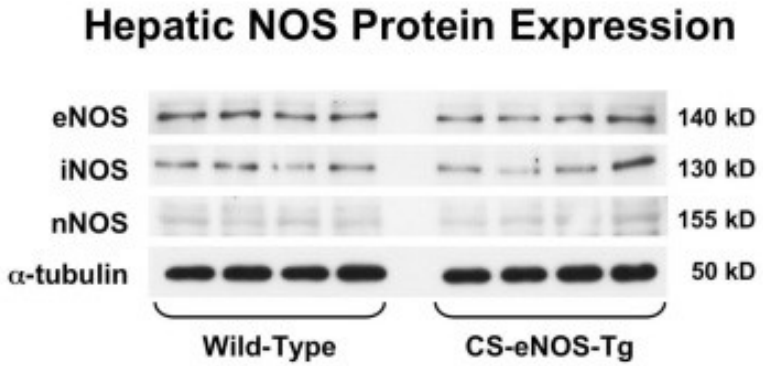


Elrod, PNAS 2008

Local N.O. Production in the Heart Results in Accumulation of N.O. Products in the Liver

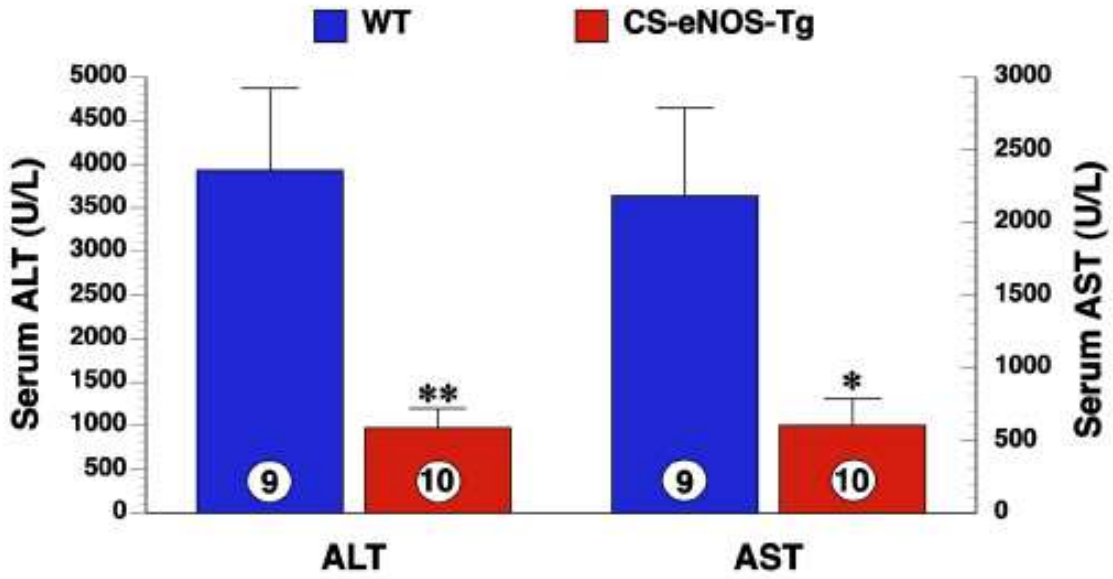






Elrod, PNAS 2008

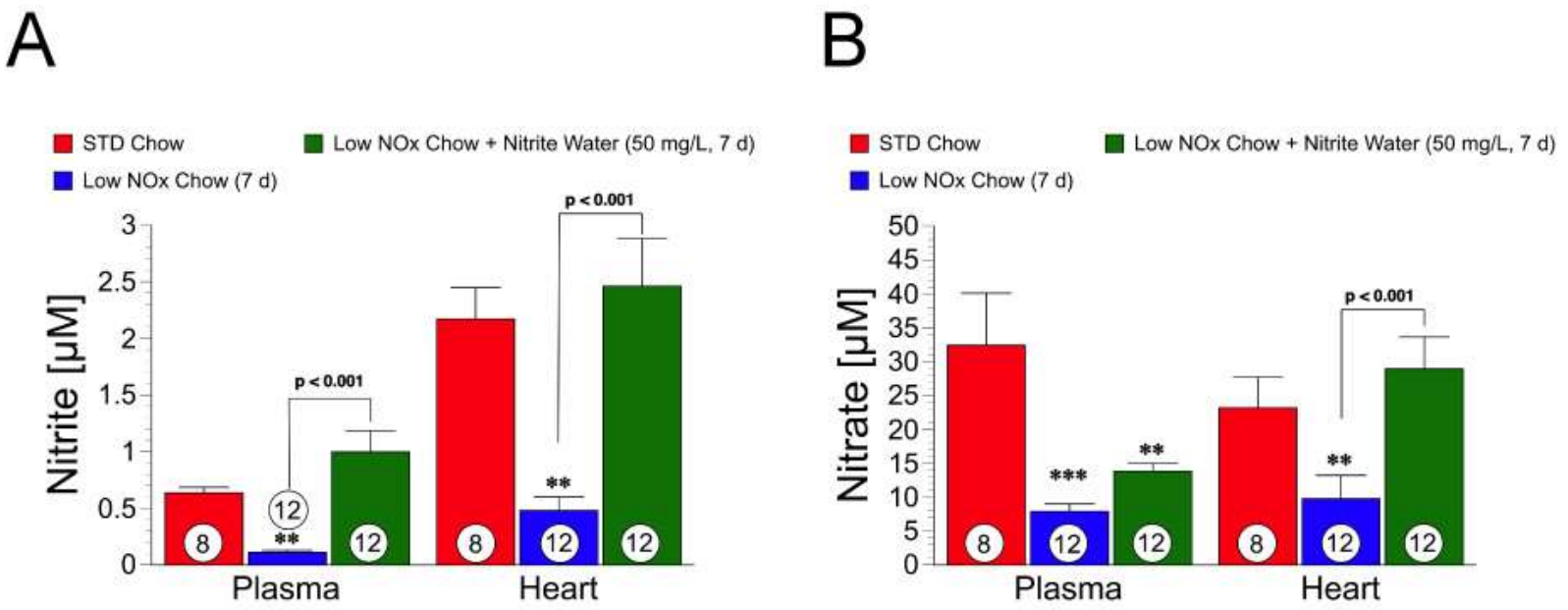
Cardiac Derived N.O. Promotes Distant Organ Protection: Evidence for an Endocrine Role of Nitrite



Elrod, PNAS 2008

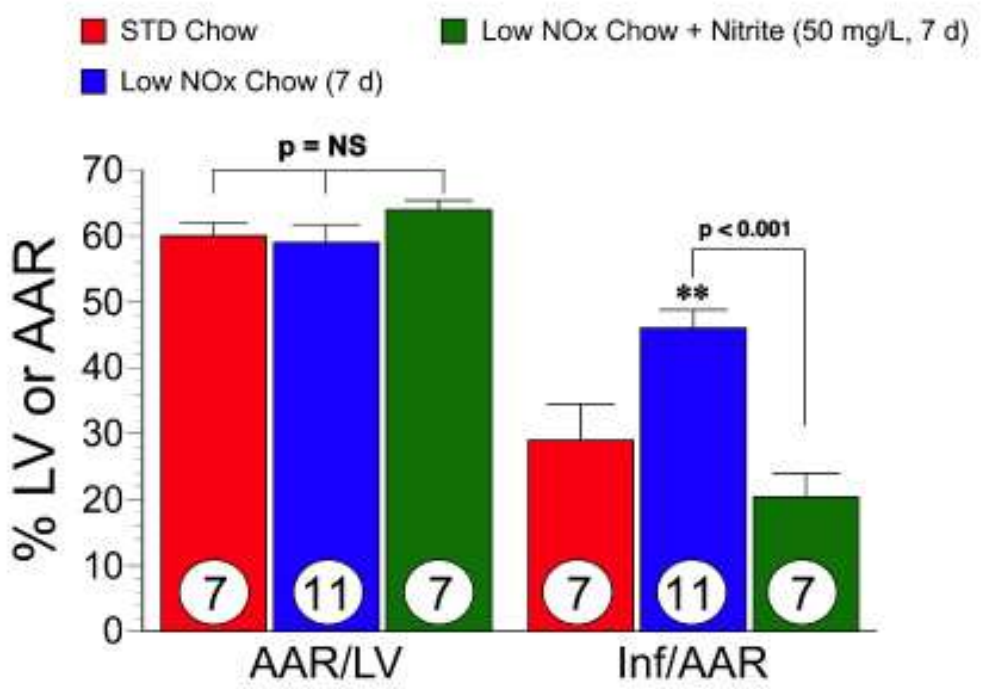
Can we replete tissue N.O. stores with **dietary nitrite** and **nitrate** and lower cardiovascular risk?

Mice on **Low NOx Diet for 1 Week** Reveal Diminished Plasma and Cardiac Nitrite and Nitrate and is Restored with Oral Nitrite Supplementation



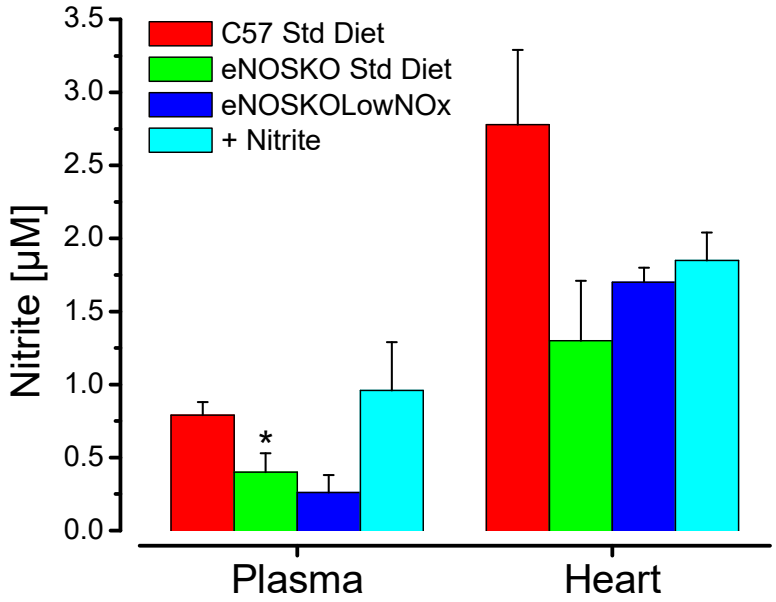
Bryan *et al* PNAS (2007)

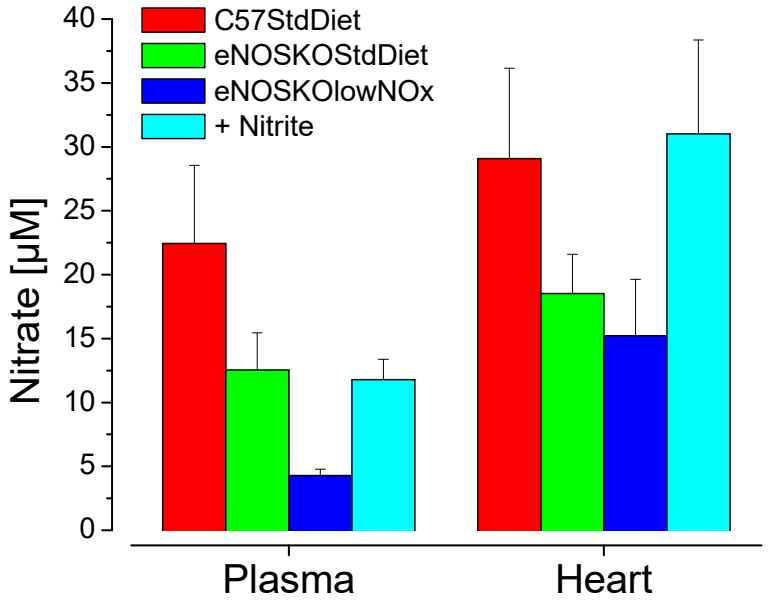
Mice on **Low NOx Diet for 1 Week** Reveal Increase Injury from Heart Attack which is Reversed with Oral Nitrite and Nitrate



Bryan *et al* PNAS (2007)

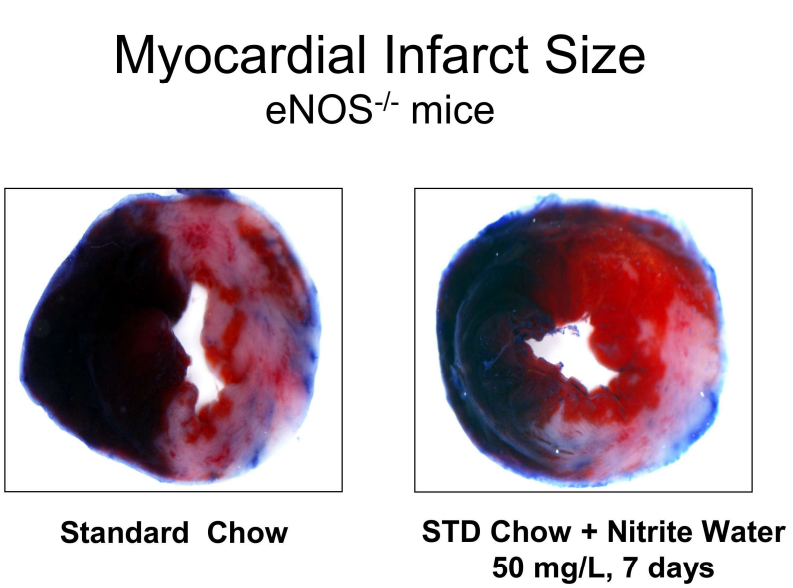
Circulating and Tissue Nitrite/Nitrate are Affected By Both NOS and Diet and **Restored by Supplemental Nitrite**





Bryan et al, FRBM 2008

Supplemental Nitrite Reverses MIR Injury in eNOS -/- mice



Bryan et al, FRBM 2008

Strategies to Restore **Nitric Oxide**

Things that disrupt nitric oxide production

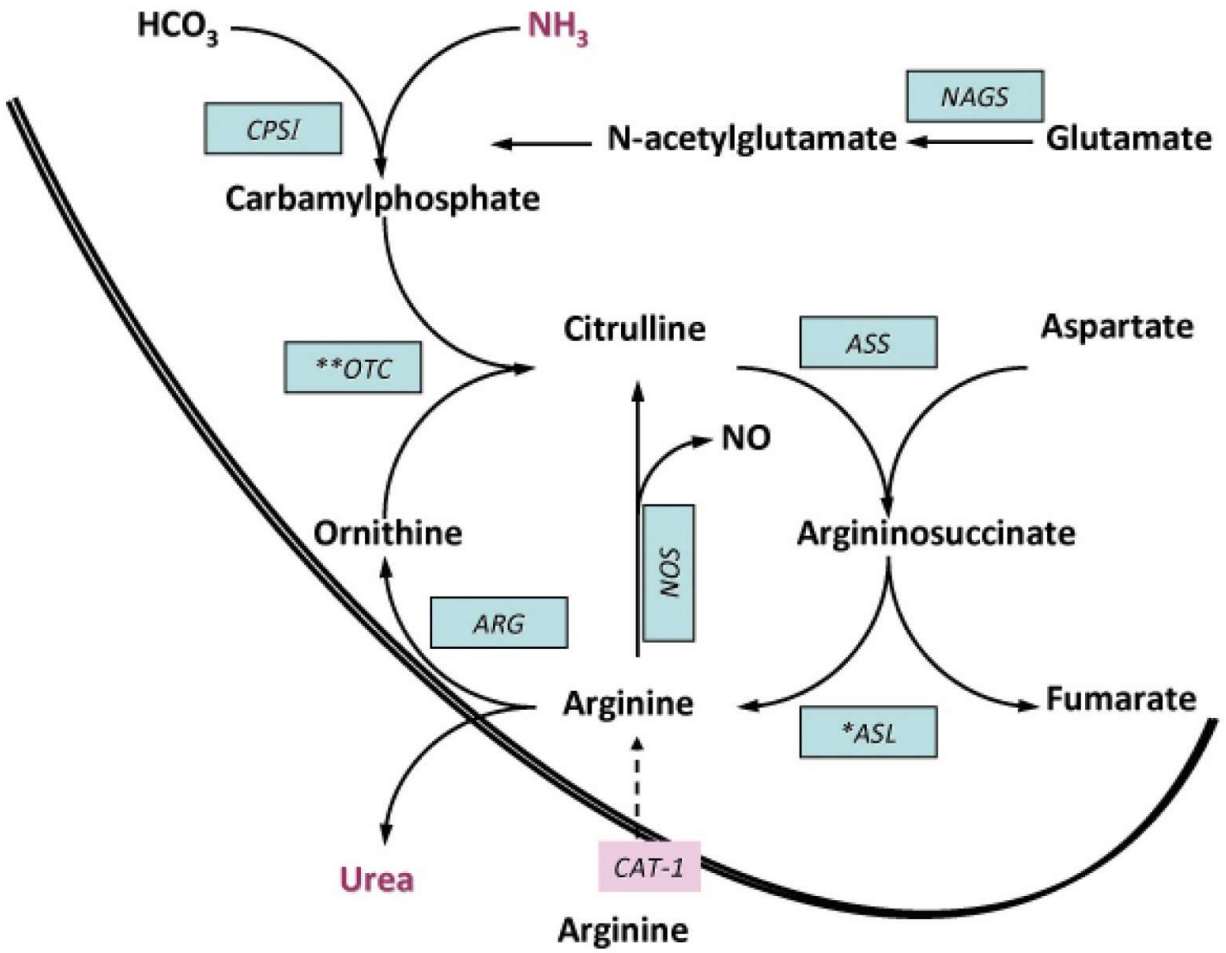
1. Antiseptic mouthwash and fluoride. Stop using mouthwash and fluoride toothpaste.
2. Antacids. Stop using antacids, specifically proton pump inhibitors
3. Stop eating high carbohydrate and highly processed junk food. High glucose causes glycation of the enzyme that makes nitric oxide and stops it from working.

Things that promote or restore nitric oxide production

1. Healthy balanced diet with lots of green vegetables
2. Moderate physical exercise
3. Infrared light therapy or infrared sauna
4. Safe and effective nitric oxide supplementation

Nitrite Supplementation Rescues **Inborn Error in Metabolism**

The Urea Cycle Converts Ammonia To Urea For Excretion



Erez et al Nat Med 2011

ASL Deficiency is an **Inborn Error In Metabolism**

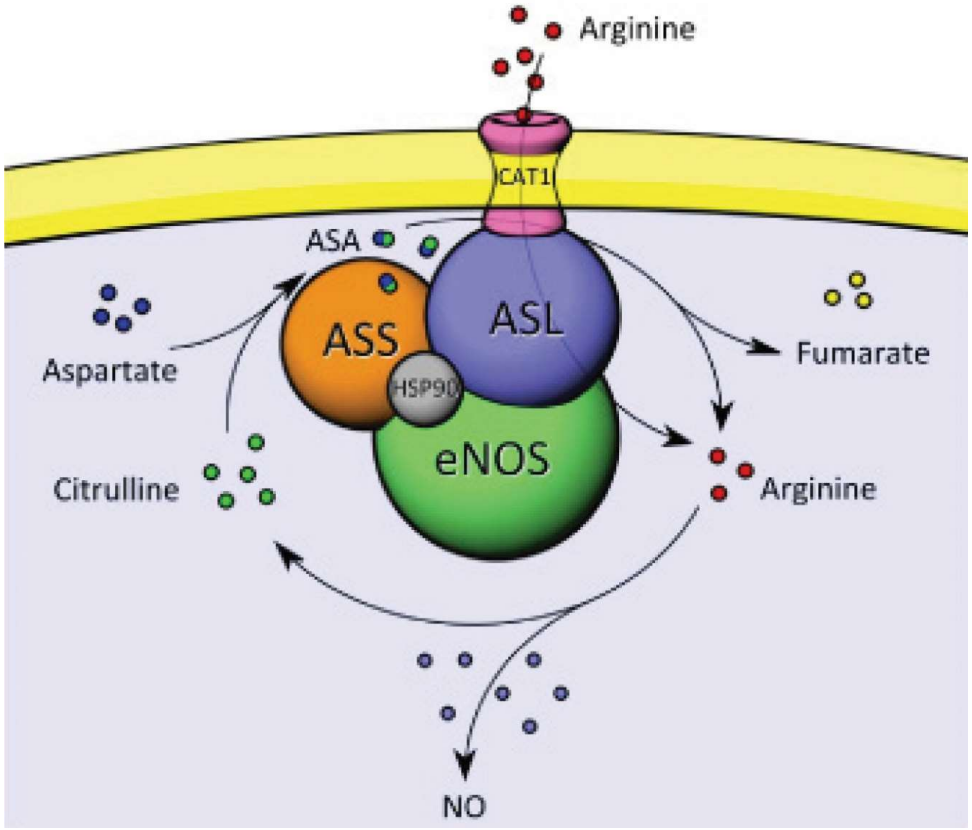
Hyperammonemia

- In addition:
  - Progressive liver dysfunction and cirrhosis
  - Coagulopathy
  - Neurological dysfunction independent of recurrent hyperammonemia
  - Hypertension
  - Renal dysfunction

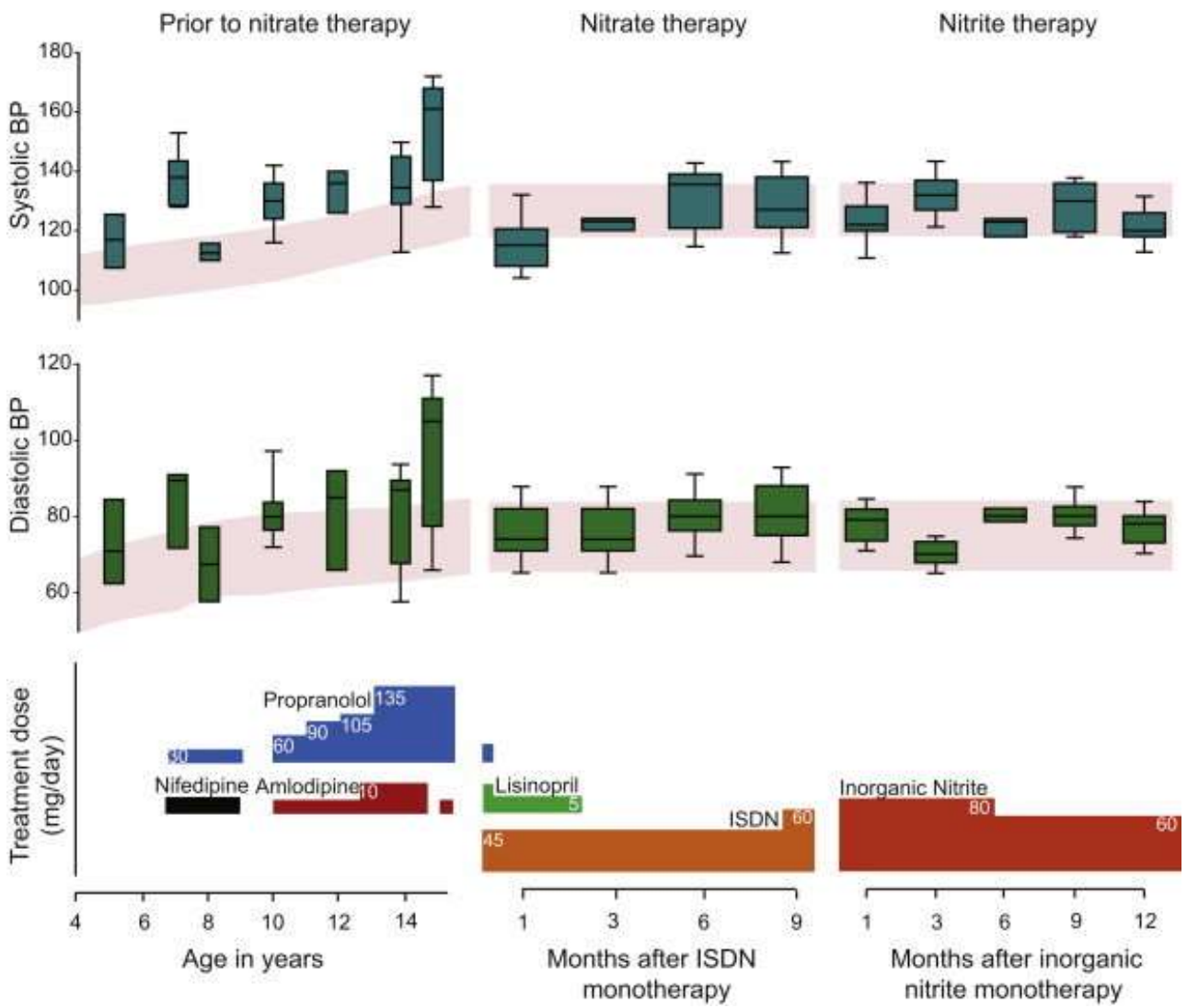
More than hyperammonemia?

Erez et al Nat Med 2011

NOS Utilizes Intracellular **L-Arginine from L-citrulline** For N.O. Production



Erez et al Nat Med 2011



Nagamani et al Am J Hum Genet. 2012 May 4;90(5):836-46

Echocardiogram measurements before and after initiation of N.O. supplementation.

Echocardiogram measurements of LV dimensions taken before and 5 months after initiation of N.O. supplementation. All parameters demonstrate normalization.

Also increased the number of circulating endothelial progenitor cells.

Left ventricle (LV) parameters	Before NO supplementation (z-score)	After NO supplementation (z-score)
LV diastolic septal thickness	2.26	1.33
LV diastolic dimension	-2.10	-0.36
LV diastolic wall thickness	3.59	2.24
LV systolic septal thickness	4.08	1.94
LV systolic dimension	-2.08	-0.67
LV systolic wall thickness	3.01	1.53

Nagamani et al Am J Hum Genet. 2012 May 4;90(5):836-46

Mechanisms of N.O. on Skin and Anti-Aging

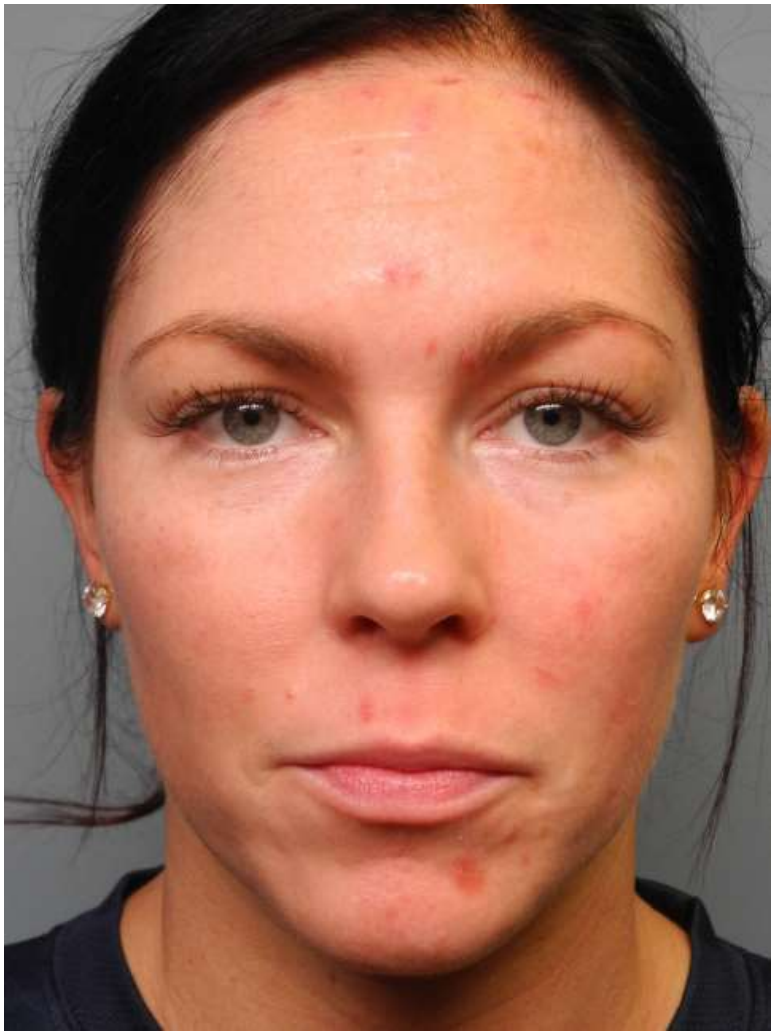
Nitric Oxide dilates the capillaries and increases healthy blood circulation to the skin. The enhanced circulation helps to bring a flood of nutrients saturating the malnourished skin with new life. It improves skin texture, elasticity, thickness, stimulating cell regeneration, and restores moisture. It reduces the appearance of wrinkles and creates tighter, smoother looking skin.

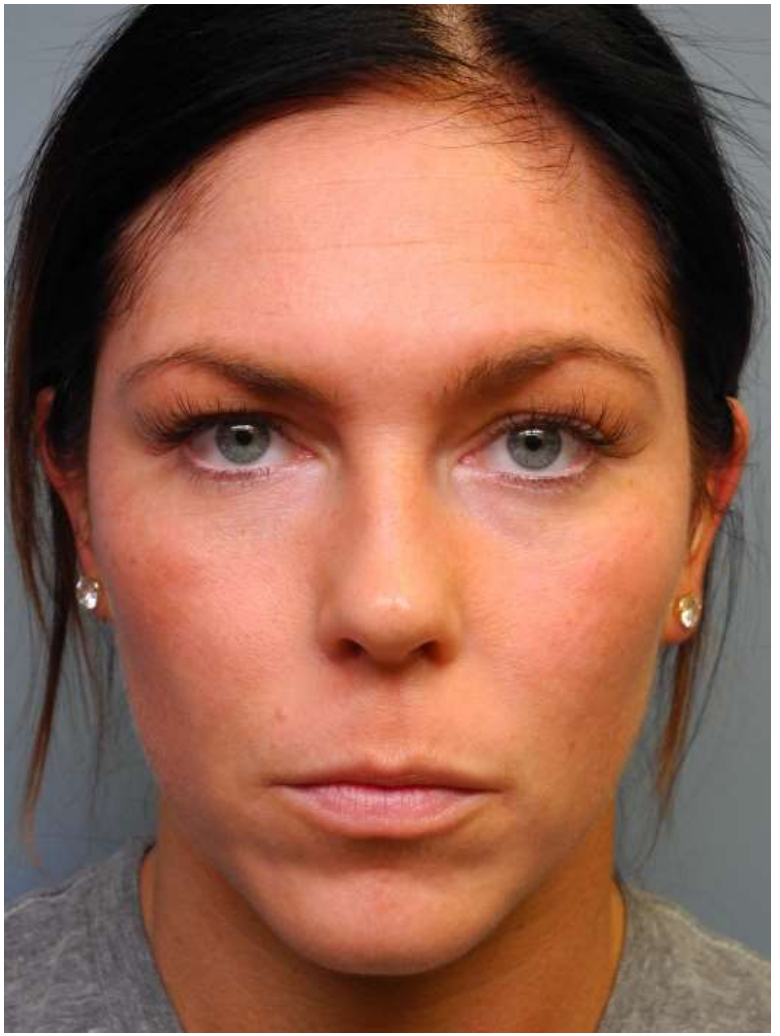
New and Innovative
Topical Nitric Oxide Serum

The FIRST and ONLY true Nitric Oxide based anti-aging skin care serum.
Nitric Oxide has been scientifically proven to *increase nutrient rich blood circulation to the skin*.

Restoring Nitric Oxide production in the small vessels of the dermis works within seconds to rejuvenate malnourished and aging skin.

- Improves the texture of the skin
- Evens the appearance of skin tone
- Increases elasticity
- Hydrating and moisturizing
- Reduces the appearance of fine lines & wrinkles
- Creates Tighter, Smoother looking Skin





COVID-19

- A **worldwide pandemic** affecting hundreds of millions of people around the world
- As of today, more than **230,000,000** people have been infected with over **4,000,000** deaths worldwide
- Early data reveal that patients with CVD were more susceptible to infection, greater disease severity and a **10X higher** mortality
- US CDC reports a **disproportionate fatalities** among patients with high prevalence of **hypertension**, which often leads to the development of cardiomyopathy and heart failure
- Abnormal **blood clotting** is an increasingly recognized complication of this disease

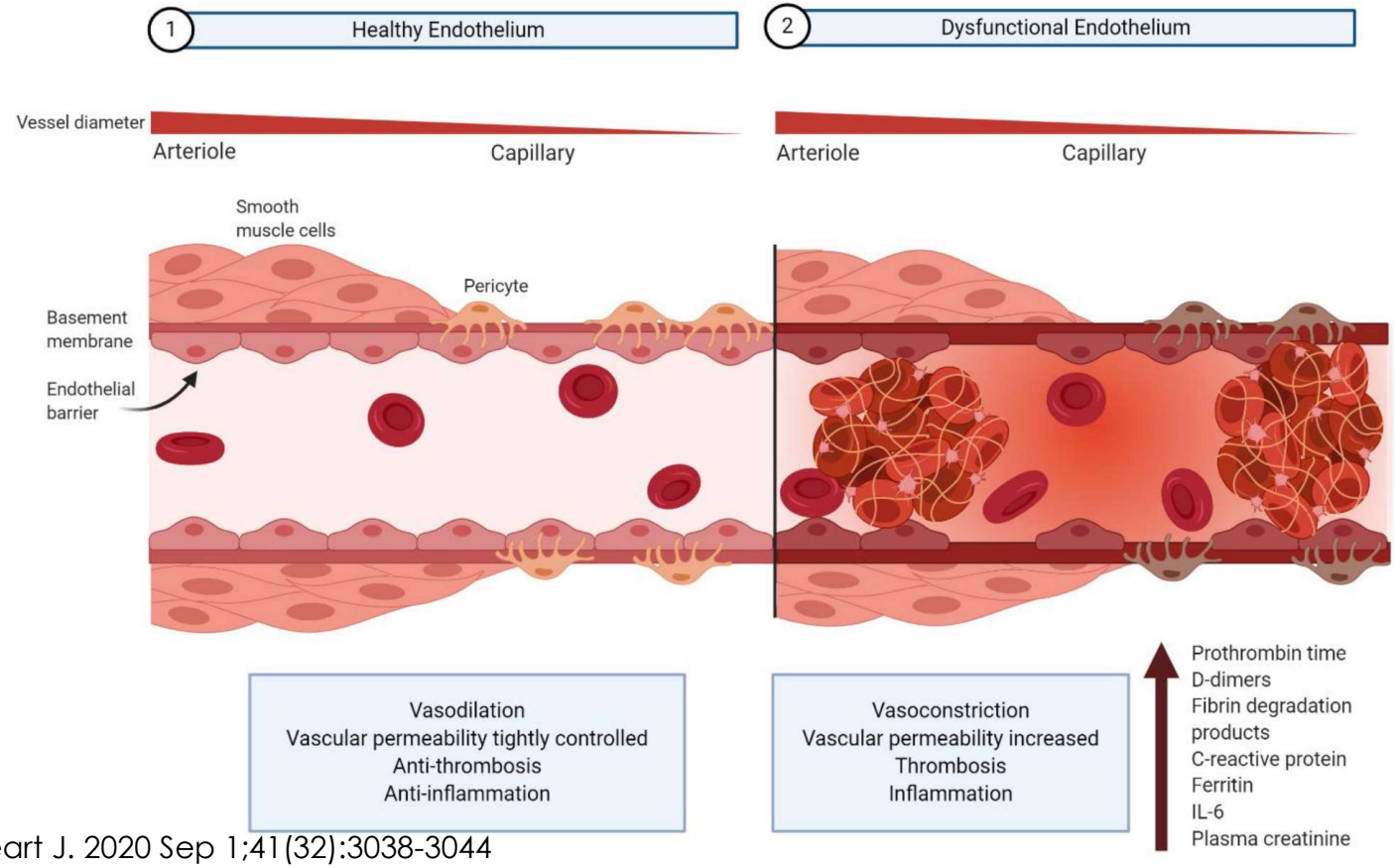
cdc.gov

Nitric Oxide and COVID-19

- N.O. is reported to improve **oxygenation**, an action needed as the disease progress
- N.O. decreases the propensity of blood to **clot**
- Recent clinical observations reveal endothelial cell infection and endothelitis in COVID patients across vascular bed in multiple organs
- Vascular endothelium is an active organ that is indispensable for the maintenance of **vascular homeostasis**; diminished N.O. levels and hypertension has been associated in high-risk patients
- Endothelial dysfunction and **insufficient N.O. production** is a principal determinant of microvascular dysfunction
- **N.O. inhibits Corona virus replication**
- Access of SARS-CoV-2 virus to the cells is through ACE2 receptor, and N.O. has been reported to **alter** the surface protein of SARS-1, implying that it is likely that N.O. may well prevent **cellular** penetration

Libby Eur Heart J. 2020 Sep 1;41(32):3038-3044

Spike Protein Leads to **Endothelial Dysfunction**



Libby Eur Heart J. 2020 Sep 1;41(32):3038-3044

Nitric Oxide Inhibits the Replication Cycle of Severe Acute Respiratory Syndrome Coronavirus

Sara Åkerström, Mehrdad Mousavi-Jazi, J

DOI: 10.1128/JVI.79.3.1966-1969.2005

Nitric oxide (N.O.) is an important signaling molecule between cells which has been shown to have an inhibitory effect on some virus infections. The purpose of this study was to examine whether N.O. inhibits the replication cycle of the severe acute respiratory syndrome coronavirus (SARS CoV) in vitro. We found that an organic N.O. donor, S-nitroso-N-acetylpenicillamine, significantly inhibited the replication cycle of SARS CoV in a concentration-dependent manner. We also show here that N.O. inhibits viral protein and RNA synthesis. Furthermore, we demonstrate that N.O. generated by inducible nitric oxide synthase, an enzyme that produces N.O., inhibits the SARS CoV replication cycle.

Proven Risk Factors and Treatment of COVID

Risk	Solution
Vitamin D < 50 ng/ml	5000 -10,000 Units Vitamin D daily
Low zinc	50 mg zinc daily
Low Vitamin C	3000 mg Vitamin C daily
Low Glutatione	900 mg N-acetyl cysteine
Low nitric oxide (hypertension, diabetes, obesity Smokers, heart disease, kidney Disease, pulmonary disease)	nitric oxide
	Ivermectin, hydroxychloroquine, etc

Noviricid
Nitric Oxide generating drug

- **FDA approved clinical trial**
- Manufactured by Nitric Oxide Innovations, LLC
- Lozenge delivers 30-40 ppm N.O. gas as it is dissolving over 5-6 minutes
- If your body cannot produce N.O., then the lozenge does it for you
- Clinical studies reveal many beneficial effects
  - Reduced inflammation
  - Normalization of blood pressure
  - Improved endothelial function
  - Dilation of blood vessels and better blood flow
  - Better immune function
  - Increased blood oxygen saturation
  - Inhibition of corona virus replication

Baseline
COVID patient

8 minutes
post N.O.
treatment

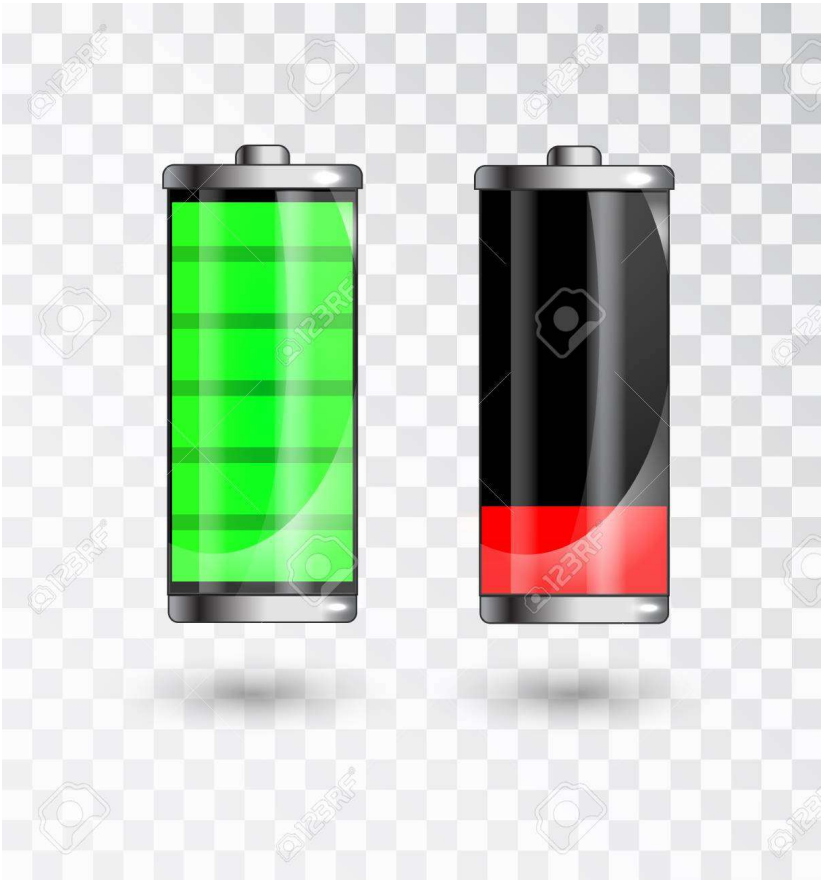
People Get Sick for **Two Reasons**

1. The body is missing something that it needs
2. The body is exposed to something toxic
   (infected root canals, chemicals, EMF, etc)

The result is loss of regulation of blood flow

Must replete missing nutrients and detox the body
(infrared sauna, clean water, clean up infections)

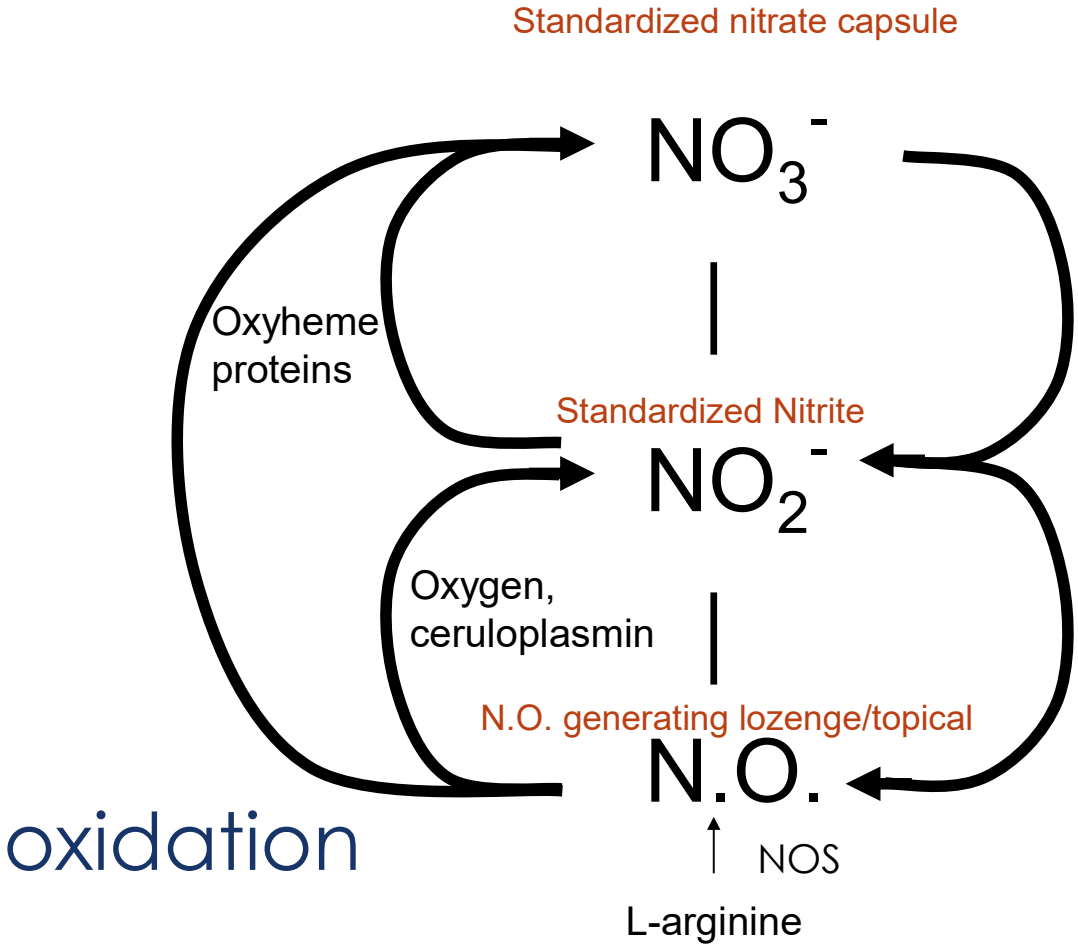
Loss of Nitric Oxide **Causes Human Disease**



Clinical Strategies to replete N.O.

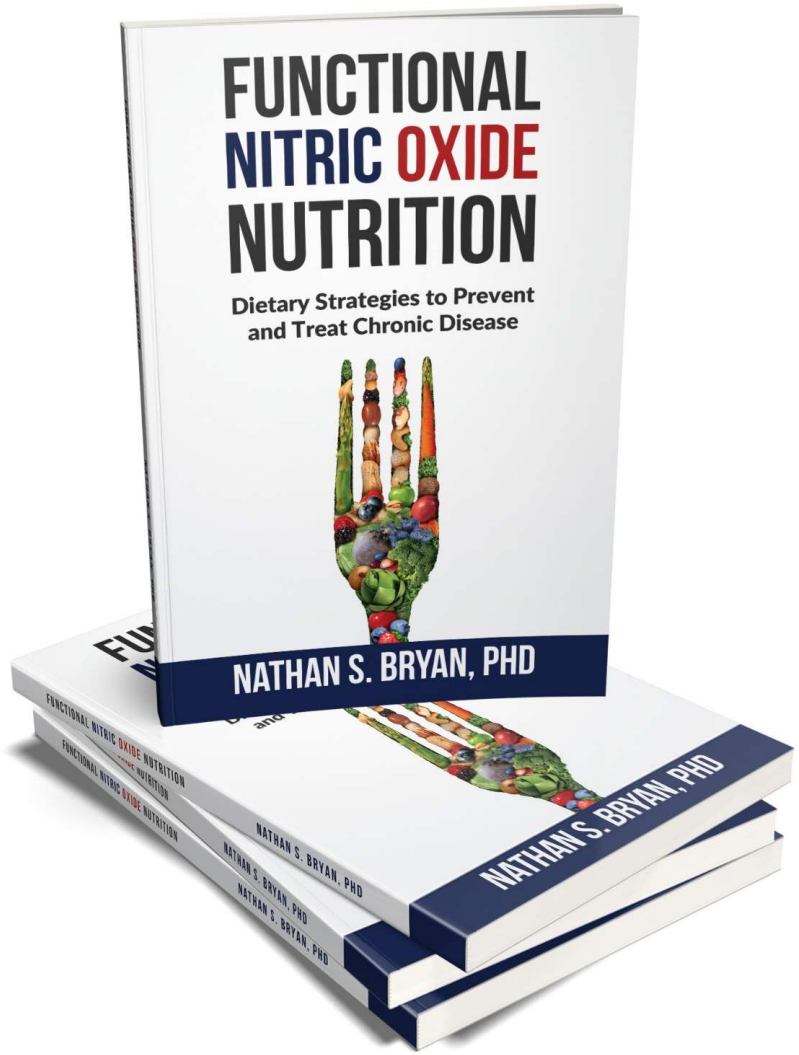
1. Supplement to standardize nitrate consumption
2. Restore endothelial function (nitrate and nitrite)
   - Stop smoking
   - Stop antacids
   - Start exercising
3. Use an infrared sauna
4. Use Fluoride free toothpaste
5. Discontinue mouthwash

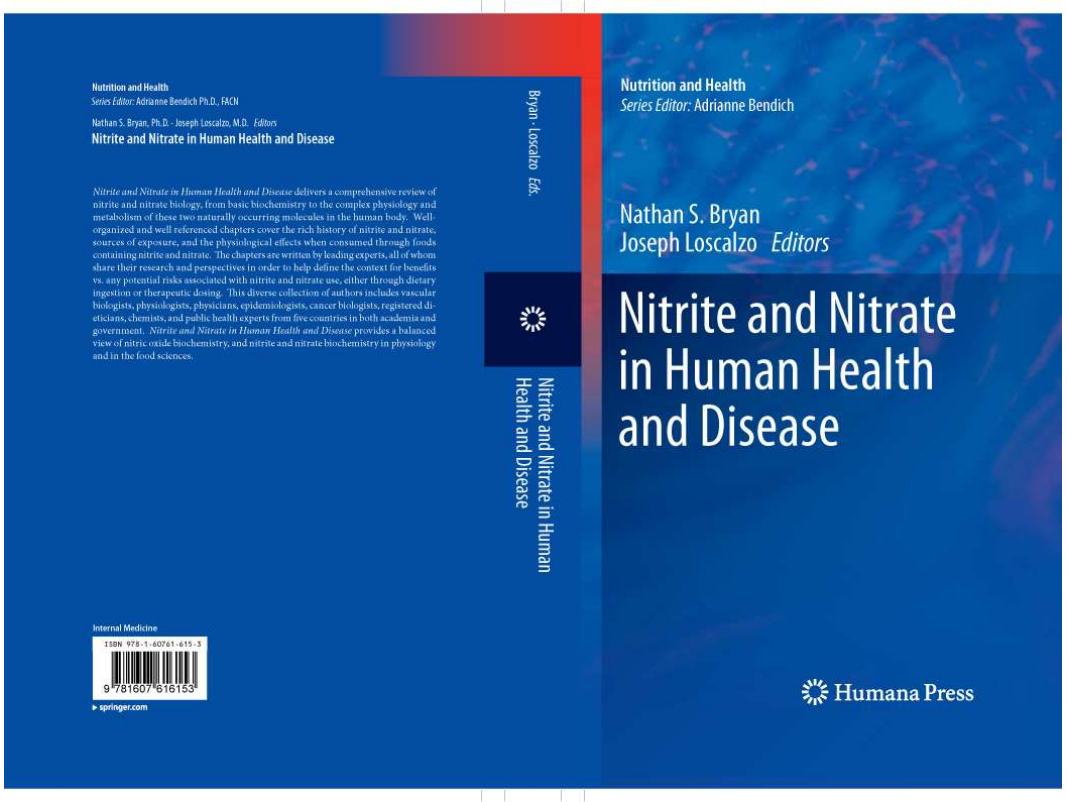
Nitrate – Nitrite – Nitric Oxide Pathway



CONCLUSIONS

- Nitric oxide controls and regulates blood flow and oxygen delivery to every cell in the body
- There is an age-related decline in N.O. production that asserts its effect on cardiovascular risk and chronic disease
- Diet and Exercise are not always sufficient for restoring N.O. production
- Strategies to restore N.O. production/homeostasis will have a profound impact on public health and on the future of medicine
- We must use safe and effective nitric oxide product technology in order to optimize our health





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