Nitric Oxide: How not enough relates to cardiovascular and age-related disease.

Nathan S. Bryan, Ph.D.

FullScript Webinar Feb 13, 2020

NO THERAPEUTIC INTERVENTION

Bryan Research Program

1. How does the human body produce NO?
2. What goes wrong in people that can't make NO?
3. What are the clinical consequences of such?
4. How do you fix or restore endogenous NO production?

- 20 years in Academic Research and Drug Discovery (LSU, BUMC, UTHealth, BCM)
- Dozens of issued US and International Patents on Nitric Oxide Technologies
- Over 100 peer-reviewed published papers on nitric oxide biochemistry/physiology
- Over 200 lectures worldwide on nitric oxide

Conflicts of Interests

- Founder and Shareholder – HumanN
- Founder and CEO – Nitric Oxide Innovations, LLC
- Founder and CEO – Pneuma Nitric Oxide, LLC
- Shareholder – SAJE Pharma
- Shareholder – DermaShower, LLC
- 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 mental health and disease
3. Recognize the clinical symptoms that result from lack of NO production.
4. Reveal evidence based therapeutic and nutritional strategies to restore nitric oxide production in patients

“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

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

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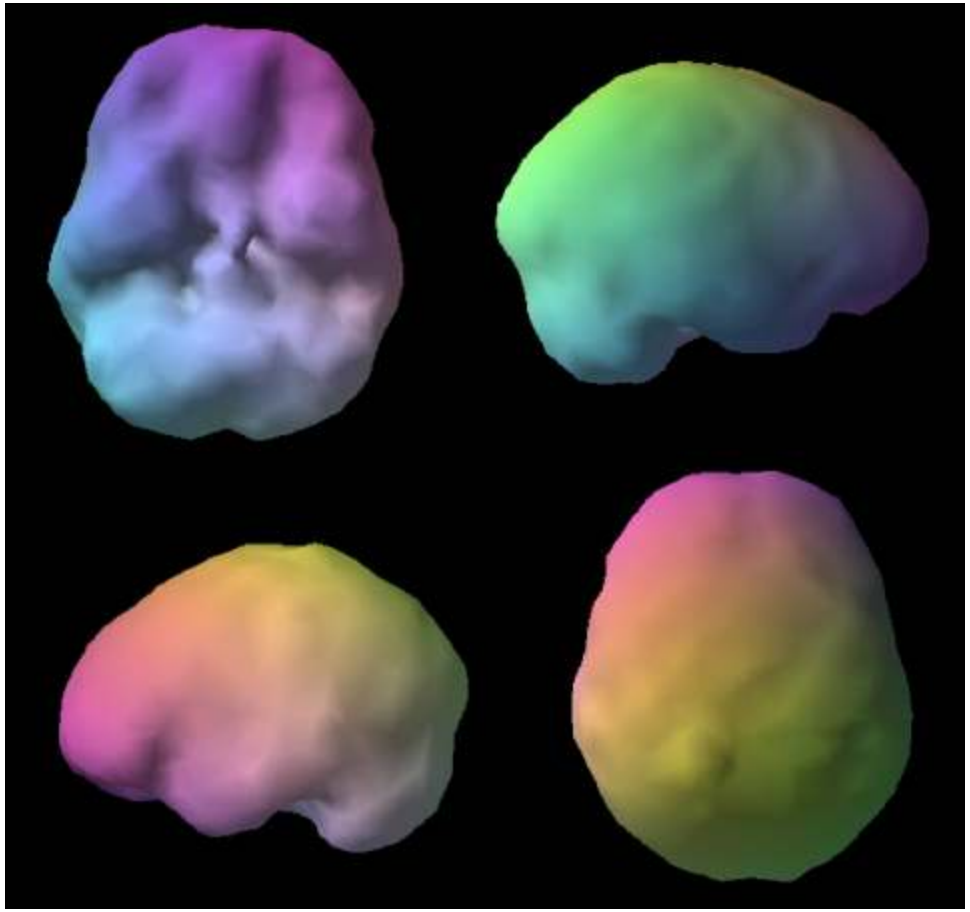
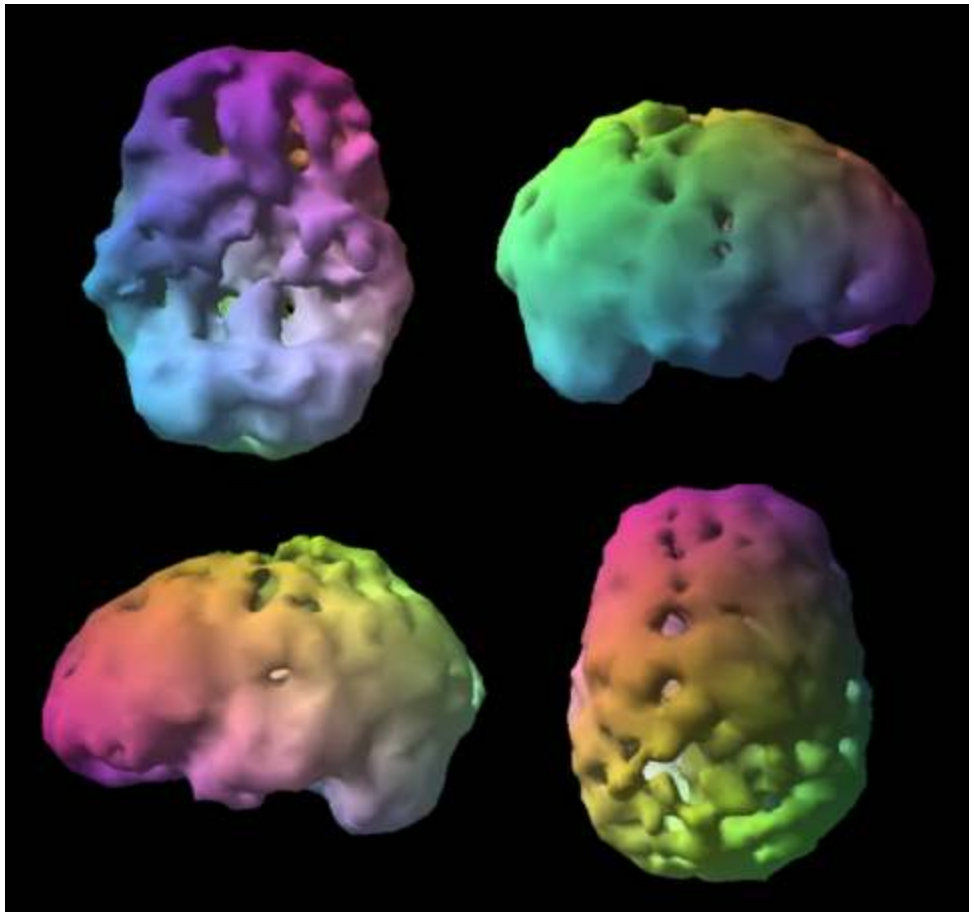


A HEALTHY BRAIN

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

Reference: www.amenclinics.com

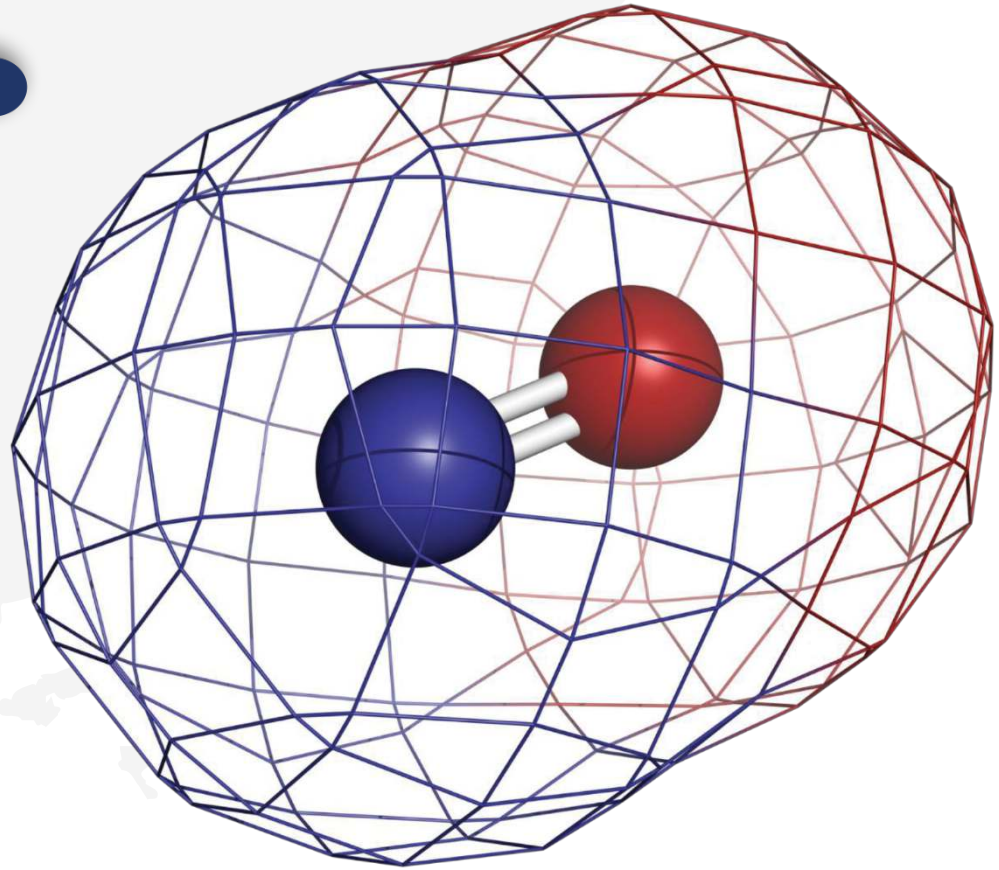
Every single chronic disease is characterized by decreased blood flow to the affected organ/tissue.

If you can restore blood flow and perfusion to specific tissues and organs, you can correct many chronic pathological conditions.

How do we restore blood flow and perfusion to the select tissues/organs?

Nitric Oxide

N::O·



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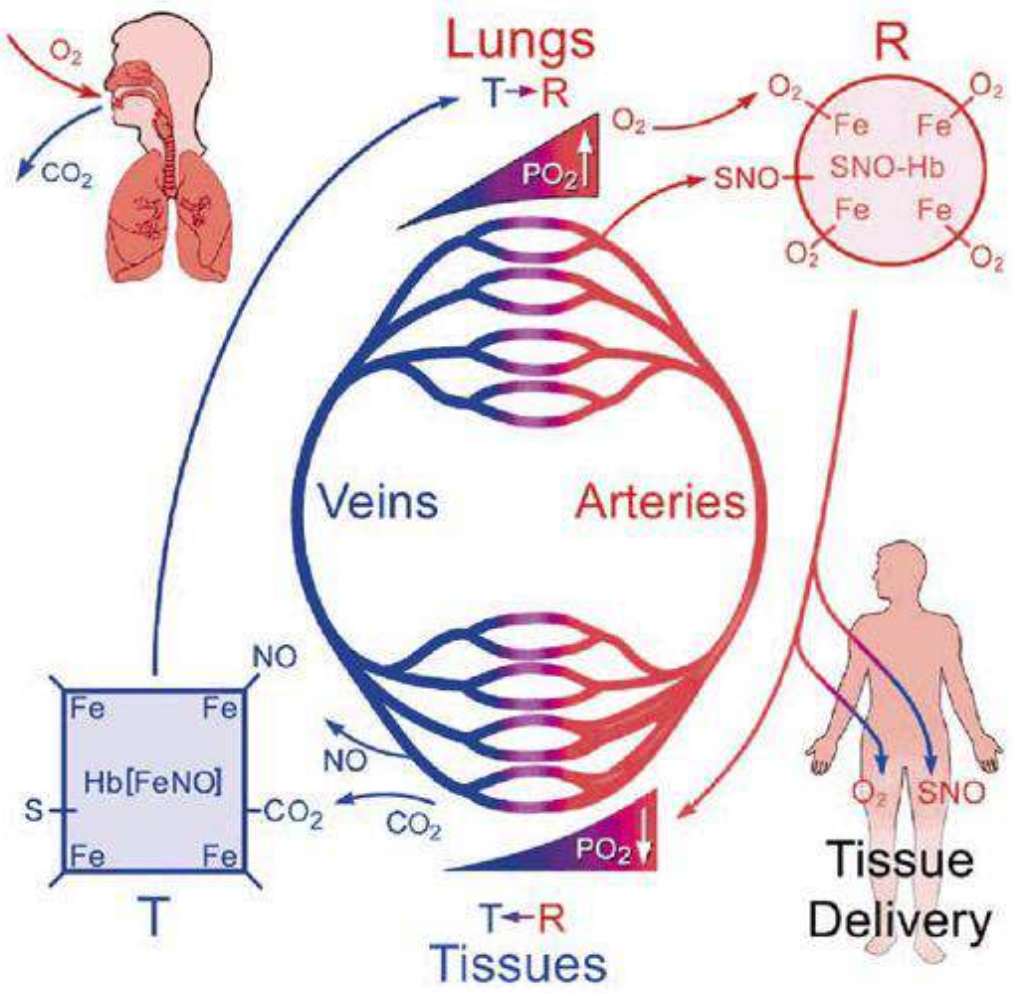
"The discovery of NO and its function is one of the most important in the history of cardiovascular medicine."

Dr. Valentin Fuster
1998 President of American Heart Association

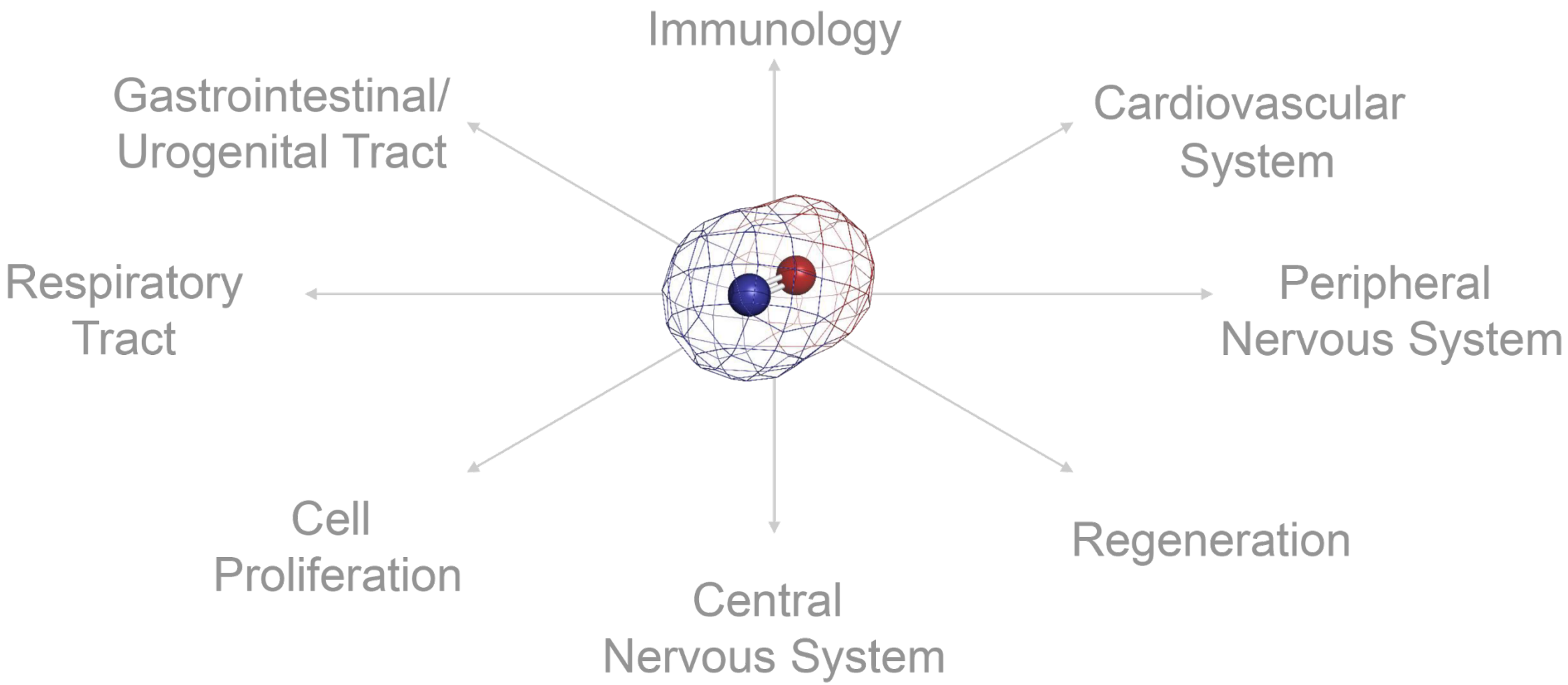
Nitric oxide is required for red blood cell delivery of oxygen from the lungs to tissue.

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**



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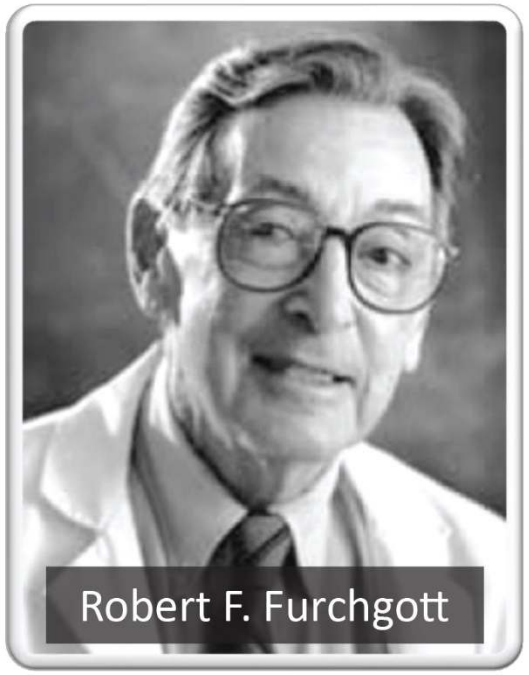
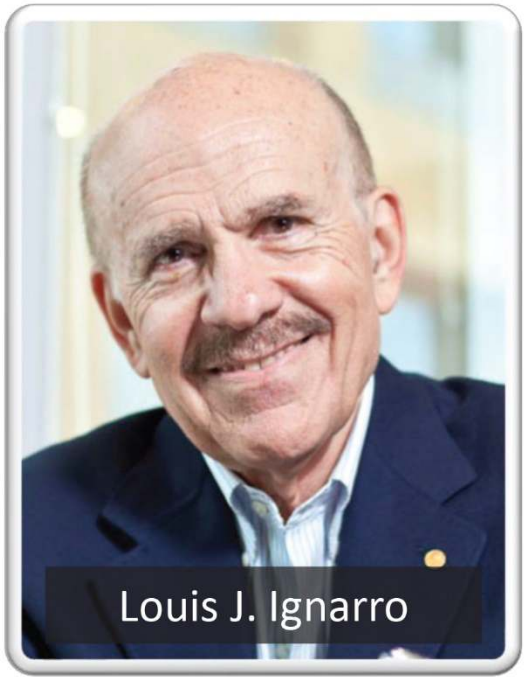


1/3 of the prize

USA
SUNY Health Science Center
Brooklyn, NY, USA

Born: 1916



1/3 of the prize

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

Born: 1941

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

Who Needs **Nitric Oxide?**

- Anyone who is aging
- Anyone over the age of 40
- People with circulation issues
- Diabetics
- People with low energy
- People with sexual dysfunction
- Anyone on antacids
- Anyone interested in disease prevention
- Anyone eating a poor diet
- ***Anyone diagnosed with vascular dysfunction***

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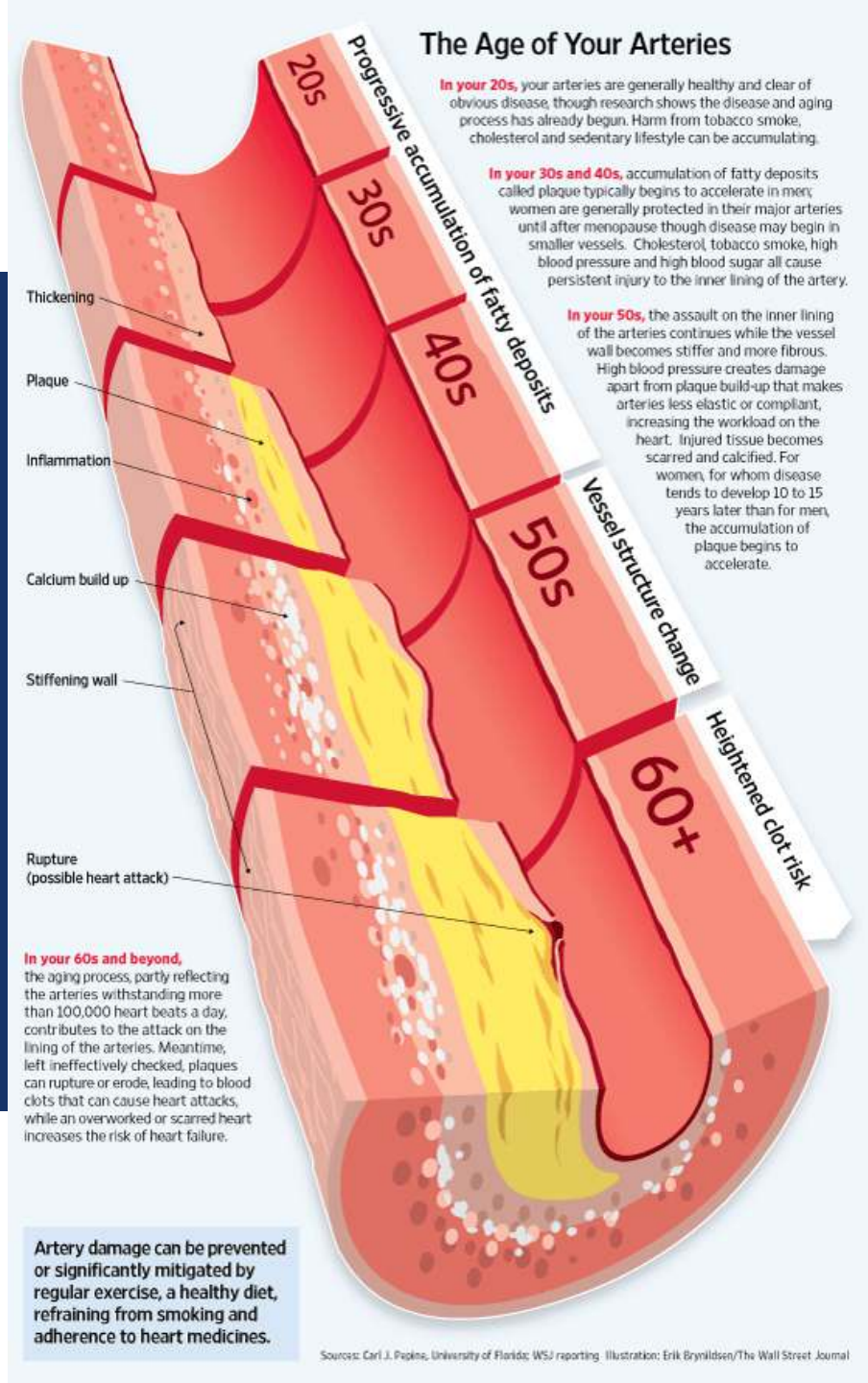
“A man is as old as his arteries.”

Thomas Sydenham, English Physician, 1624-1689

The Age of your **Arteries**



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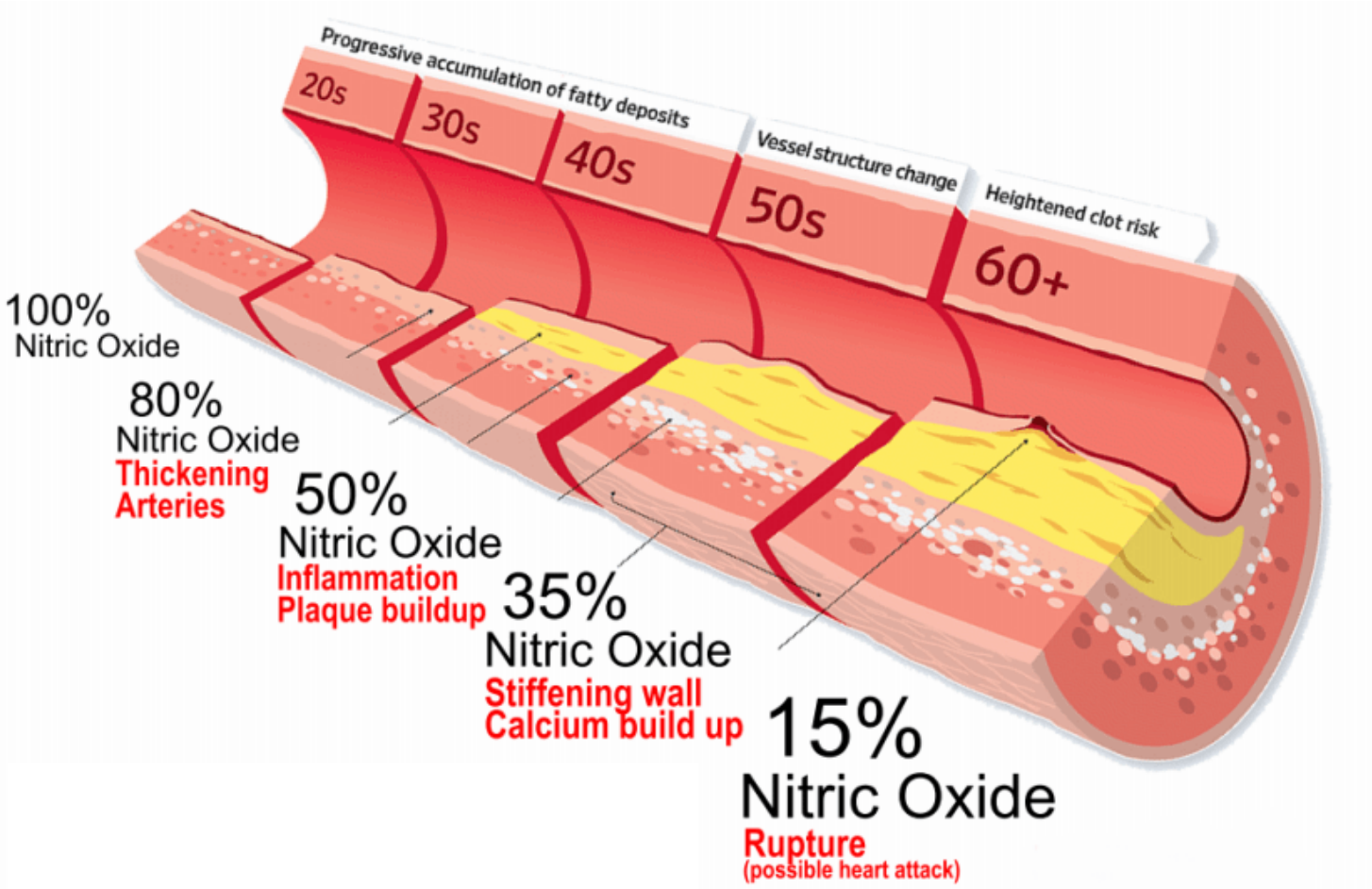

Loss of **NO** is Associated with **Atherosclerosis.**

As we age, we lose 85% of our ability to make Nitric Oxide.

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How do we control and regulate Nitric Oxide production?

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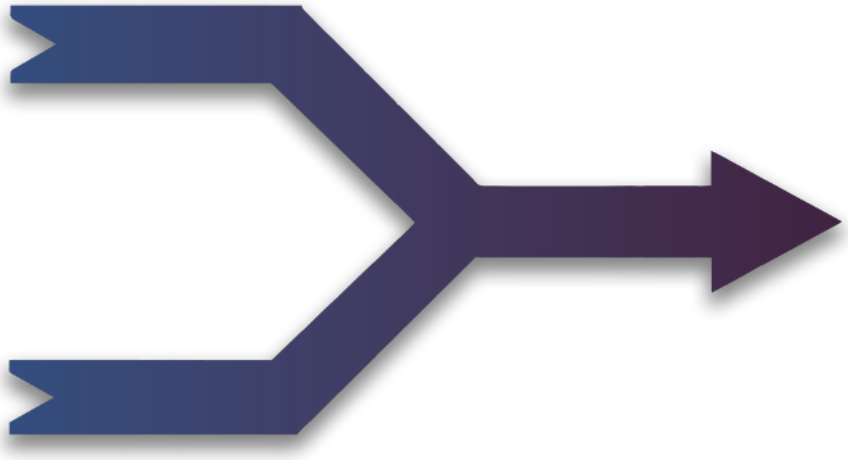
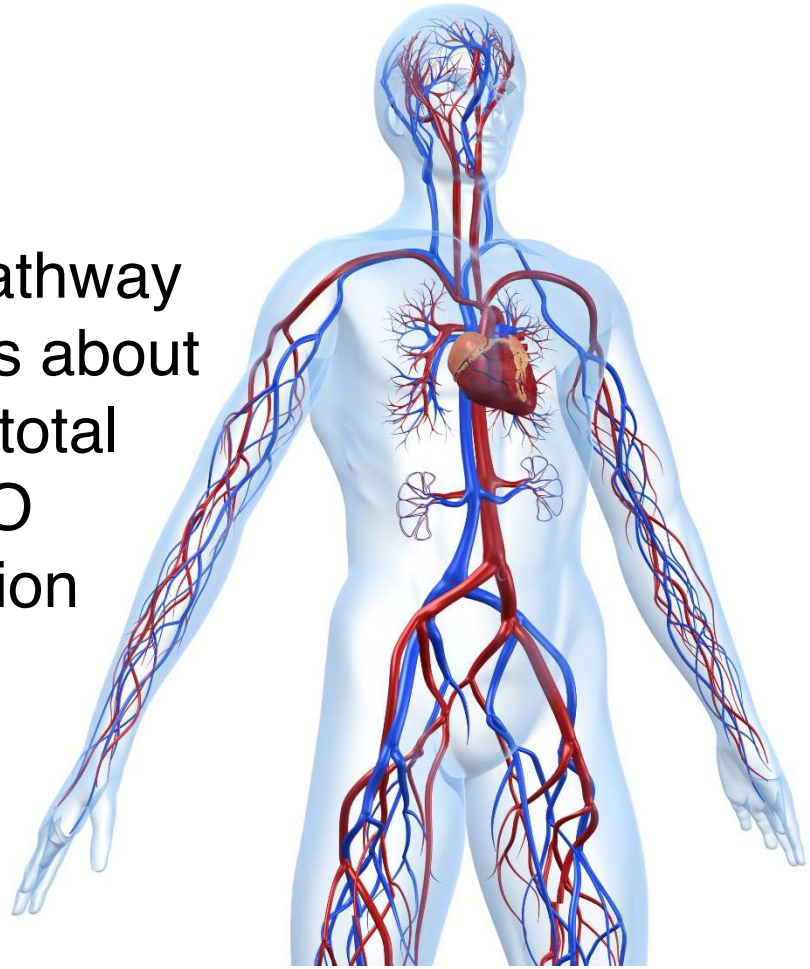
Two **Nitric Oxide** Production Pathways

1. Oxidation of L-arginine (NOS)



2. Nitrate-Nitrite-Nitric Oxide

Each pathway provides about 50% of total body NO production



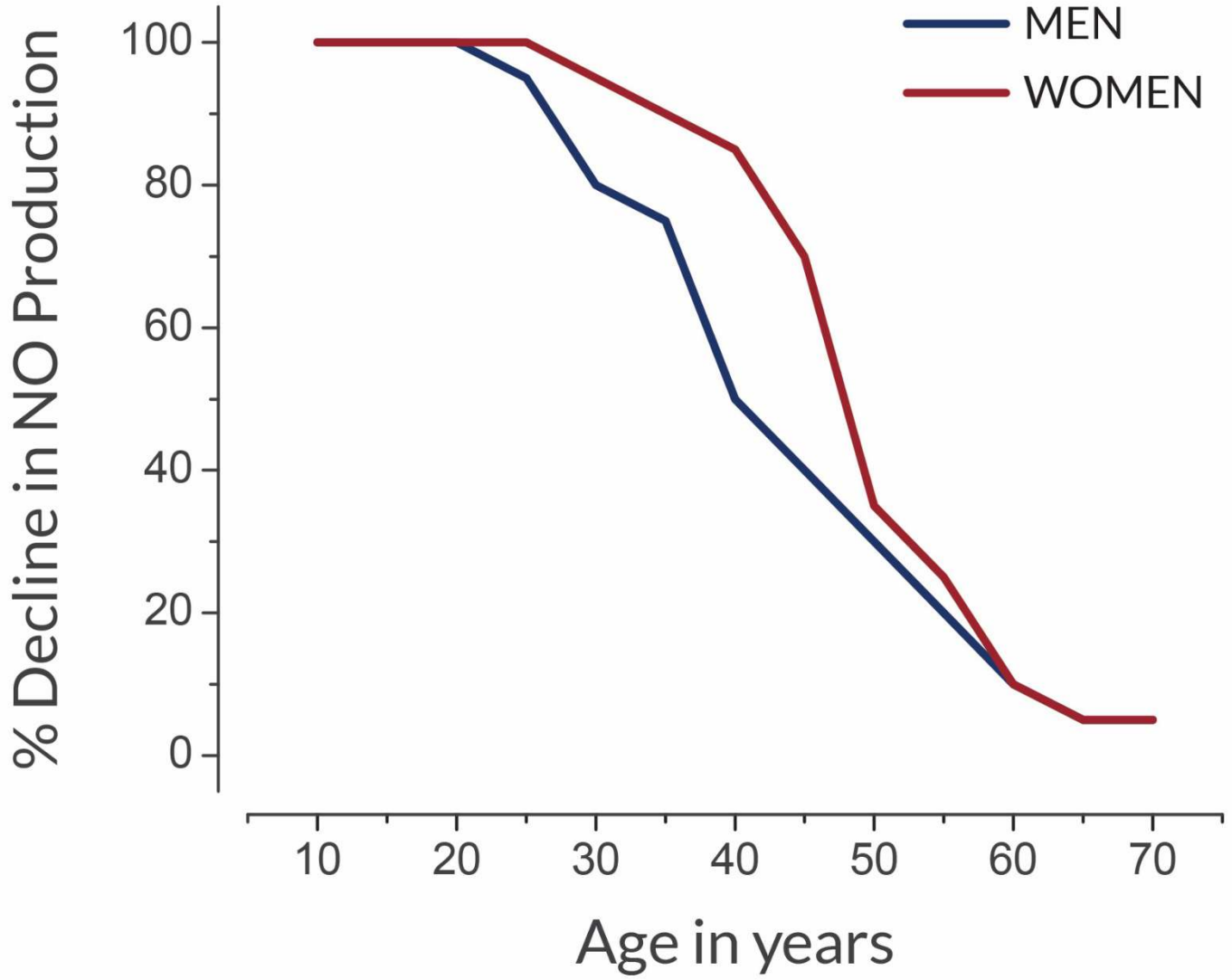
Endothelial Production of NO Declines with Age

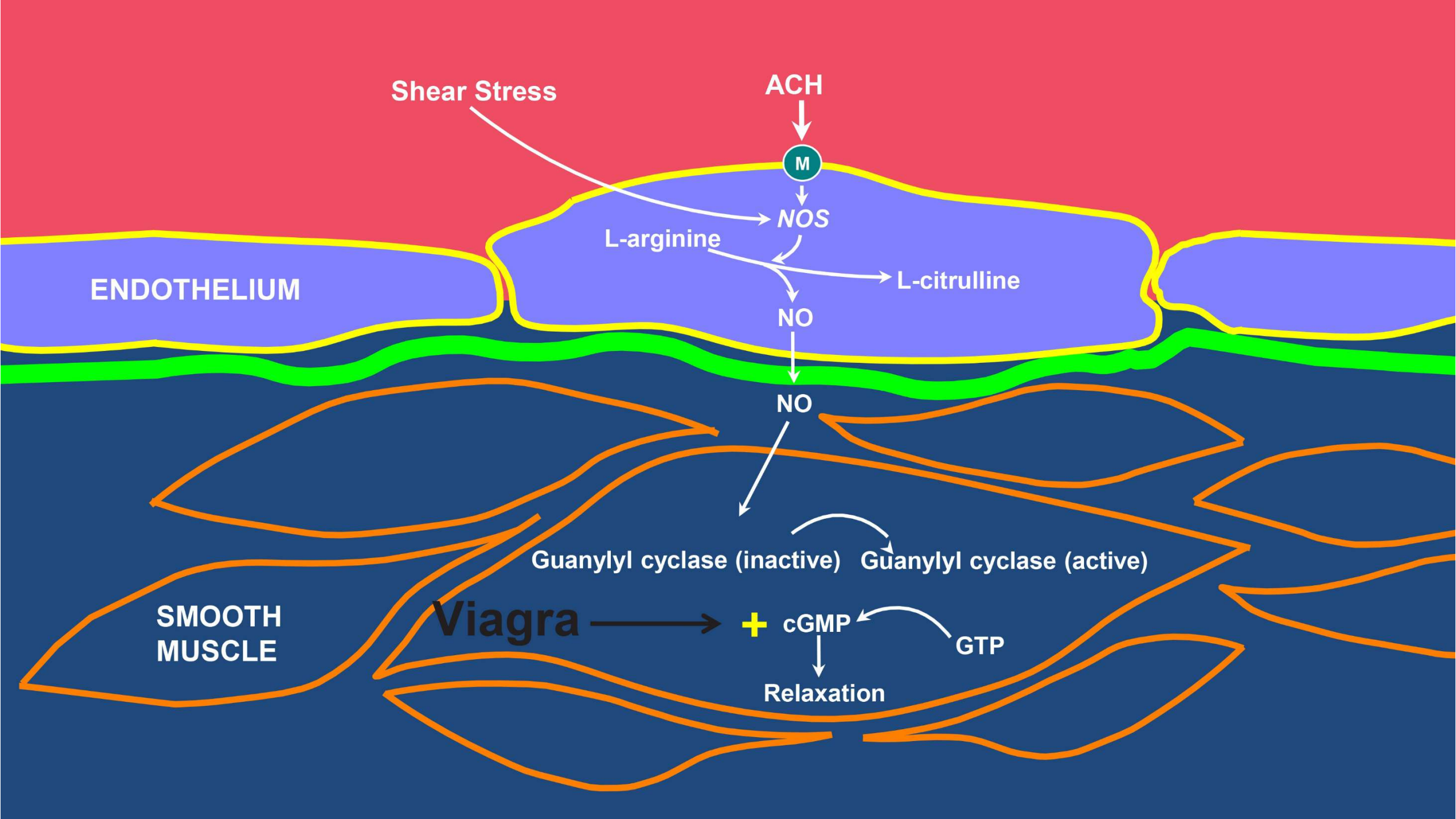
Gerhard et al Hypertension 1996

Celermajer et al JACC 1994

Taddei et al Hypertension 2001

Egashira et al Circulation 1993

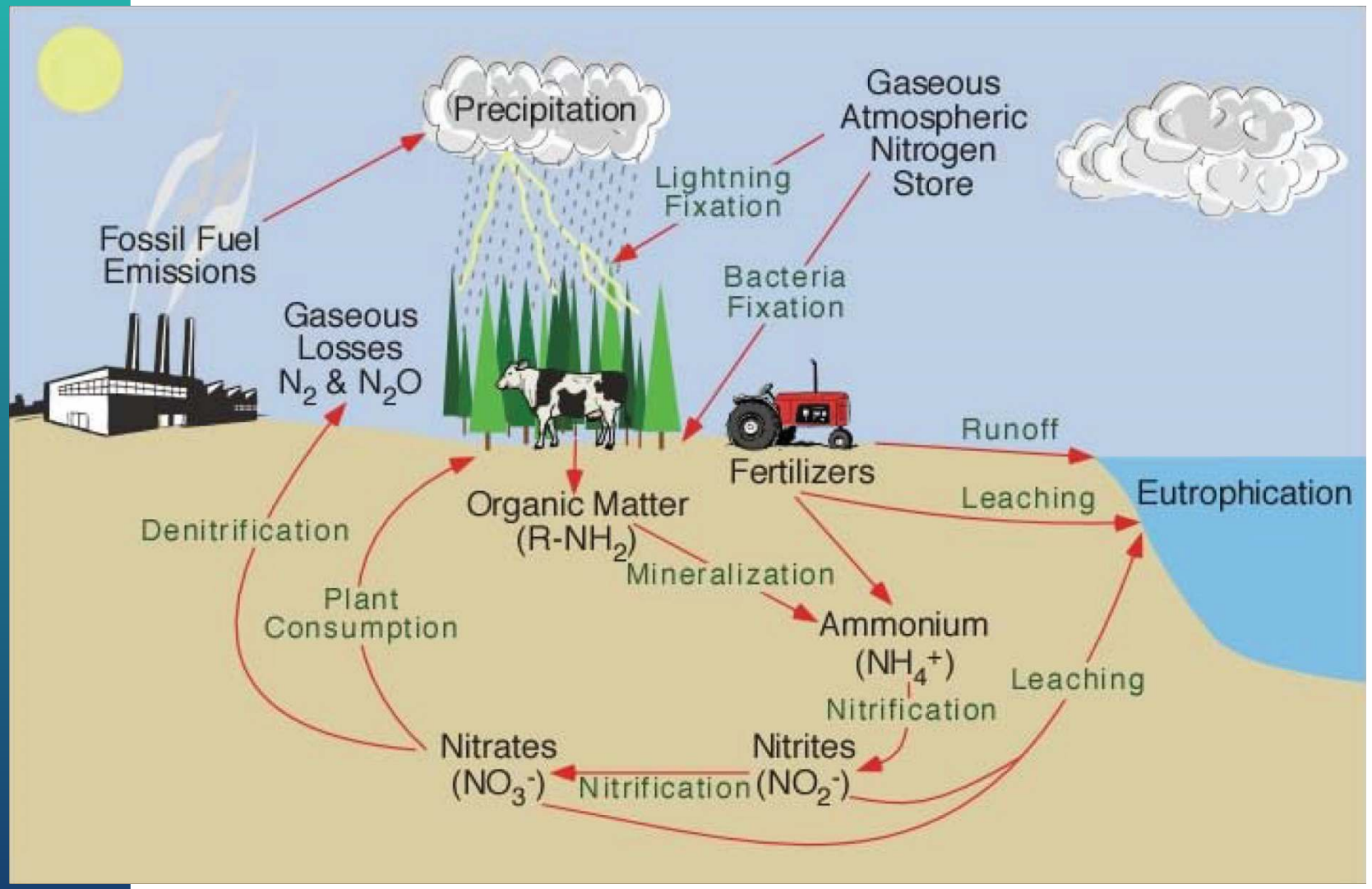



Shear Stress
ACH
M
NOS
L-arginine
L-citrulline
ENDOTHELIUM
NO
NO
Guanylyl cyclase (inactive)
Guanylyl cyclase (active)
SMOOTH MUSCLE
Viagra
+
cGMP
GTP
Relaxation

Can proper nutrition, food or Supplements provide NO 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.



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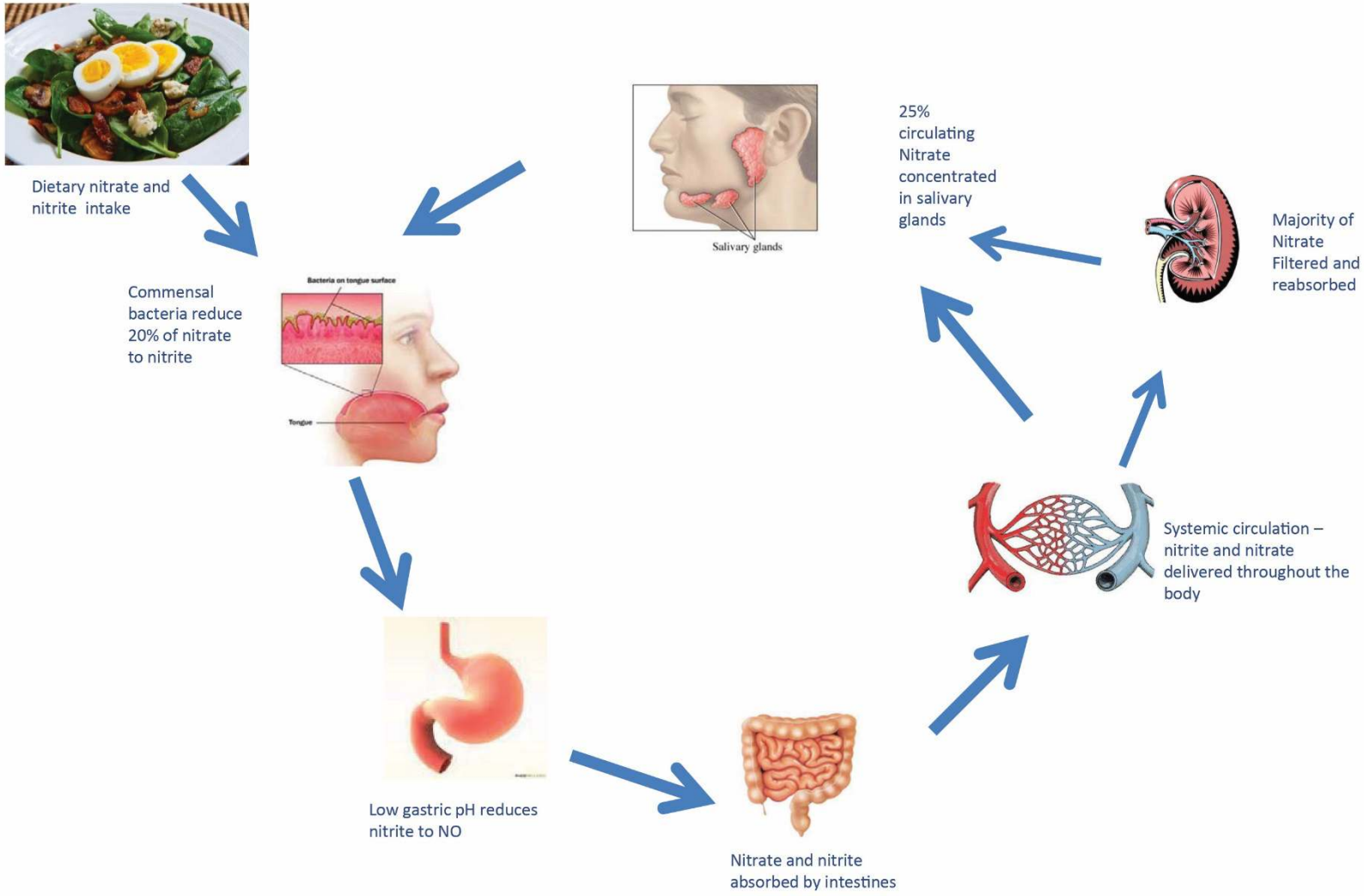
New Paradigm - Human Nitrogen Cycle



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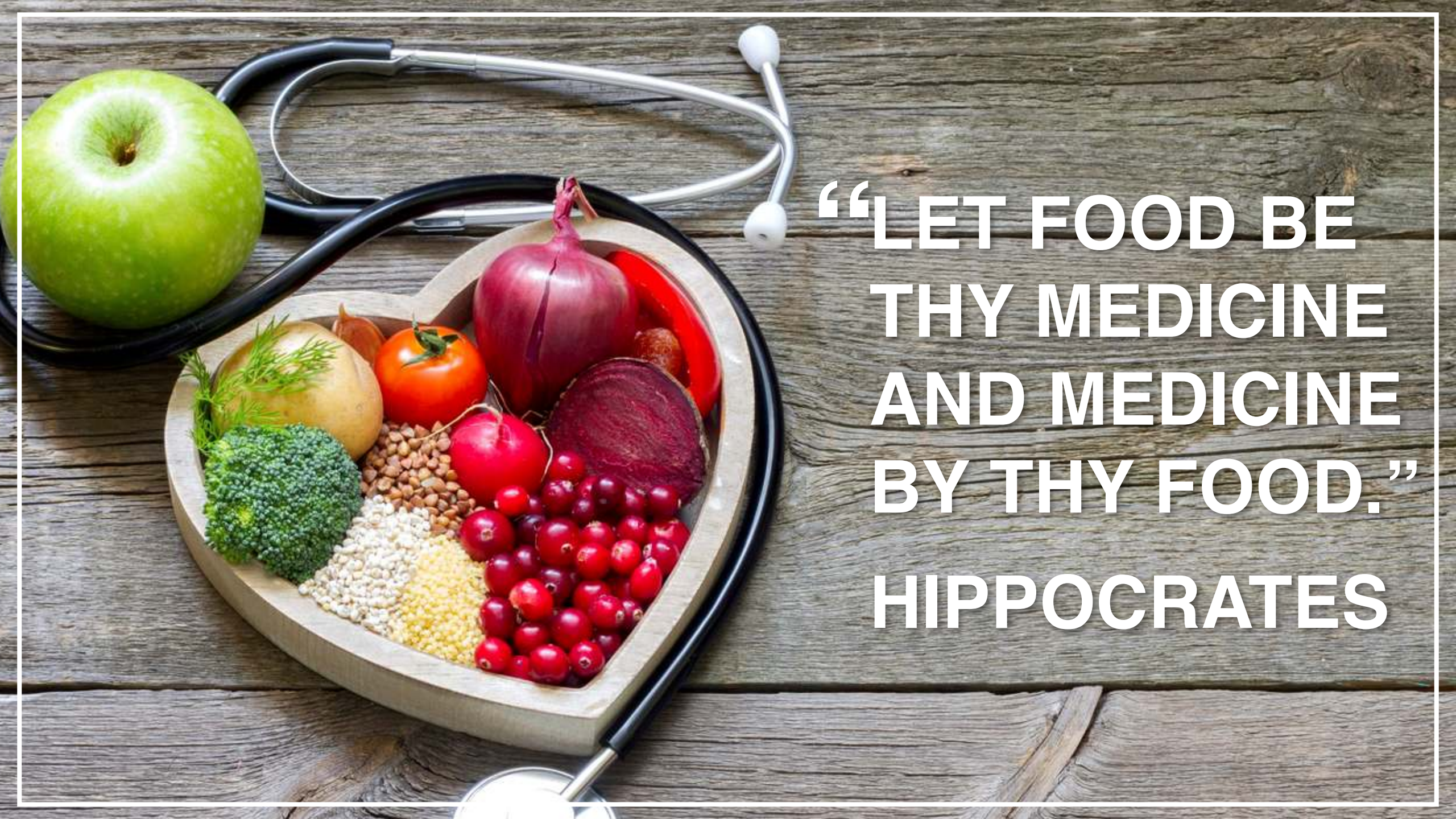
“LET FOOD BE THY MEDICINE AND MEDICINE BY THY FOOD.”
HIPPOCRATES

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

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

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Regional and Category Differences In **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.

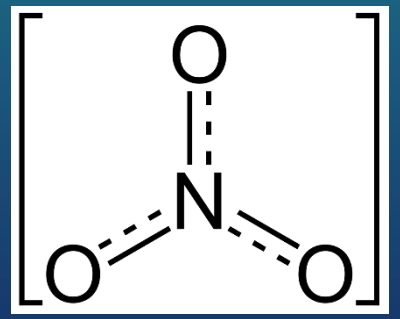
Nitrate is inert in Humans.

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



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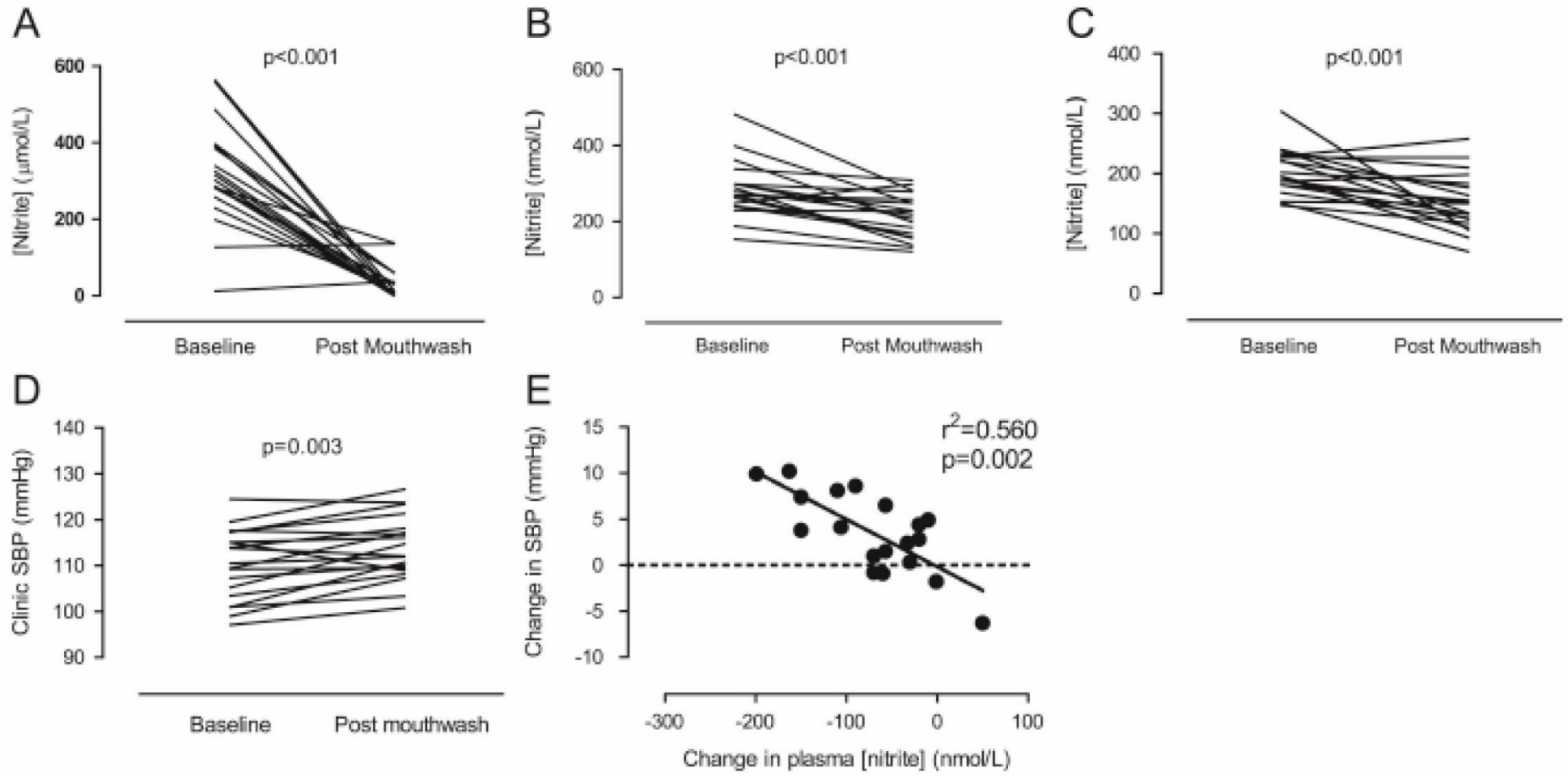
Plant based diets and/or Potassium Nitrate based products will only work in less than one third of Americans due to simple lifestyle habits

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



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

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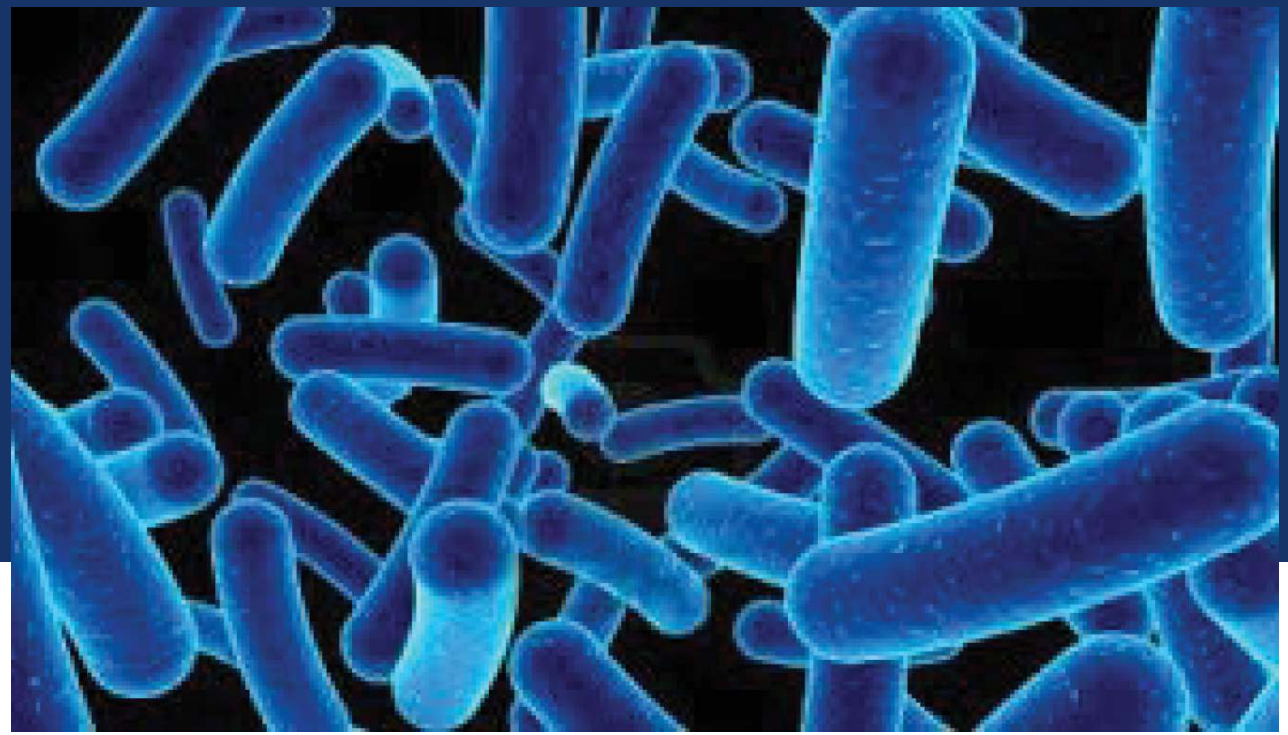
Genetic Diversity

23,000 genes



3,000,000 genes

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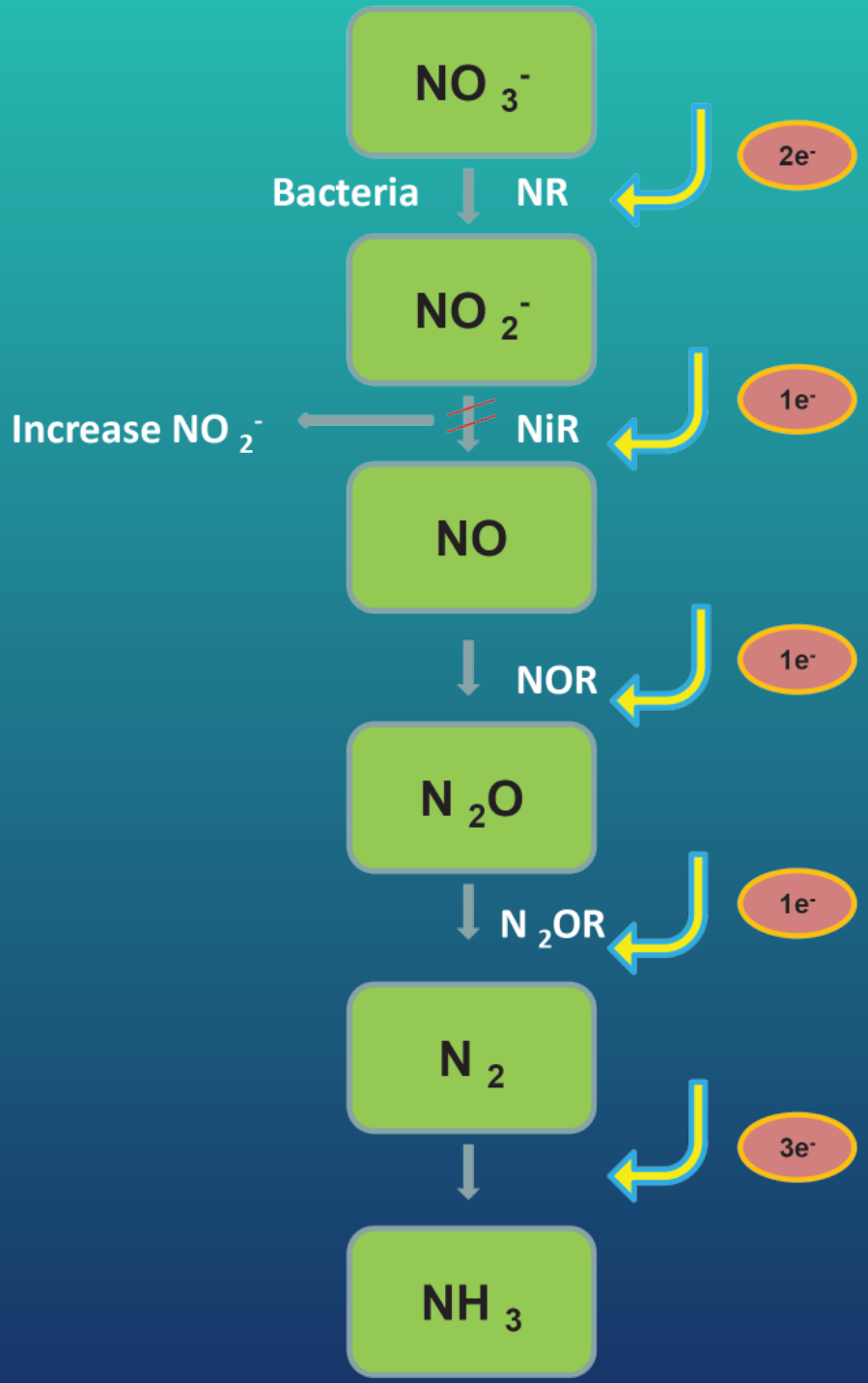
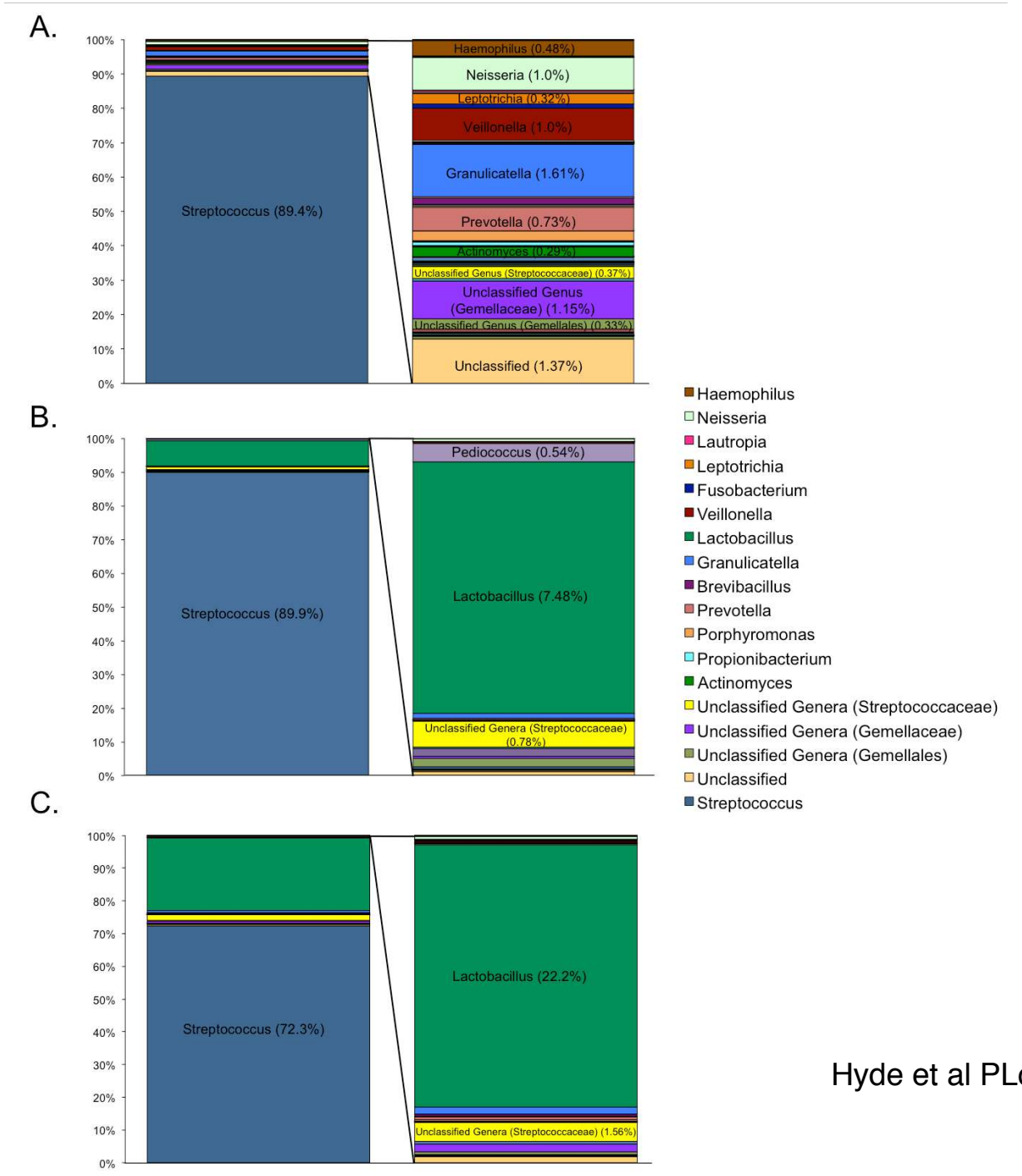


Ideal Community:

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



Best

Intermediate

Worst

Hyde et al PLoS One (2014)

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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?

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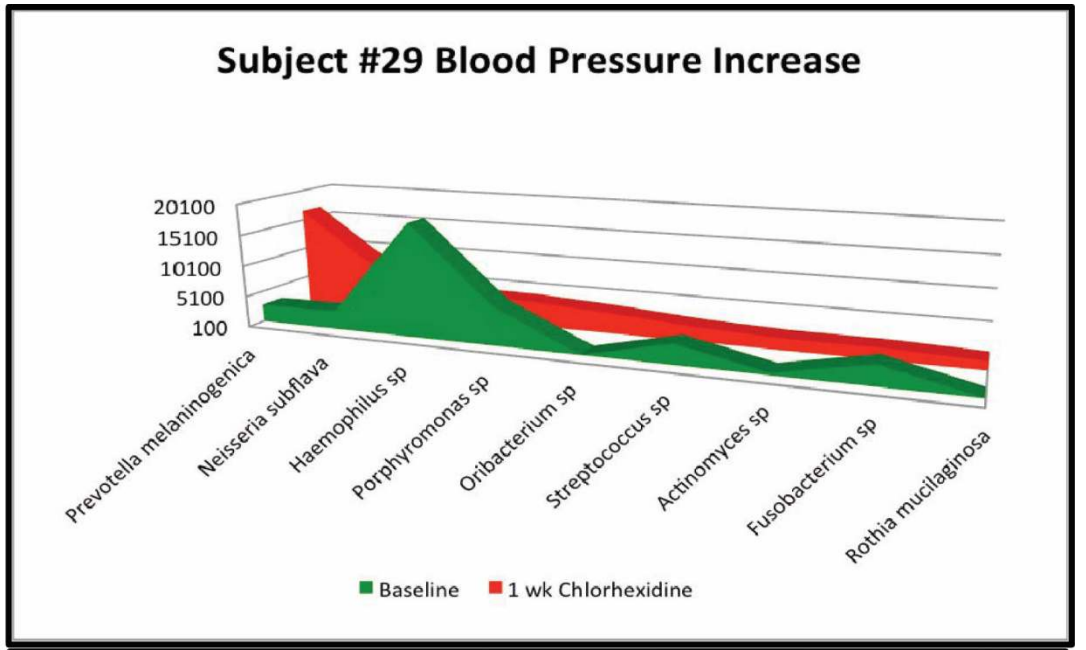
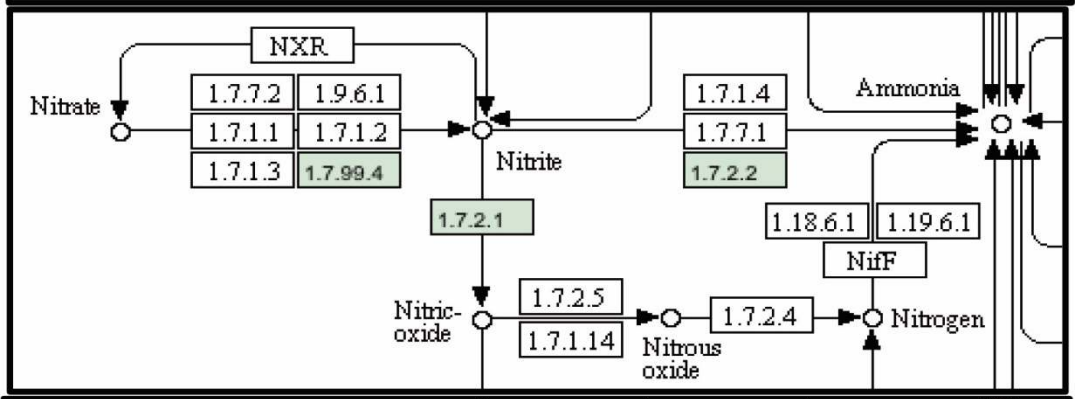
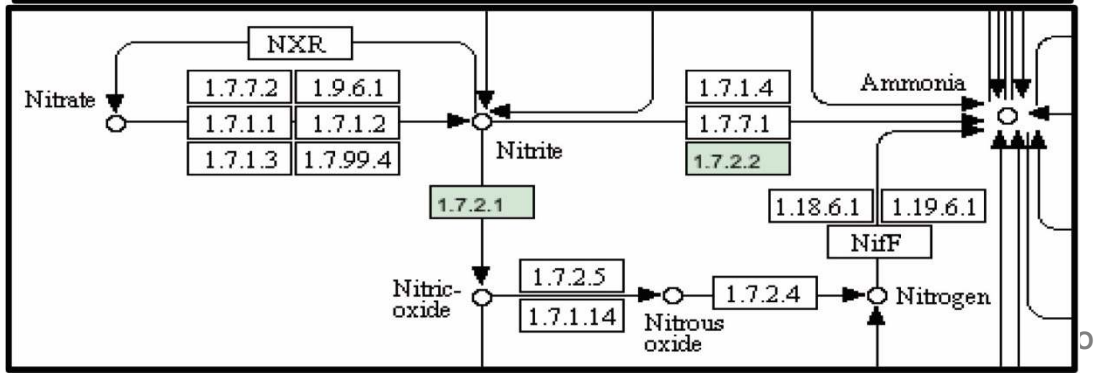
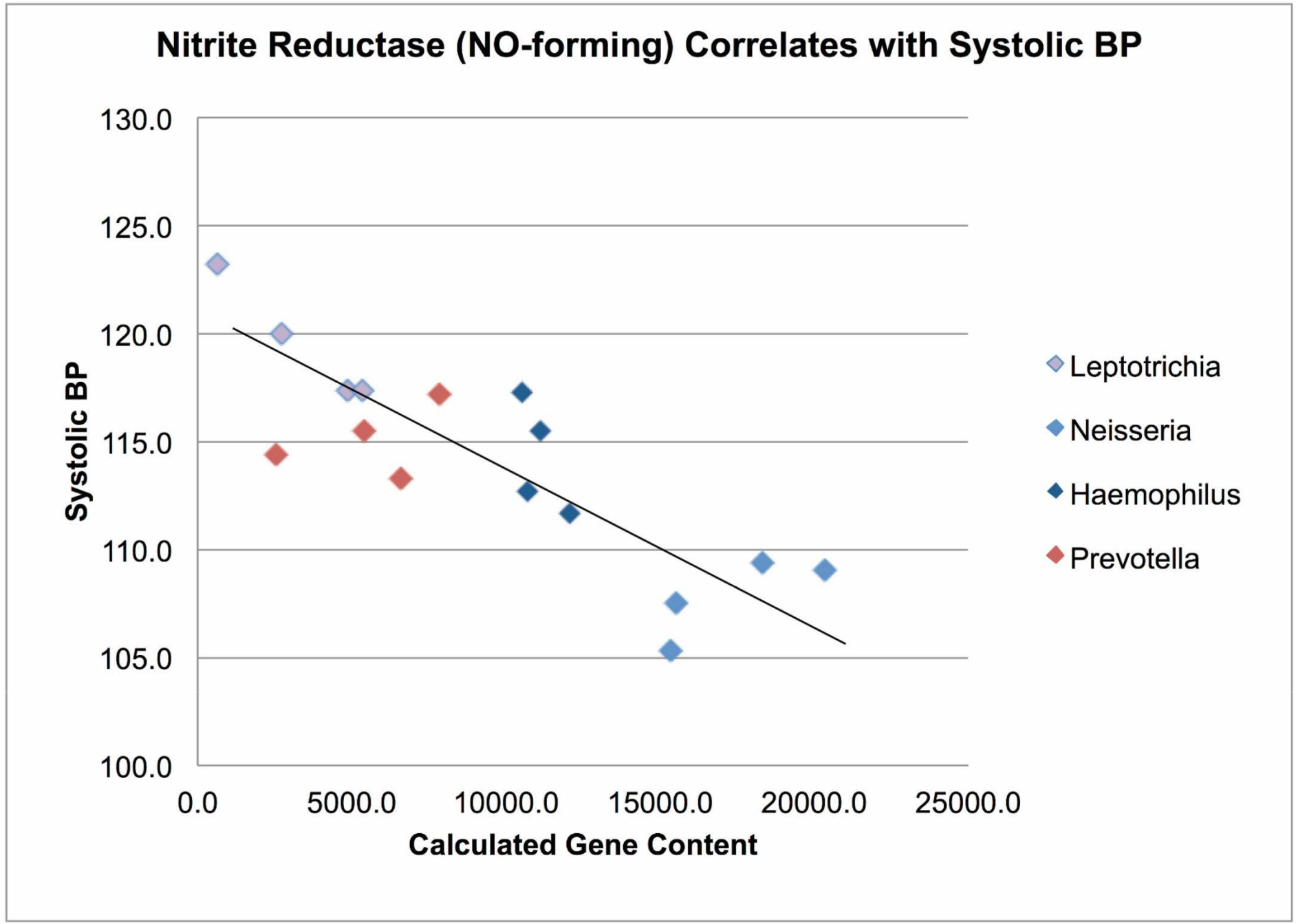
One week Chlorhexidine treatment caused 26 mmHg increase in systemic blood pressure.

This was associated with change in bacterial communities that disrupted nitrate reduction and NO production.

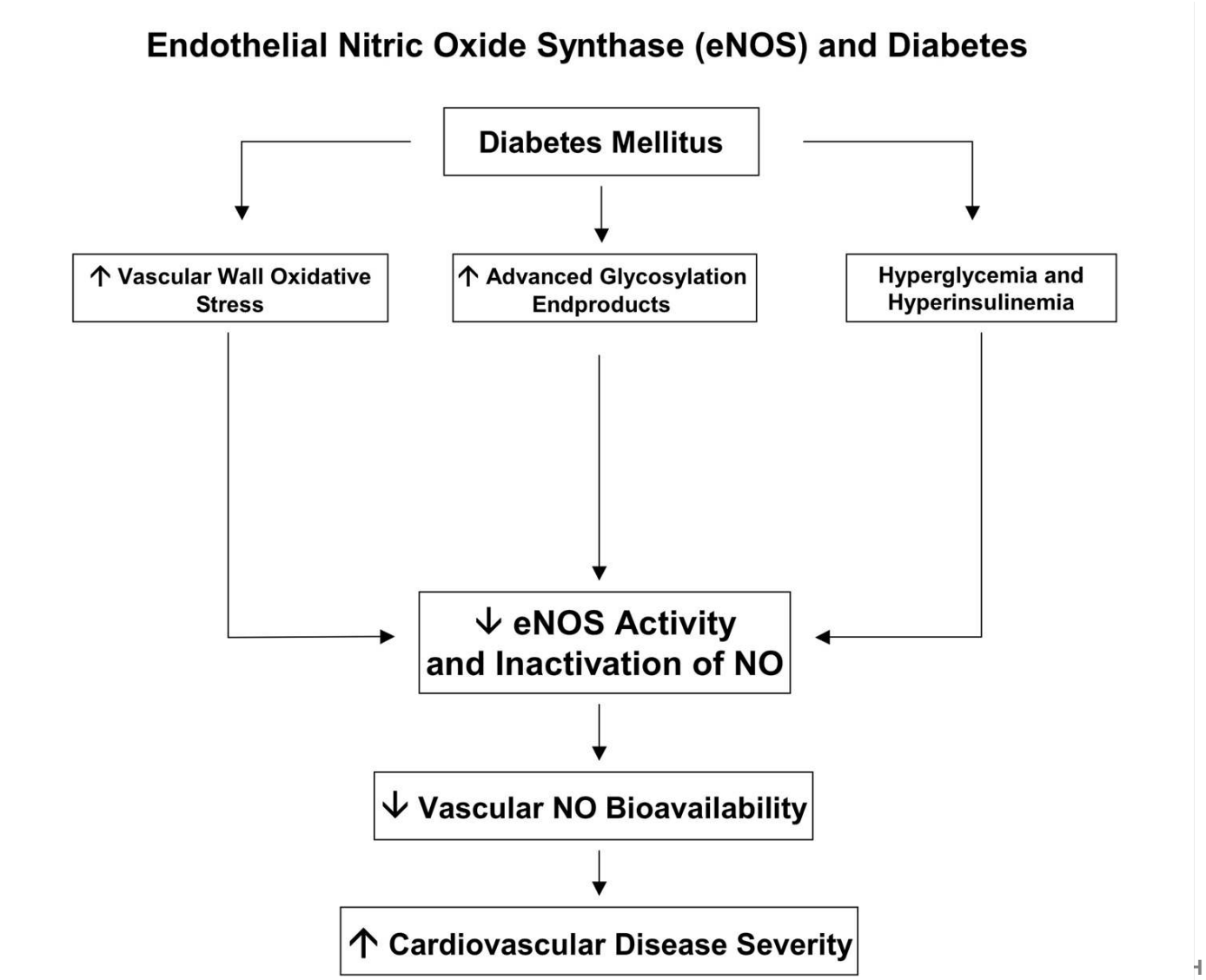







Nitrite Reductase (NO-forming) Correlates with Systolic BP
130.0
125.0
120.0
115.0
110.0
105.0
100.0
Systolic BP
0.0
5000.0
10000.0
15000.0
20000.0
25000.0
Calculated Gene Content
Leptotrichia
Neisseria
Haemophilus
Prevotella

Diabetes Leads to Insufficient NO Production



HERAPEUTIC INTERVENTION

Insufficient NO Production Leads to Diabetes

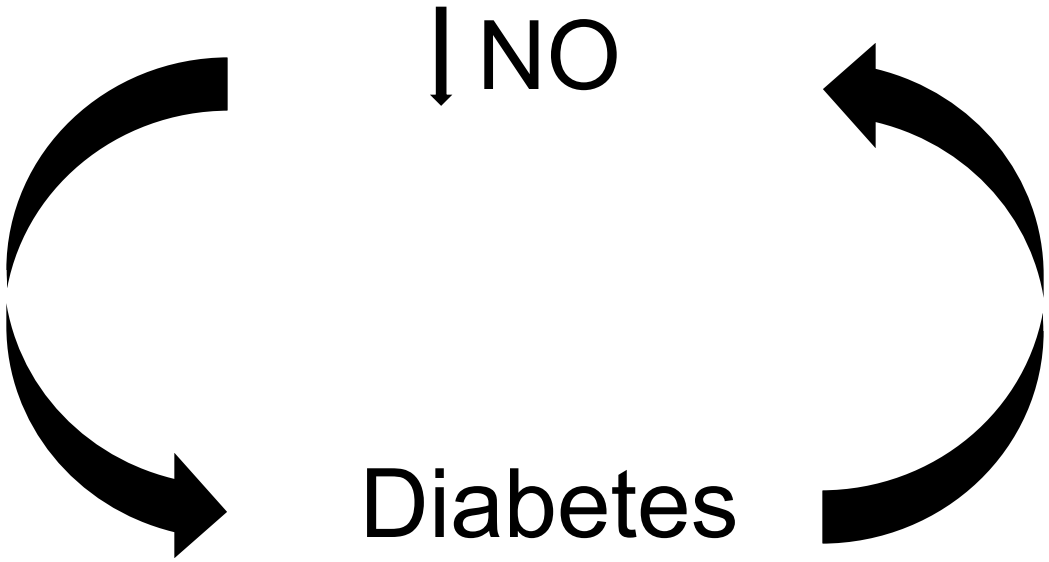
eNOS$^{-/-}$ mice display a disturbed blood-glucose concentration curve

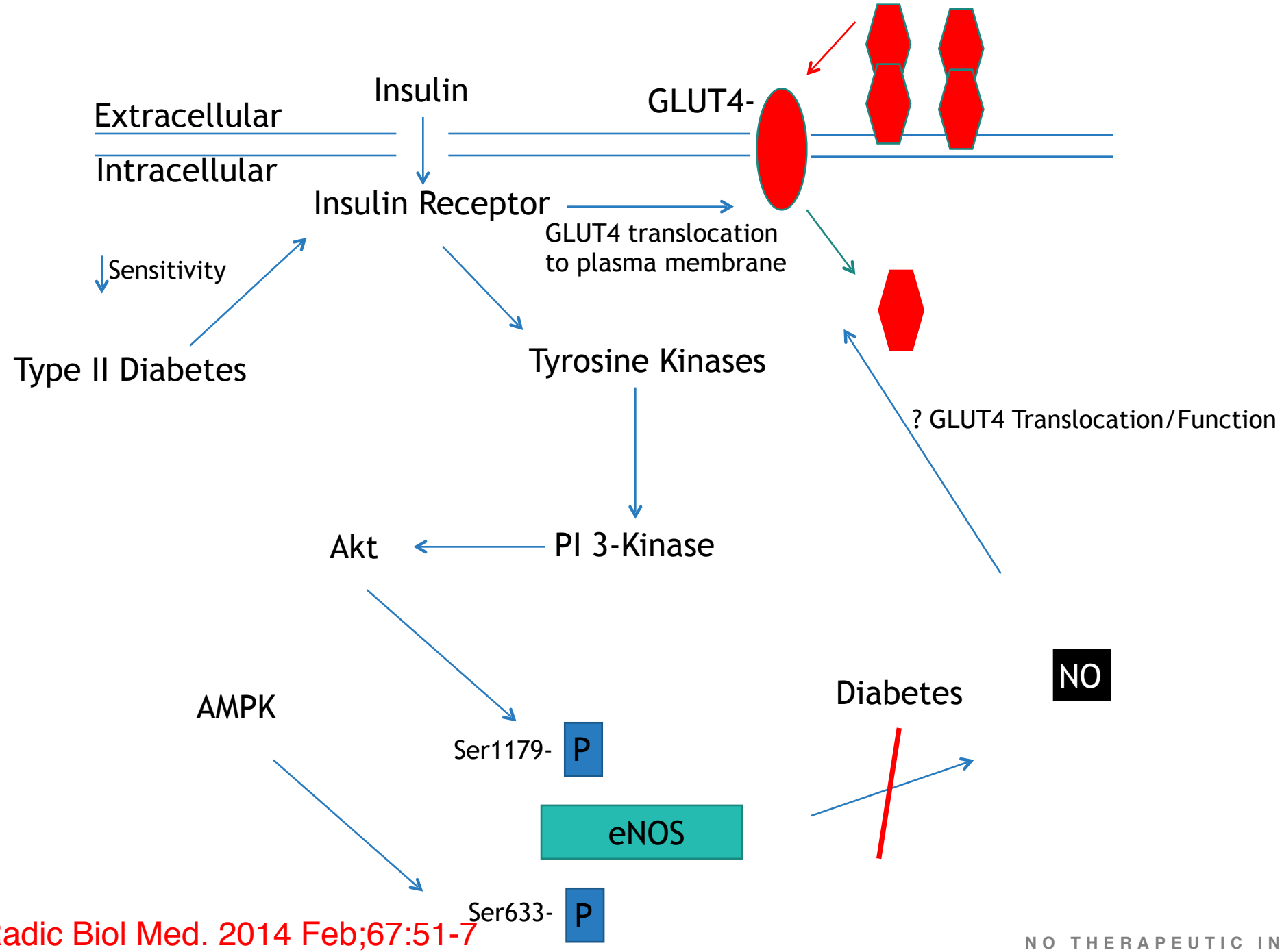
eNOS-/- mice have high proinsulin/insulin ratios

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 NO production.

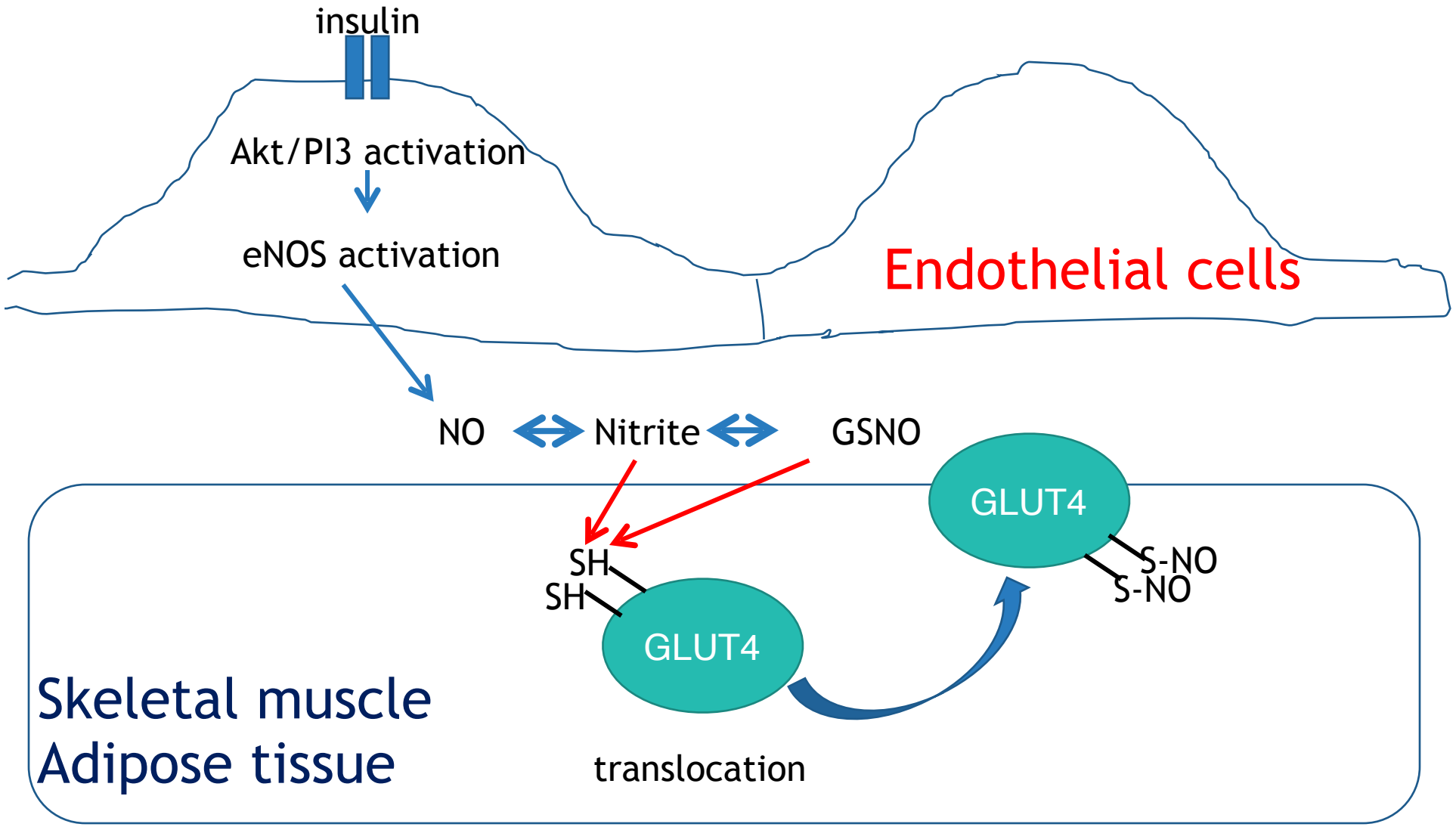
Perpetual Cycle of NO and Diabetes





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

NO THERAPEUTIC INTERVENTION



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

Traditional Chinese Medicine

Traditional Chinese Medicine (TCM) has been used as a main stream of medical care throughout Asia for centuries. But it is still considered an alternative medical system in the western world. Mostly because of a lack of understanding of their mechanisms of action and/or the active compounds.

Many cardiovascular diseases are characterized by a NO insufficiency. There are a number of published reports on the association of TCM and NO-related effects in cardiovascular field. However, their mechanism of action is far from clear.

TCMs for Cardiovascular Indications

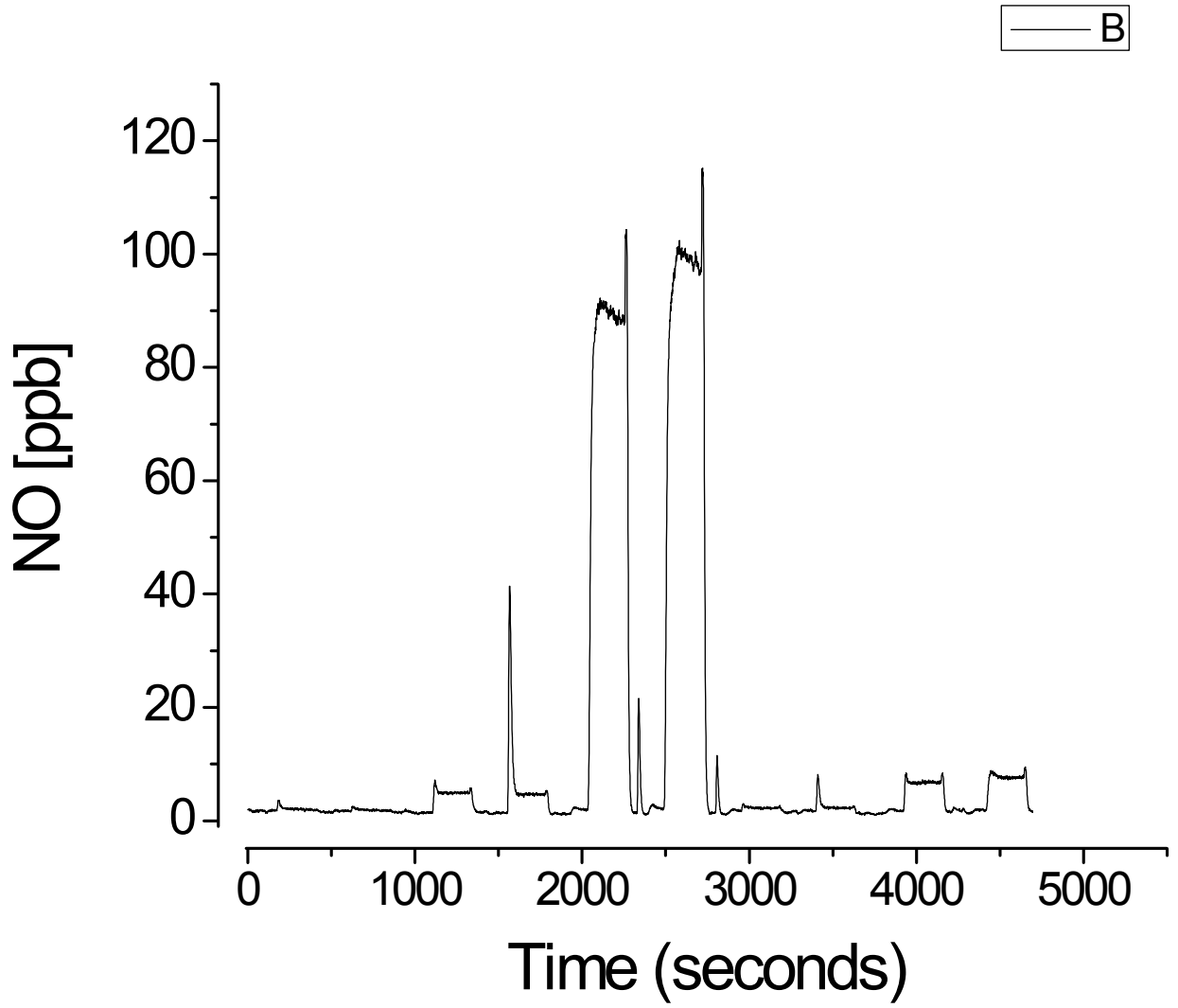
Table 1
Common traditional Chinese medicines and their primary indications as given to patients

	Name of Chinese herb			Primary indication
	Chinese	Latin	English	
DS	DanShen	*Radix salviae miltiorrhizae*	Danshen root	CAD
GL	GuaLou	*Fructus trichosanthis*	Snakegourd fruit	CAD, acute MI, hyperlipidemia
XB	XieBai	*Bulbus allii macrostemi*	Longstamen onion bulb	CAD, acute MI, hyperlipidemia
SC	SanChi	*Radix notoginseng*	Sanchi	CAD
RX	RuXiang	*Resina olibani*	Frankincense	Hypertension
CS	ChiShao	*Radix paeonia rubra*	Red Peony Root	CAD
HS	HongSheng	*Radix ginseng*	Ginseng	Heart failure, CAD
SBP	BingPiang	*Borneolum syntheticum*	Borneol	Increase other herb's function for CAD or brain disease
NBP	TianRanBingPiang	*Cinnamomum*	Borneol	Increase other herb's function for CAD or brain disease

CAD, coronary artery disease; MI, myocardial infarction.

Tang et al FRBM 2009

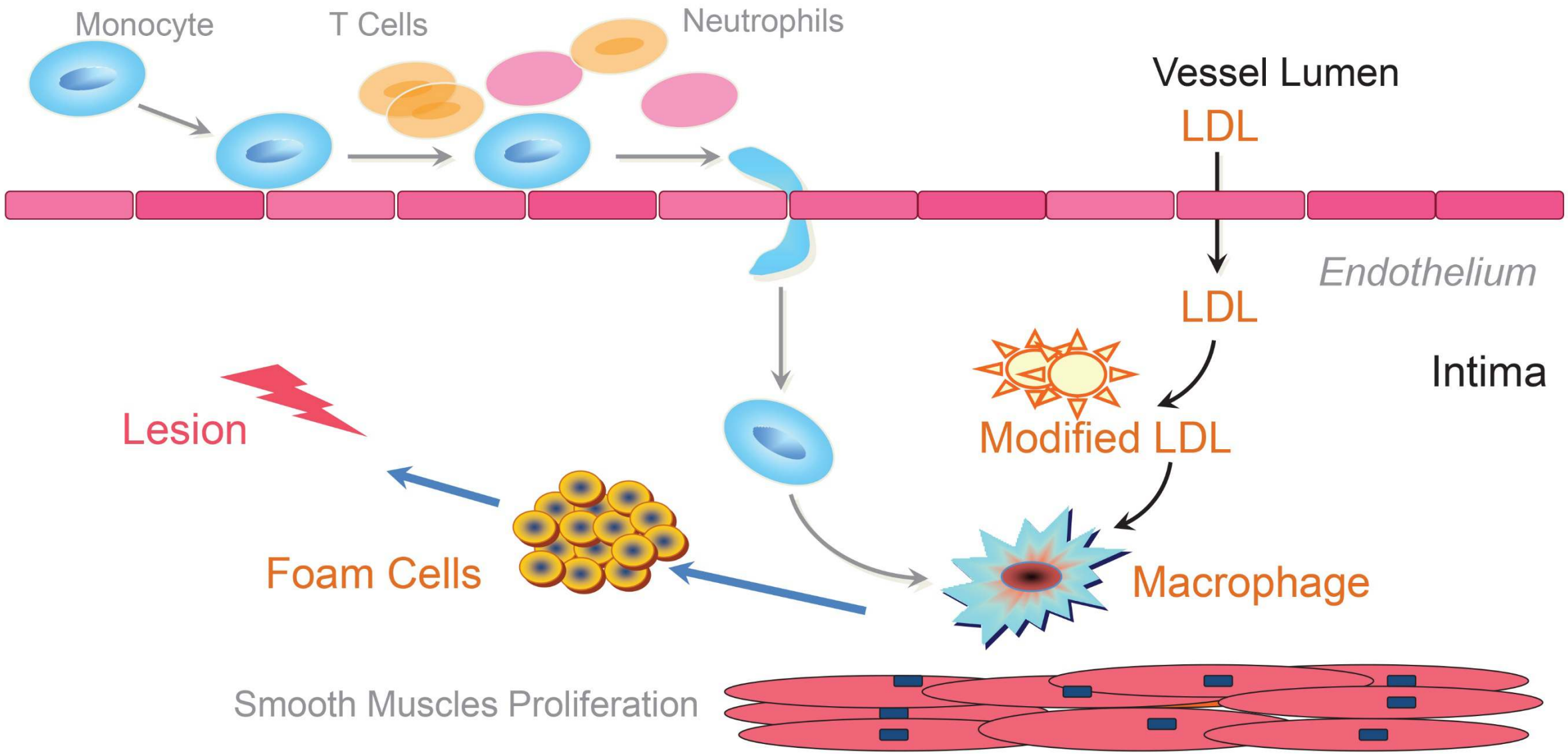
Kinetics of NO Formation



Tang et al FRBM 2009

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

Atherogenesis



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Atherogenic Diet

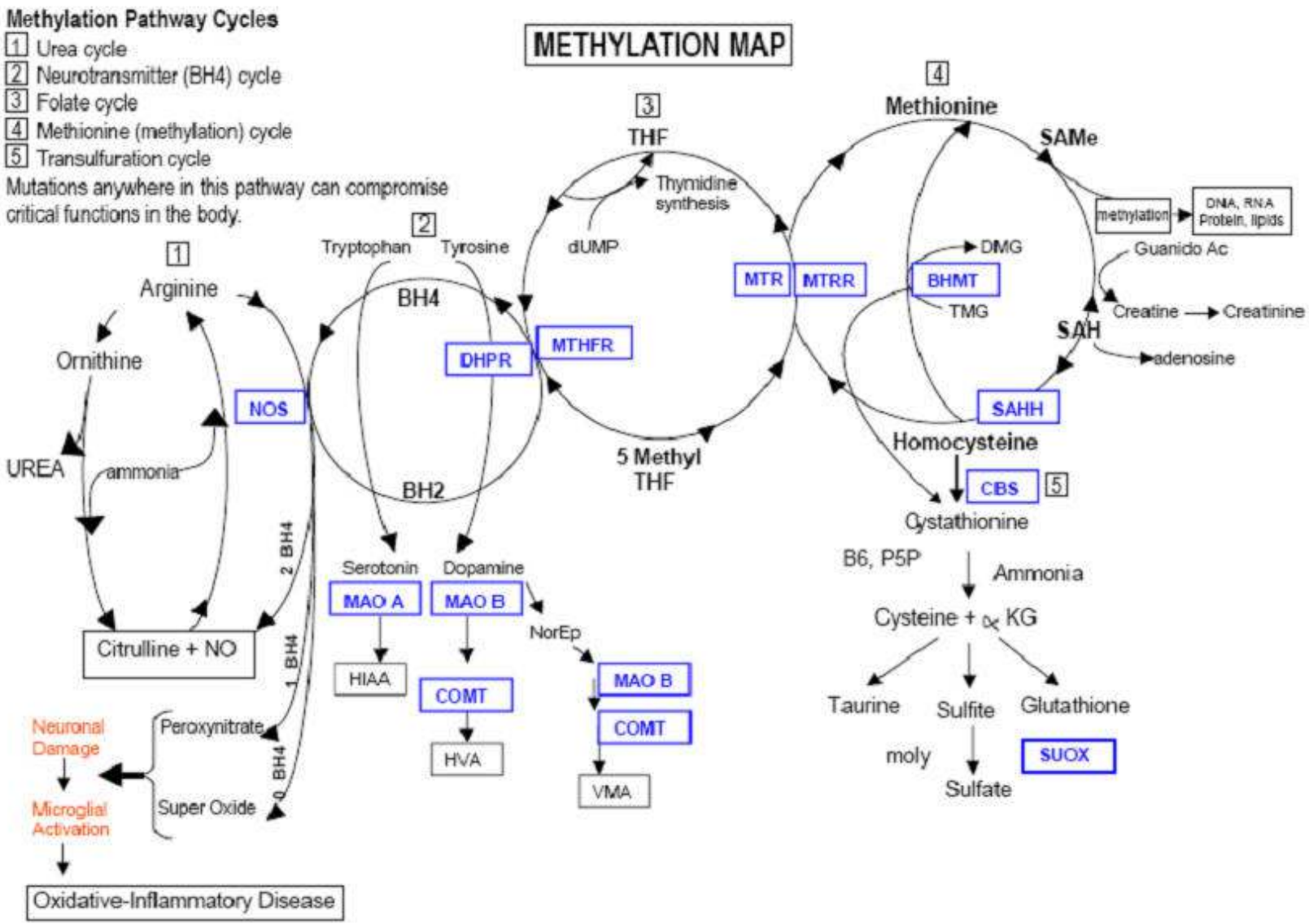
Stokes et al Am J Physiol Heart Circ Physiol. 2009 May;296(5):H1281-8

NO THERAPEUTIC INTERVENTION

Atherogenic Diet + NO

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

What about Genetic Testing?
Do Specific SNPs Affect NO Production



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Development of Safe and Effective **NO-based Technology**

1. Provide an exogenous source of NO
2. Promote endogenous endothelial production of NO
3. Account for differences in non-responders to nitrate therapy and L-arginine
4. Plant-based natural product chemistry (clean and testable)
5. Clear product experience (demonstrate changes in vascular structure and function
6. Strong and sound basic science behind technology
7. Clinically proven in peer-reviewed, placebo-controlled trials
8. Intellectual Property for protection

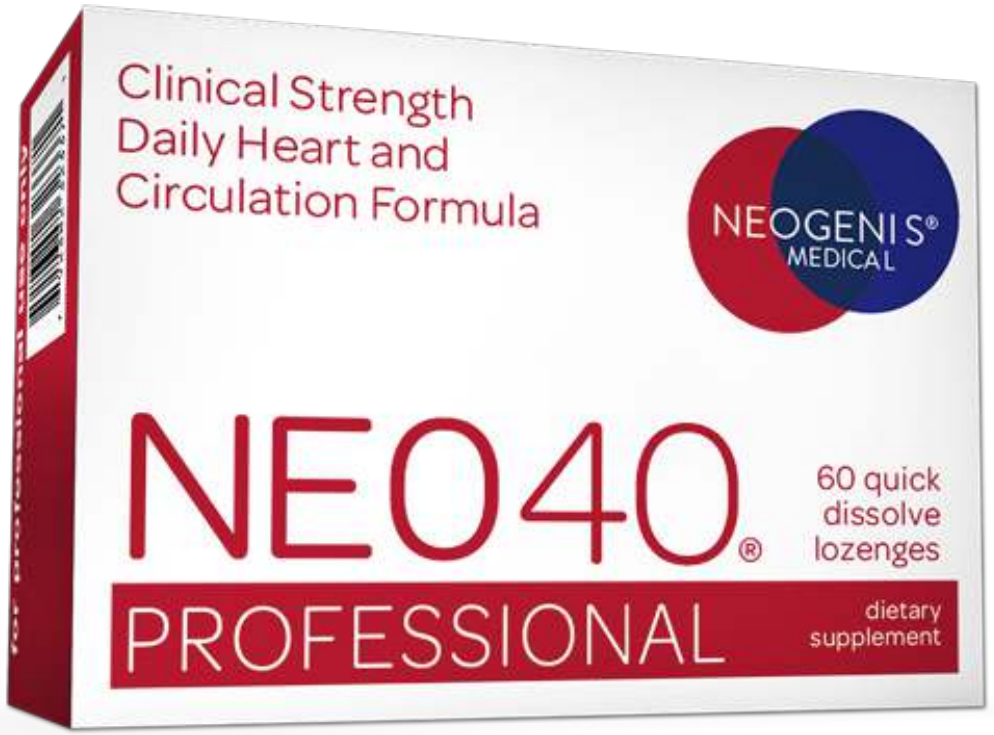
Neo40® Pro is Superior Technology

The Benefits:

- The ONLY technology in the world to provide an exogenous source of NO
- Promotes endothelial production of NO
- Provides the body the nutrients necessary for restoring NO

The Proof & Track Record:

- Clinically proven in 5 published trials
- No tolerance development
- Drug-like effects without side effects
- Clear product experience



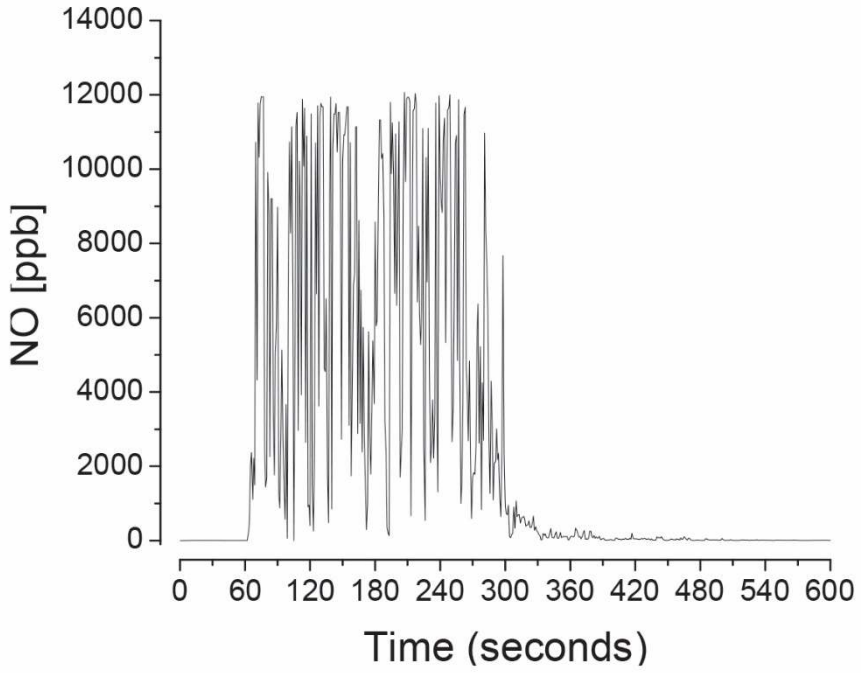
US patents

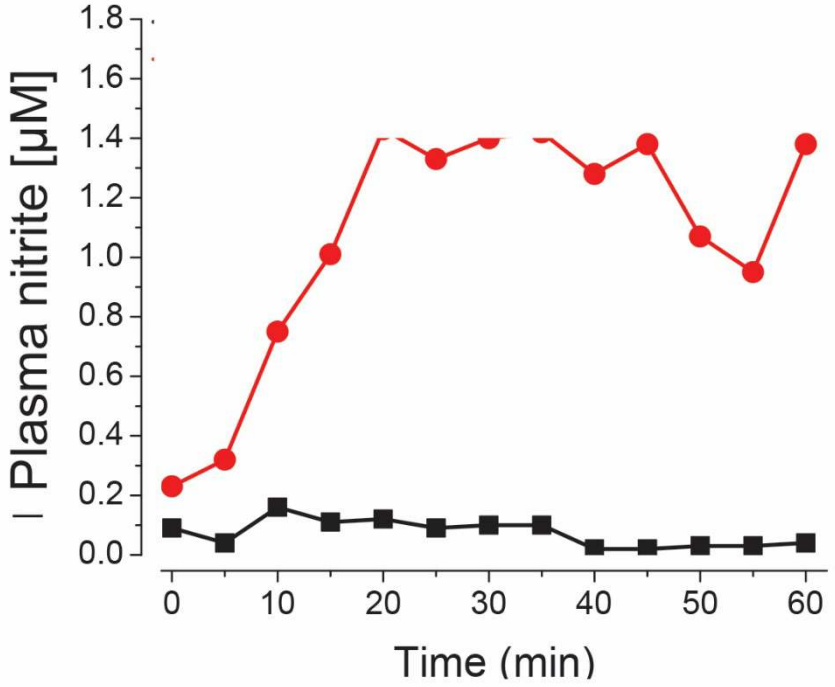
8,298,589
8,303,995
8,435,570
8,962,038
9,119,823
9,241,999

NO THERAPEUTIC INTERVENTION

NO Clinical Trial Results

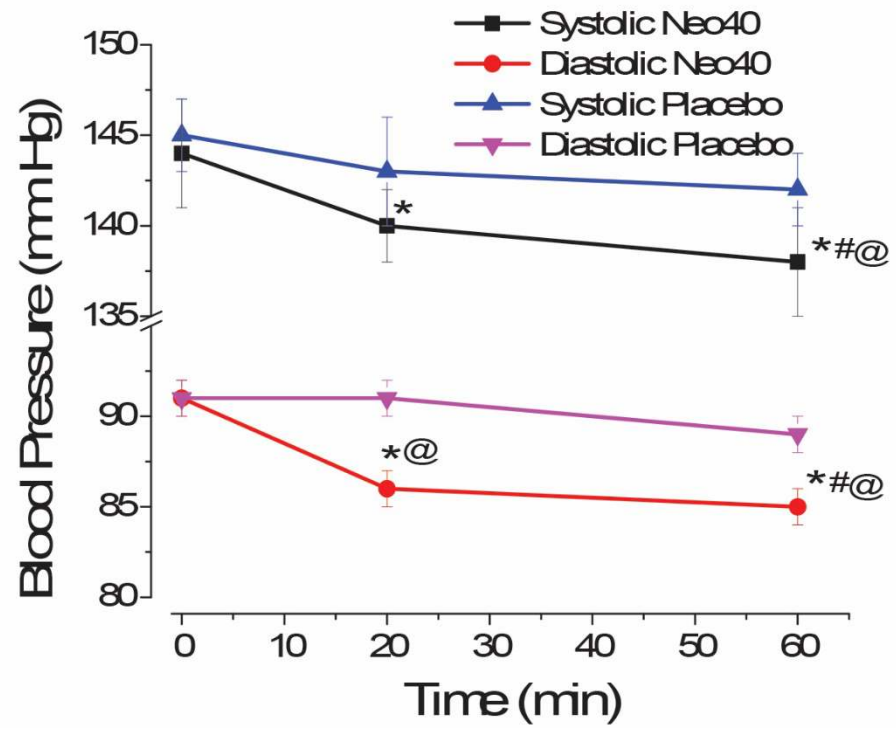
Strong & Sustained Nitric Oxide Activity

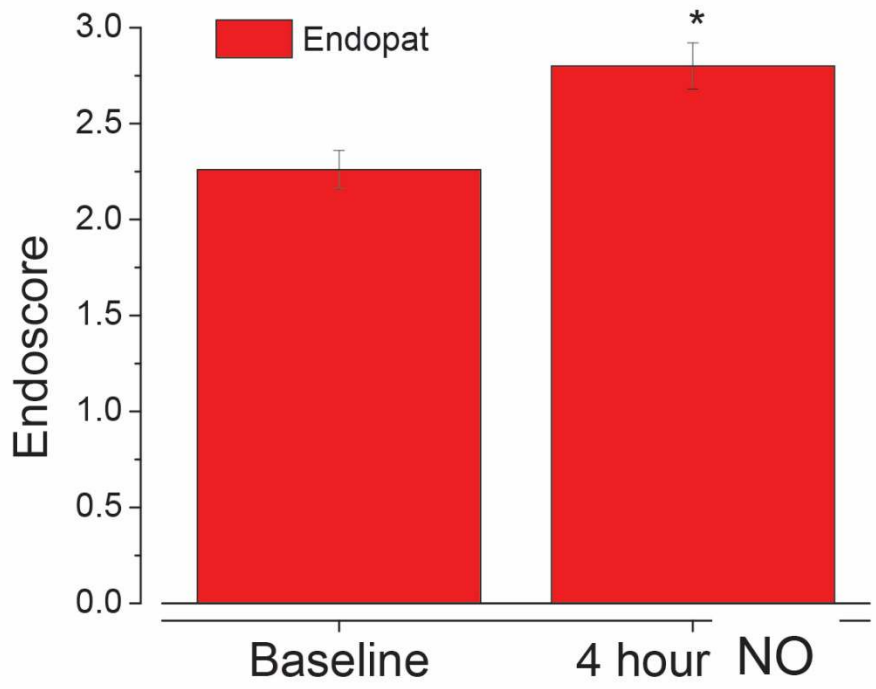




Zand et al Nutrition Research 2011

NO Supports **Healthy Blood Pressure** And **Improves Endothelial Function**

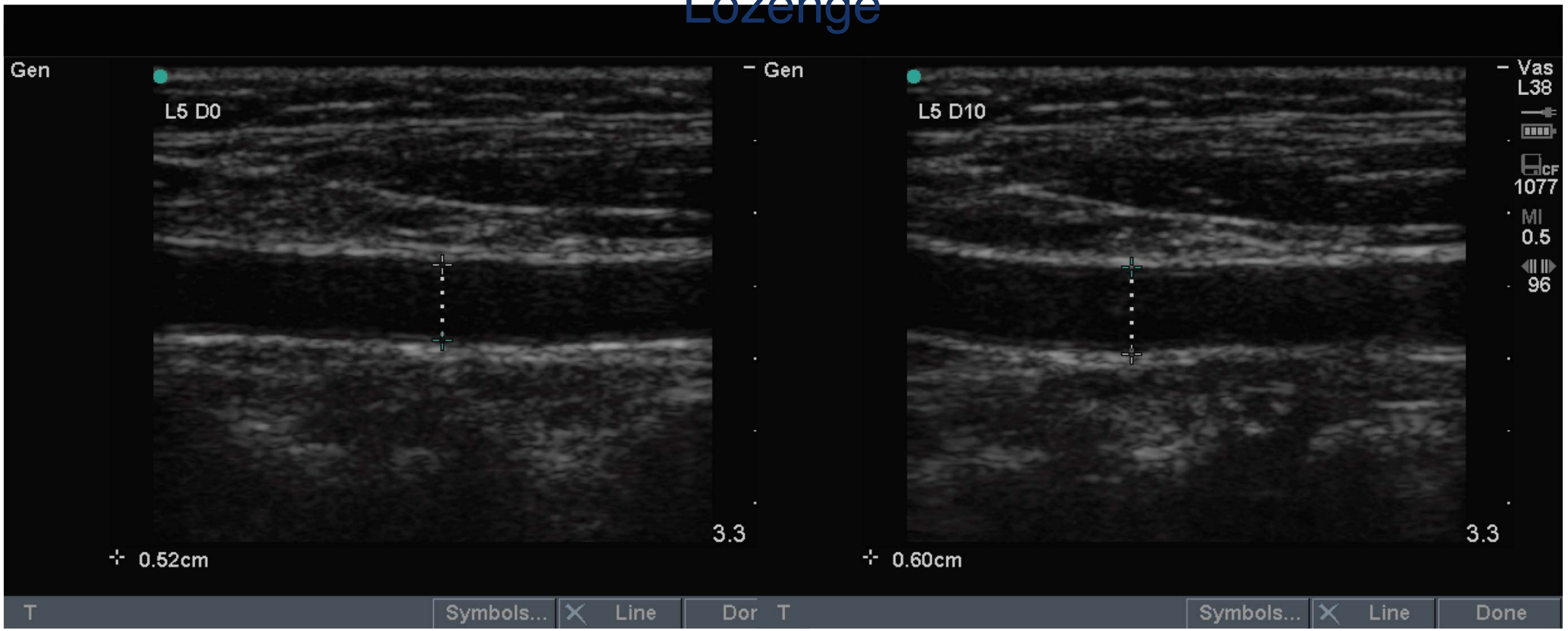




Flow mediated dilation

Houston, Hays JCH 2014

Representative Ultrasound Before and 10 minutes after NO Lozenge



13% increase in vessel diameter causes a **34% increase** in blood flow

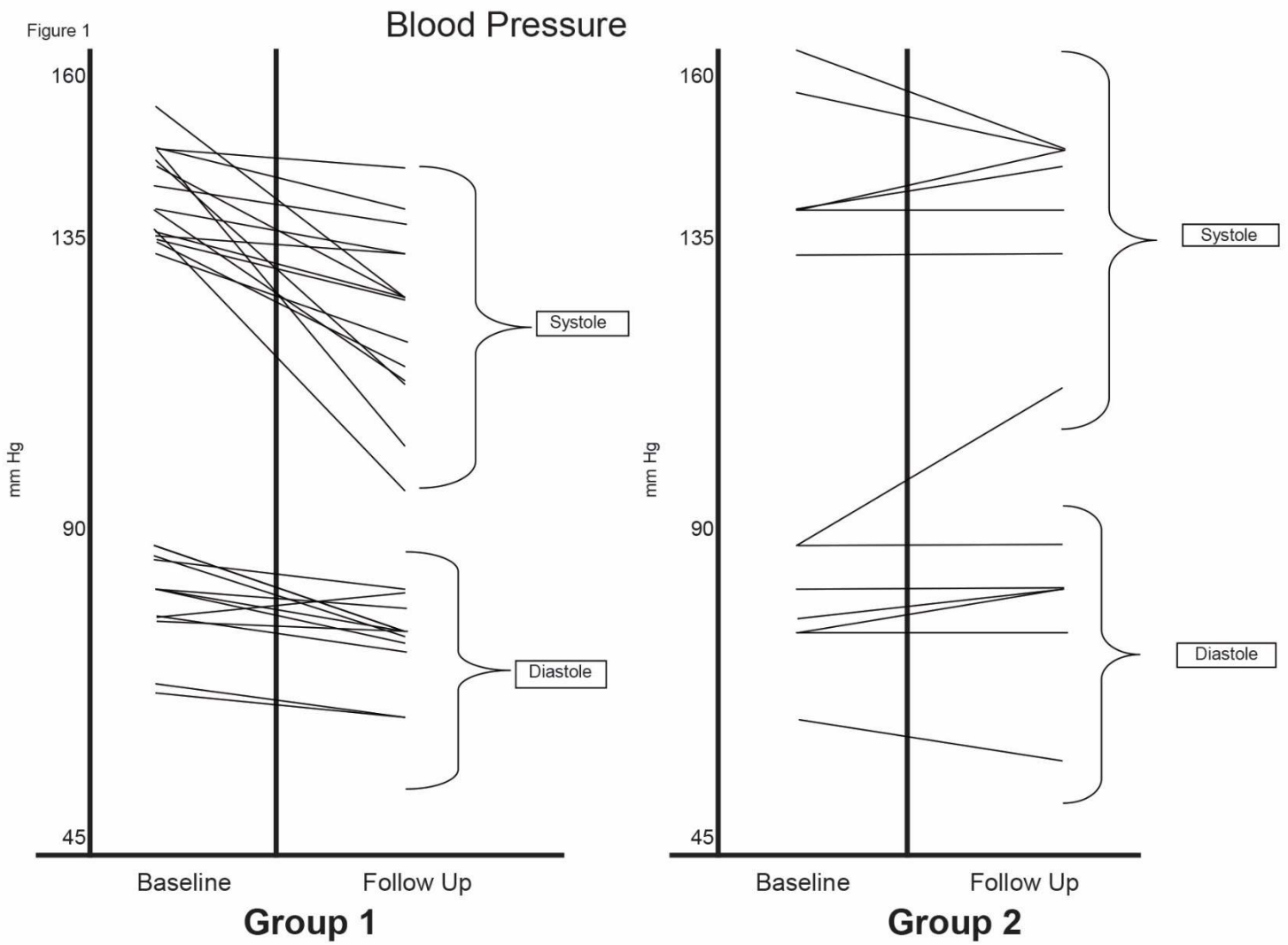
NO THERAPEUTIC INTERVENTION

Pre-Hypertension Trial

Cedars Sinai Medical Center

PI: Ernst Schwarz MD, PhD

Biswas et al JCPT 2014



NO THERAPEUTIC INTERVENTION

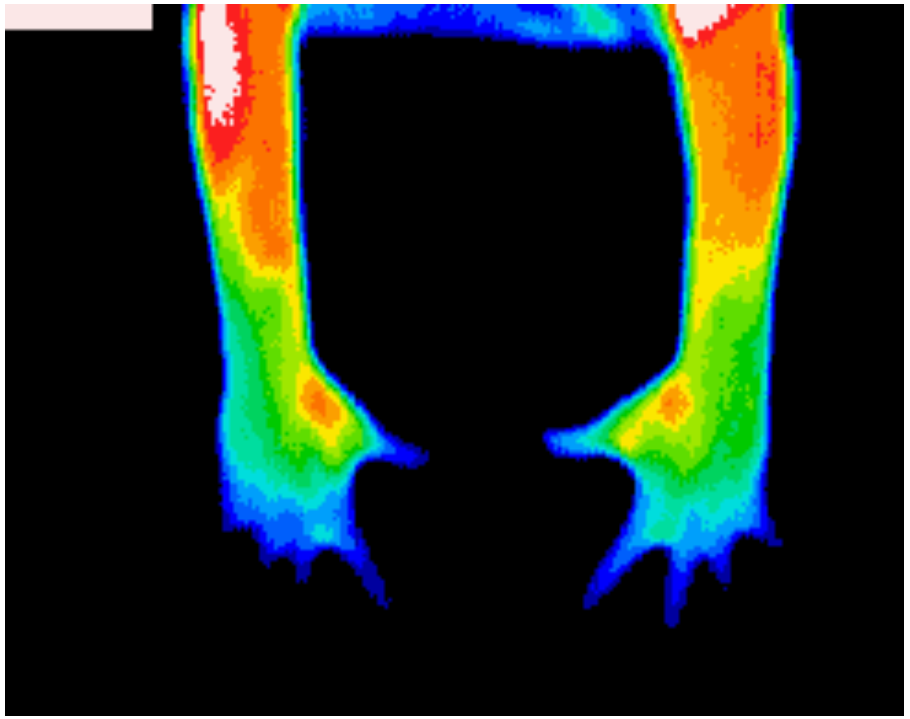
30 Day Placebo Controlled Trial

	Group 1 (mean ± SD)			Group 2 (mean ± SD)			Baseline: NO vs placebo (p-value)	Follow-Up: NO vs placebo (p-value)
	Baseline	Follow-Up	Δ	Baseline	Follow-Up	Δ		
BP (mmHg, systole; diastole)	138±12; 84±5	126±12; 78±4	12; 6 reduction (p<0.001)	138±21; 80±8	135±17; 82±8	N.S.	0.19; 0.012	0.26; 0.25
Heart Rate (bpm)	75±9	76±8	N.S.	80±10	79±8	N.S.	0.14	0.33
6-Minute Walk Test (meters)	596±214	650±197	55 improvement (p<0.005)	590±8	606±225	N.S.	0.25	0.35
SF-36v2 (PCS; MCS)	48±10; 40±9	50±8; 45±7	p<0.05	43±10; 37±9	37±11; 37±7	significant worsening (p<0.05)	0.08; 0.06	0.08; 0.03

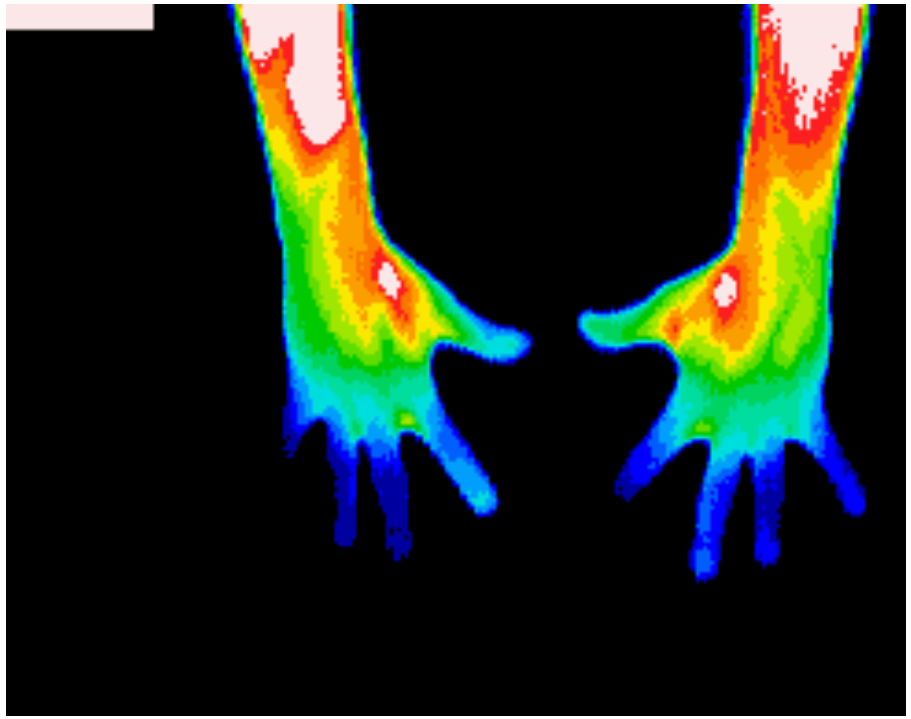
Biswas et al J CPT 2014

Thermographic Images

Before NO



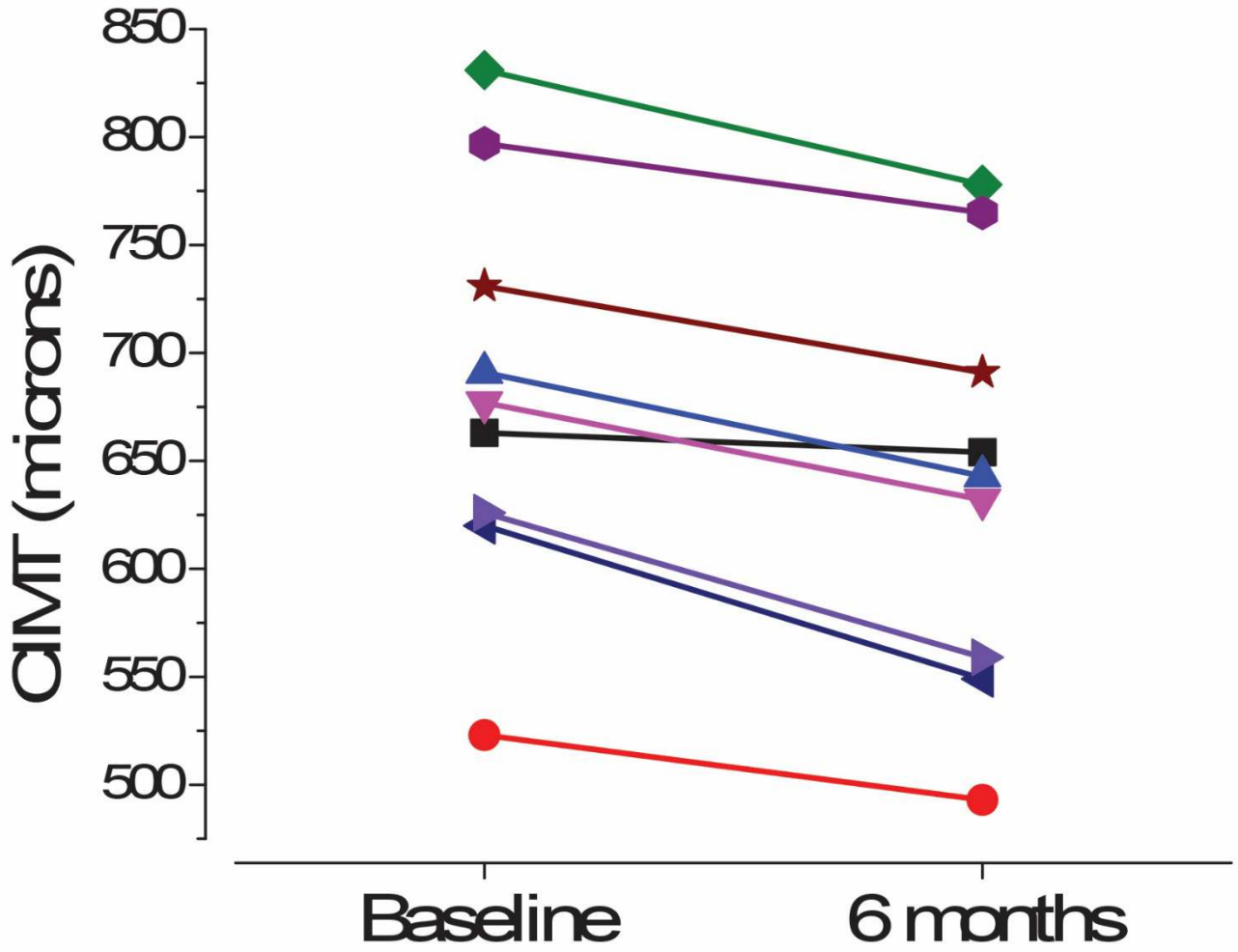
10 min After NO



49 yof chronic smoker with Raynauds

NO THERAPEUTIC INTERVENTION

NO Supplement Leads to Plaque Regression

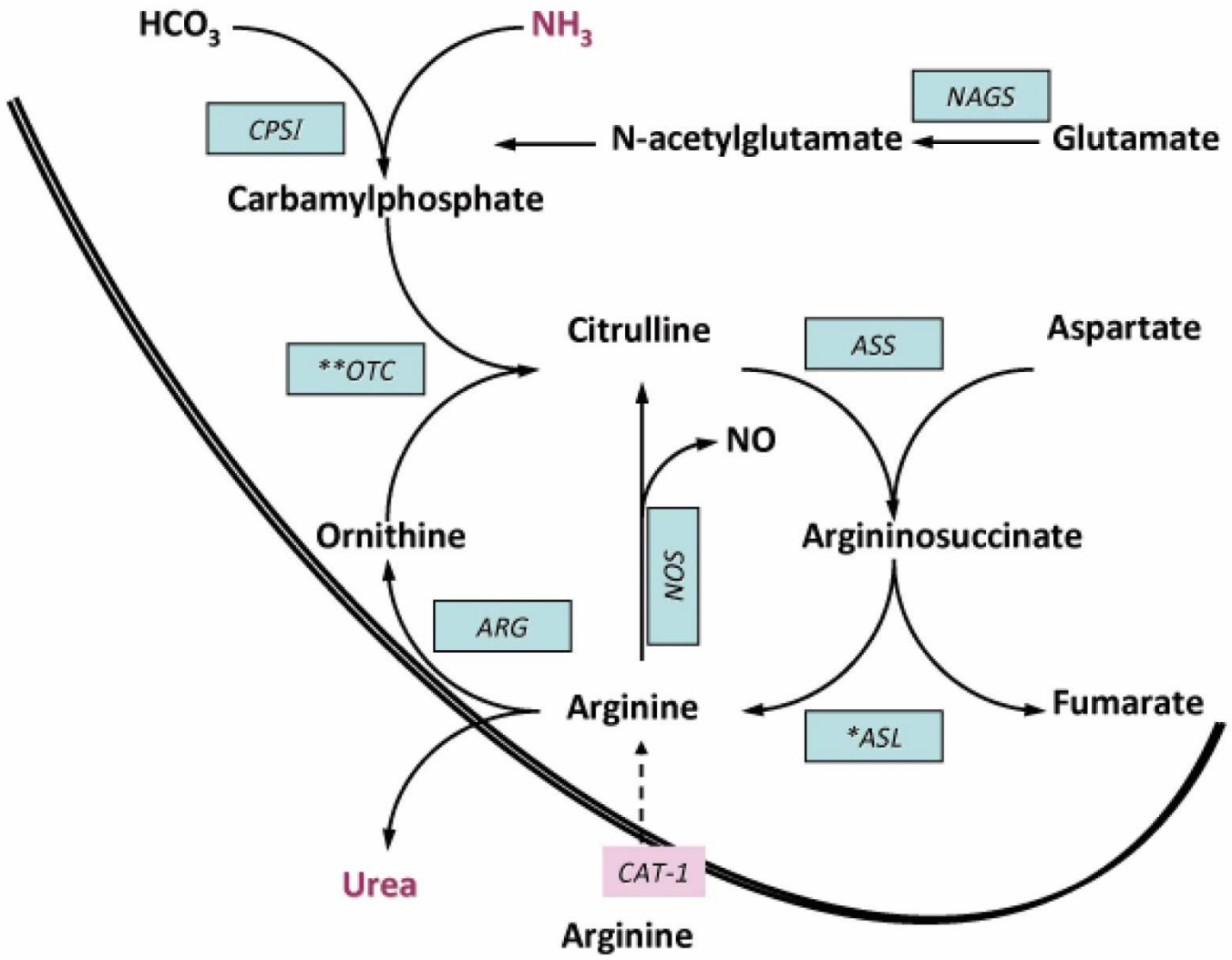


Edwin Lee MD – case report

NO lozenge Supplementation Rescues Inborn Error in Metabolism

ERAPEUTIC INTERVENTION

The Urea Cycle Converts Ammonia To Urea For Excretion

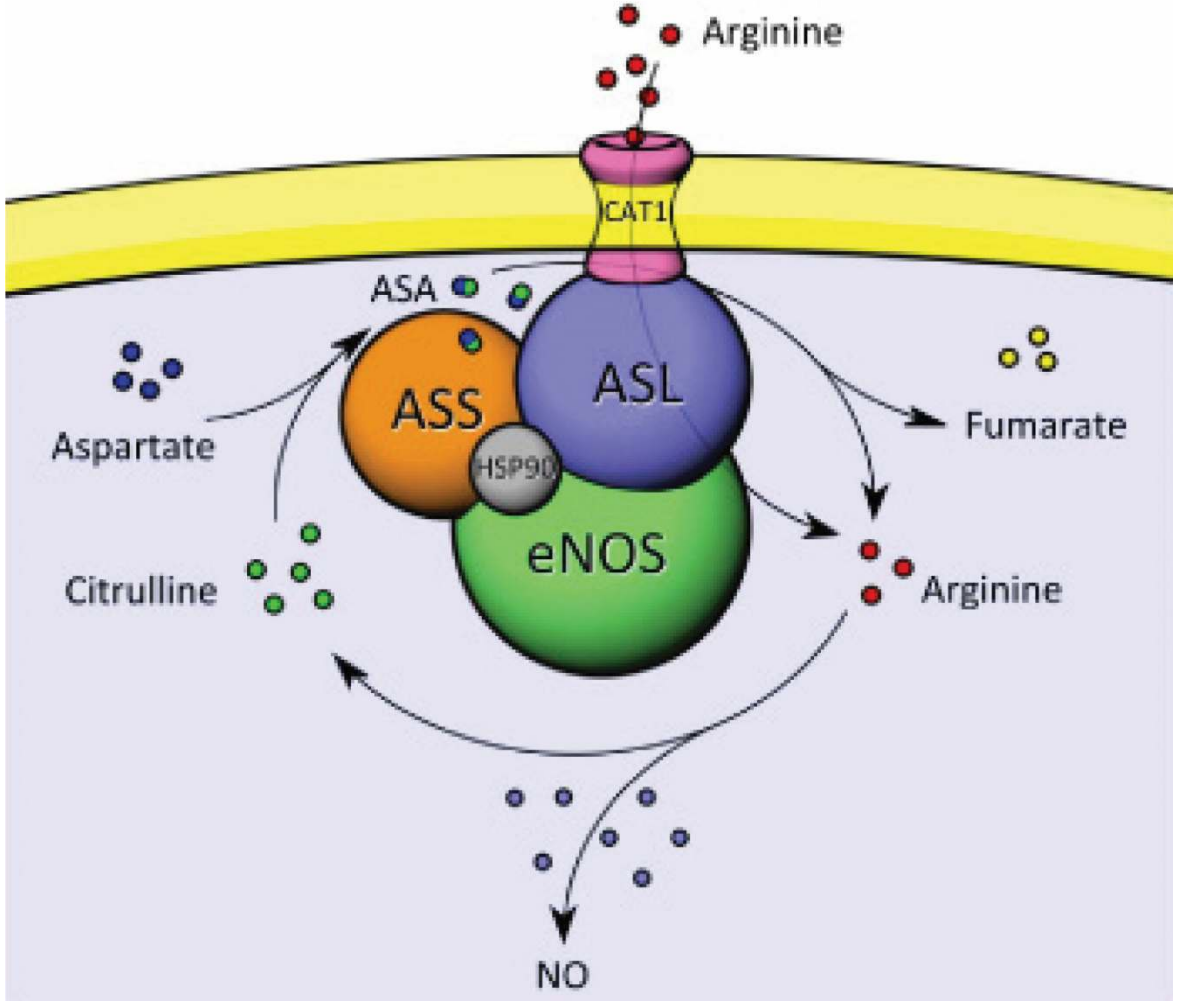


NO THERAPEUTIC INTERVENTION

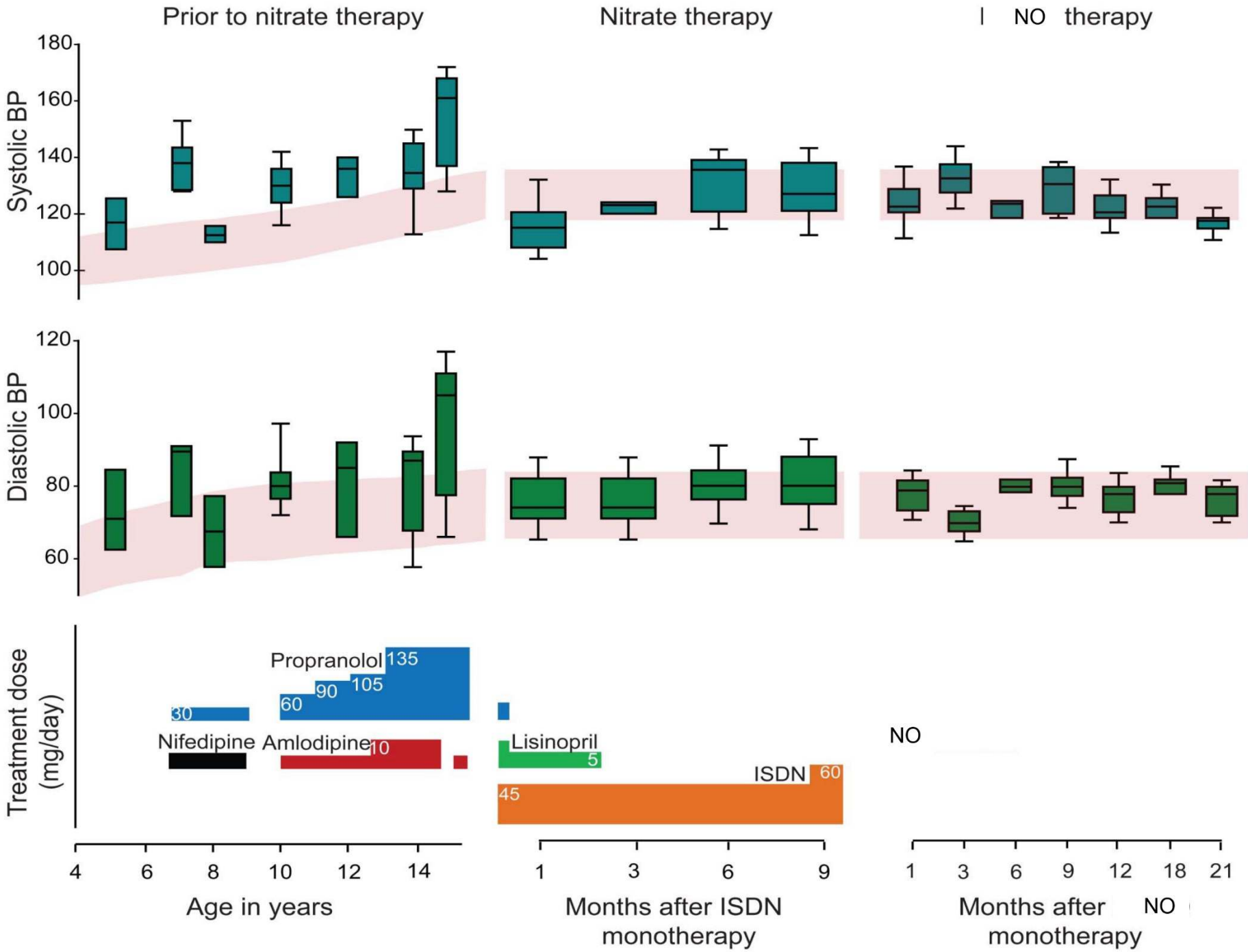
ASL Deficiency Is An Inborn Error In Metabolism

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

NOS Utilizes Intracellular **L-Arginine from L-citrulline** For NO Production



Erez et al Nat Med 2011


Prior to nitrate therapy
Nitrate therapy
NO therapy
Systolic BP
180
160
140
120
100
Diastolic BP
120
100
80
60
Treatment dose (mg/day)
Propranolol
135
105
90
60
30
Nifedipine
Amlodipine
10
Lisinopril
5
ISDN
60
45
NO
4
6
8
10
12
14
Age in years
1
3
6
9
Months after ISDN monotherapy
1
3
6
9
12
18
21
Months after NO monotherapy

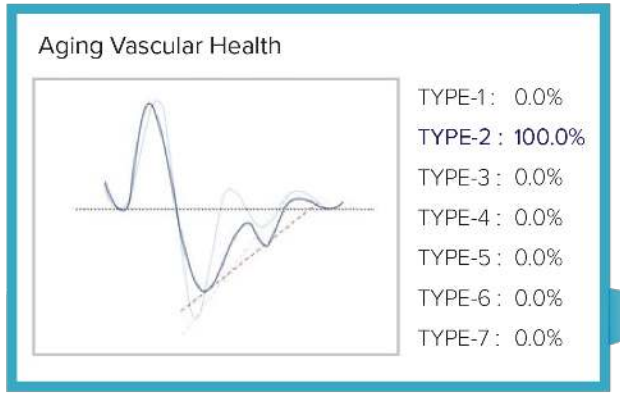
Echocardiogram measurements before and after initiation of NO supplementation.

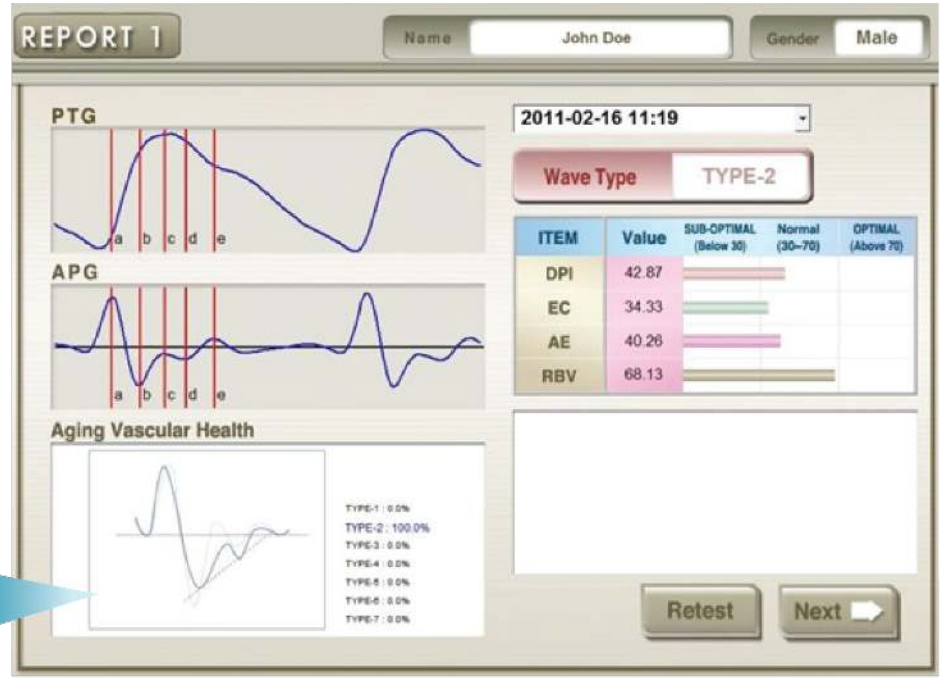
Echocardiogram measurements of LV dimensions taken before and 5 months after initiation of NO supplementation. All parameters demonstrate normalization.

Also increased the number of circulating endothelial progenitor cells.

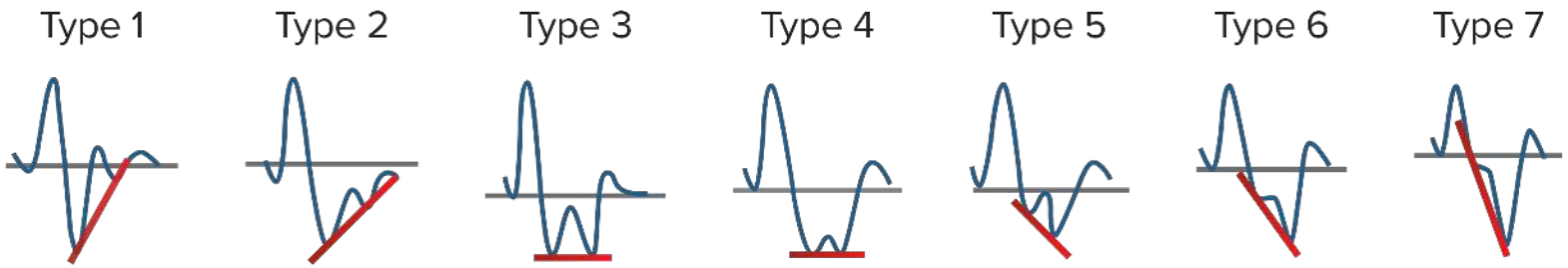
Left ventricle (LV) parameters	Before NO supplementation (z-score)	After NO supplementation (z-score)
LV diastolic septal thickness	2.26	1.33
LV diastolic dimension	-2.10	-0.36
LV diastolic wall thickness	3.59	2.24
LV systolic septal thickness	4.08	1.94
LV systolic dimension	-2.08	-0.67
LV systolic wall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

Microvascular Dysfunction





WAVEFORM PATTERNS



NO THERAPEUTIC INTERVENTION

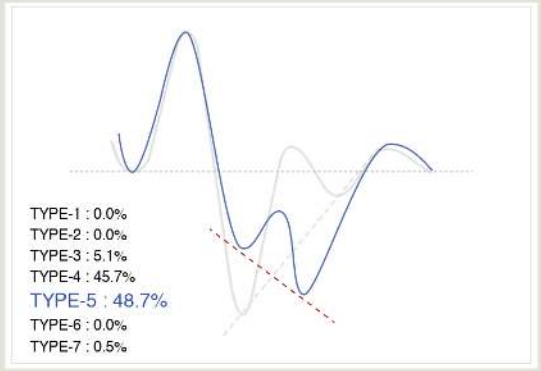
Nitric Oxide Therapeutic Intervention Outcome Data

PATIENT 1

BASELINE

Gender / Age	F / 74	Reg. Date	2018-08-16 12:21

Aging Vascular Health



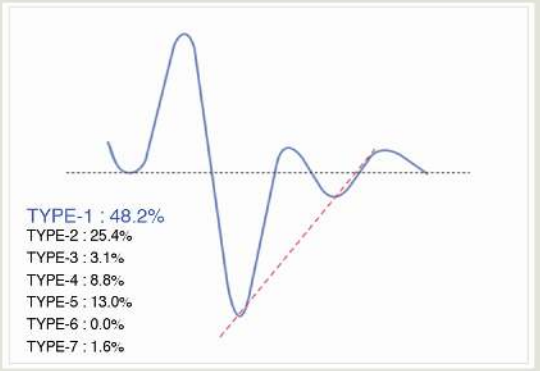
ITEM	VALUE	SUB-OPTIMAL (Below 30)	Normal (30~70)	OPTIMAL (Above 70)
DPI	29.82			
E C	29.92			
A E	24.34			
RBV	25.44			

Wave Type	TYPE-5

90 DAYS POST

Gender / Age	F / 75	Reg. Date	2018-11-13 11:37

Aging Vascular Health



ITEM	VALUE	SUB-OPTIMAL (Below 30)	Normal (30~70)	OPTIMAL (Above 70)
DPI	98.00			
E C	98.00			
A E	98.00			
RBV	94.40			

Wave Type	TYPE-1

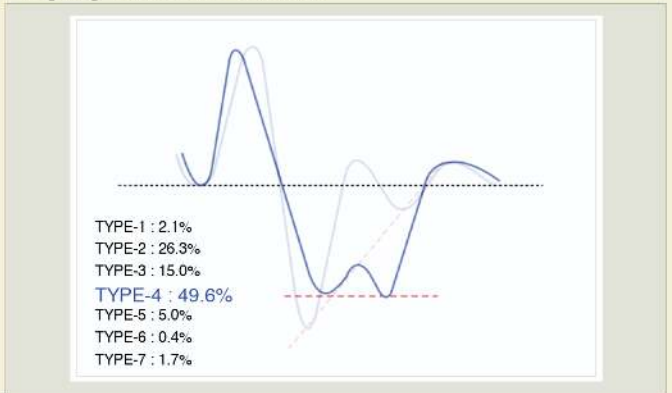
NO THERAPEUTIC INTERVENTION

PATIENT 2

BASELINE

Gender / Age	F / 70	Reg. Date	2018-07-19 12:50

Aging Vascular Health



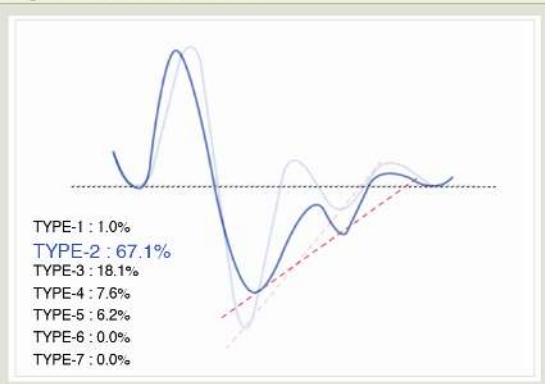
ITEM	VALUE	SUB-OPTIMAL (Below 30)	Normal (30~70)	OPTIMAL (Above 70)
DPI	18.98			
E C	37.52			
A E	9.51			
RBV	42.94			

Wave Type	TYPE-4

60 DAYS POST

Gender / Age	F / 70	Reg. Date	2018-09-18 14:34

Aging Vascular Health



ITEM	VALUE	SUB-OPTIMAL (Below 30)	Normal (30~70)	OPTIMAL (Above 70)
DPI	56.09			
E C	67.55			
A E	51.71			
RBV	61.14			

Wave Type	TYPE-2

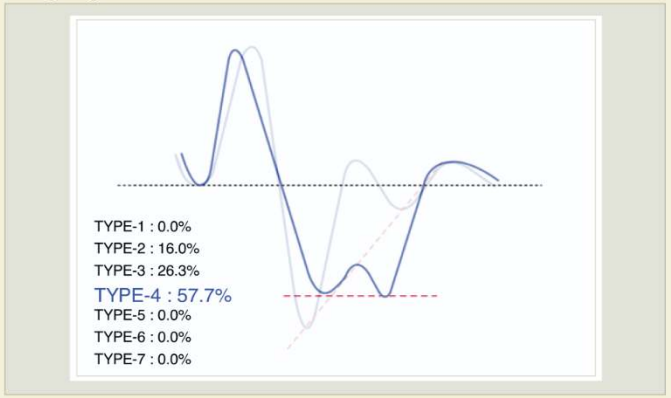
NO THERAPEUTIC INTERVENTION

PATIENT 3

BASELINE

Gender / Age	M / 60	Reg. Date	2018-03-09 13:51

Aging Vascular Health



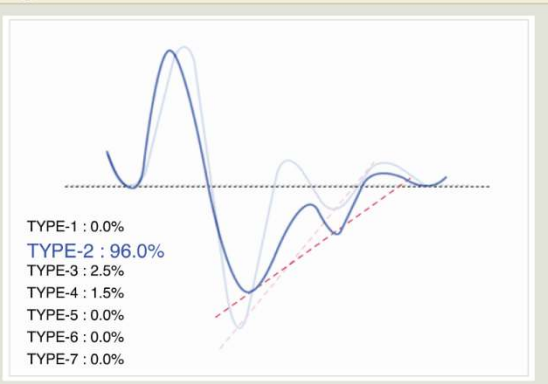
ITEM	VALUE	SUB-OPTIMAL (Below 30)	Normal (30~70)	OPTIMAL (Above 70)
DPI	28.79			
E C	29.37			
A E	25.31			
RBV	59.17			

Wave Type	TYPE-4

60 DAYS POST

Gender / Age	M / 60	Reg. Date	2018-05-11 14:21

Aging Vascular Health



ITEM	VALUE	SUB-OPTIMAL (Below 30)	Normal (30~70)	OPTIMAL (Above 70)
DPI	49.51			
E C	43.29			
A E	44.96			
RBV	68.67			

Wave Type	TYPE-2

NO THERAPEUTIC INTERVENTION

Mechanisms of NO 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 Wrinkles and Creates Tighter, Smoother Skin.

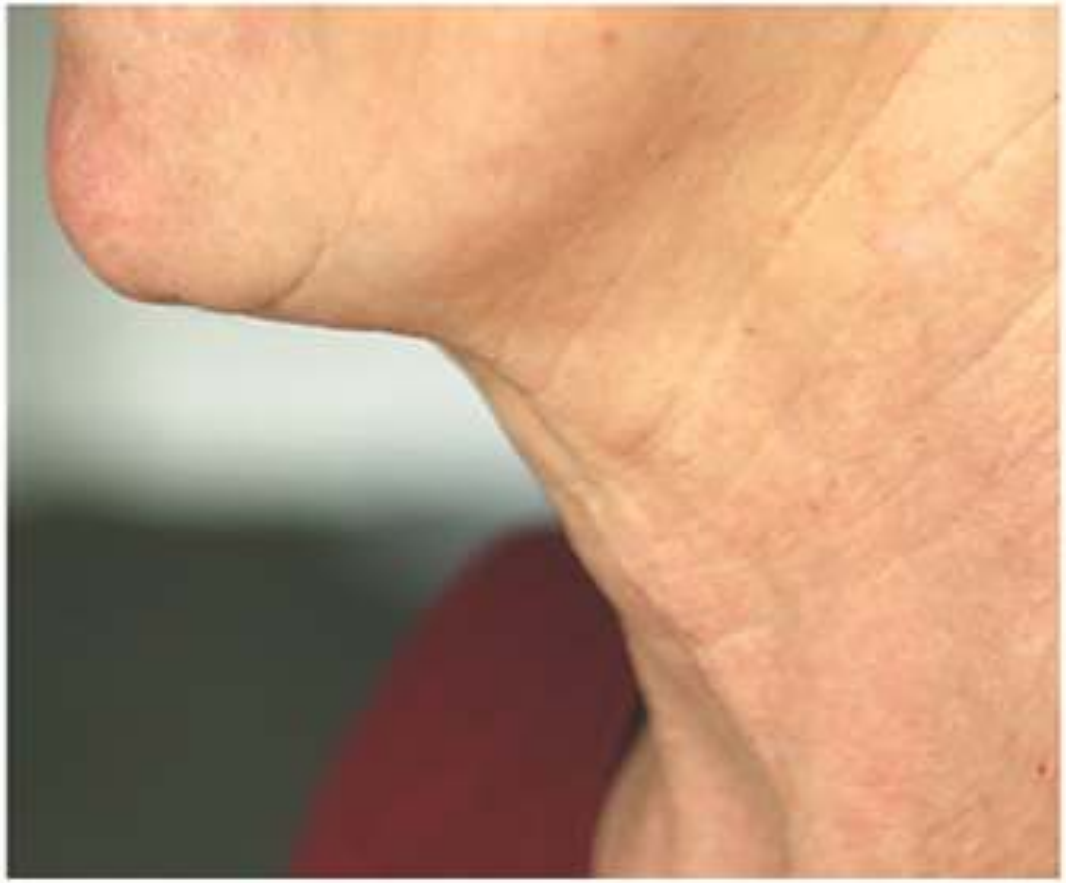
Innovative Dual Chamber Nitric Oxide Delivery

- Generates active Nitric oxide when contents mixed together
- Easy-to-Use and Convenient
- Immediately increases blood flow and circulation
- Dilates vessels and recruits capillaries
- Improves appearance of fine lines and wrinkles
- Improves the tone, texture and complexion of the skin
- You can see the technology work in seconds
- Skin is primed to receive all skin care products

You Can See Pneuma Work Within Seconds

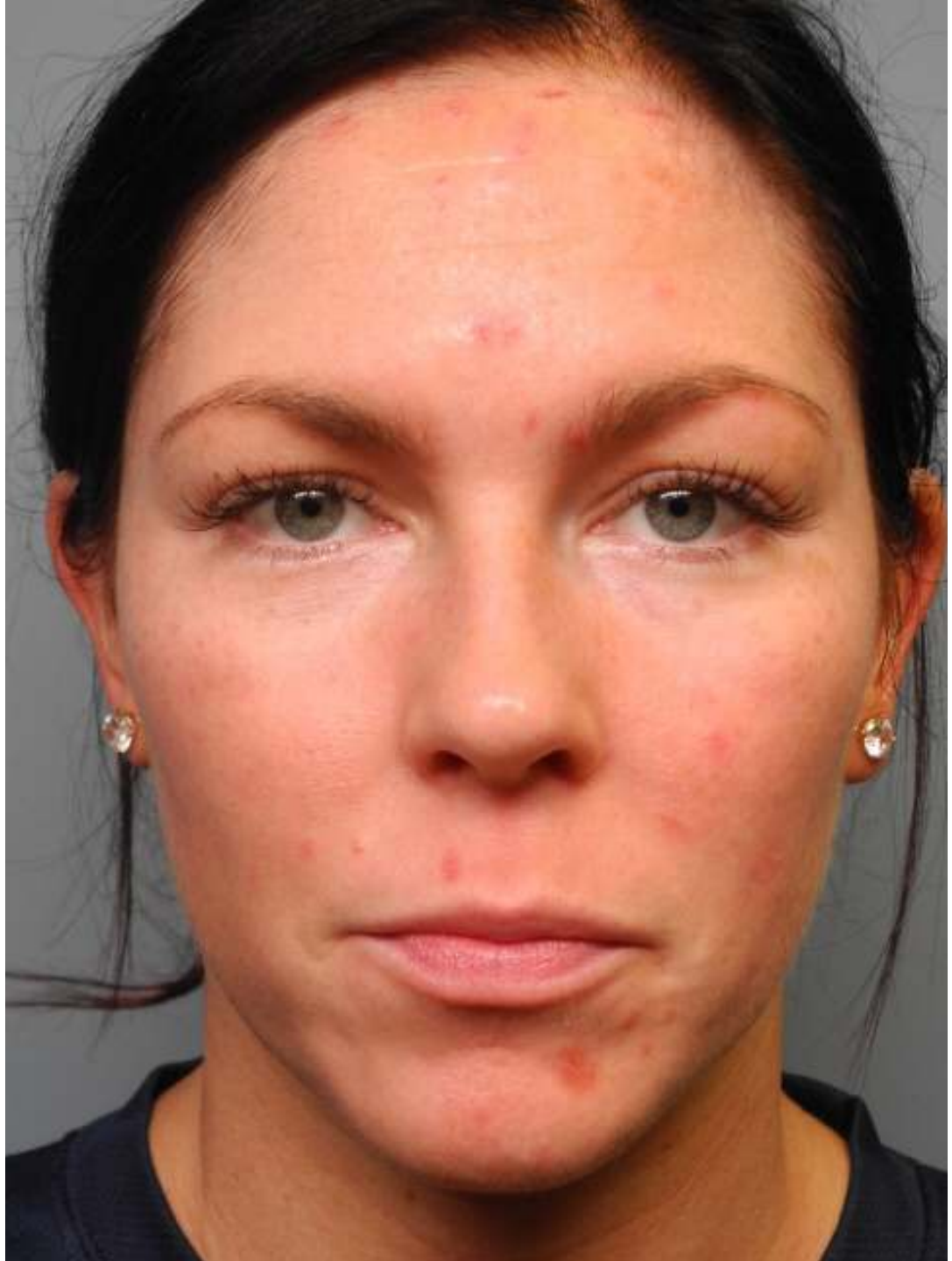
- EcoPhysics Gas phase nitric oxide detector
- Nitric oxide gas can be detected and quantified when it is produced
- Used to test whether products generate or activate nitric oxide production
- Pneuma nitric oxide generates nitric oxide gas and you can visualize nitric oxide working on the skin

NO THERAPEUTIC INTERVENTION



NO THERAPEUTIC INTERVENTION

NO THERAPEUTIC INTERVENTION



TION

NO THERAPEUTIC INTERVENTION

Before After

Smooths skin

NO THERAPEUTIC INTERVENTION

NO THERAPEUTIC INTERVENTION

NO THERAPEUTIC INTERVENTION

NO THERAPEUTIC INTERVENTION

BUT……

June 2014

NO THERAPEUTIC INTERVENTION

Today

NO THERAPEUTIC INTERVENTION

NTERVENTION

NTERVENTION

NTERVENTION

How do you improve nitric oxide production in your patients to restore blood flow?

Are there products that have been shown to increase blood flow in humans?

L-arginine utilization is controlled by the enzymatic function of nitric oxide synthase and not by L-arginine or L-citrulline deficiency

(These products cannot and will not work in people with endothelial dysfunction)

Dietary nitrate utilization is controlled by

1. Amount of nitrate consumed
2. Presence or absence of nitrate reducing bacteria
3. Stomach acid production

(Nitrate based products, potassium nitrate or beet root products, cannot and will not work in most Americans due to mouthwash, antibiotic and antacid use)

Nitrate Bioactivity Similar to Thyroid Hormone Activity

Nitrate NO_3^- INACTIVE

Nitrite NO_2^- ACTIVE

Nitric Oxide NO ACTIVE

T4 INACTIVE

T3 ACTIVE

T2 ACTIVE

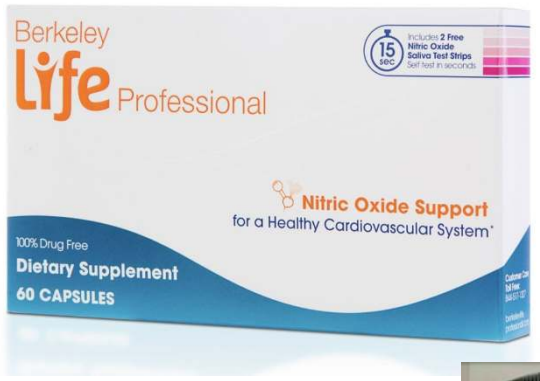
NITRATE IS INERT IN HUMANS!!!!!

NO THERAPEUTIC INTERVENTION

Disruption of **Nitrate-Nitrite-NO** Pathway

1. Insufficient dietary intake of nitrate/nitrite rich foods (green leafy vegetables, beets, etc.)
2. Problems with nitrate uptake in duodenum (sialin (SLC17A5) transporter mutations – Salla Disease)
3. Insufficient saliva production (Sjogrens syndrome)
4. Lack of oral commensal bacteria to reduce nitrate to nitrite (use of antibiotics (over 200M users)/antiseptic mouthwash (over 200M users), poor oral hygiene)
5. Insufficient stomach acid production – Achlorhydria (use of PPI's (over 200M), H. Pylori infection, iron overload)
6. Increased oxidative stress that scavenges NO

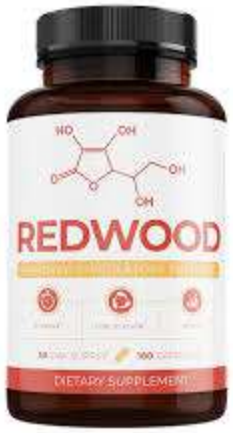
NO THERAPEUTIC INTERVENTION


Berkeley
life Professional
15 sec
Includes 2 Free Nitric Oxide Saliva Test Strips
Self test in seconds
Nitric Oxide Support
for a Healthy Cardiovascular System*
100% Drug Free
Dietary Supplement
60 CAPSULES

actavis
NDC 0228-2620-11
Rx Only
Isosorbide
Mononitrate
Tablets, USP 20 mg
100 tablets

humann
neo40
professional
Clinical Strength
Daily Heart & Circulation Formula
Dietary Supplement
30 quick dissolve tablets

humann
superbeets
Circulation Superfood
Black Cherry FLAVOR
Concentrated Beet Crystals
NET WT. 5.3 OZ (150g)


REDWOOD
DIETARY SUPPLEMENT

NOXNUTRIENTS
M3
MIRACLE
OLECULE
AX
ULTIMATE
NITRIC OXIDE NUTRITION

pure
encapsulations
Nitric Oxide
Ultra
(capsules)
hypo-allergenic
dietary supplement
120 CAPSULES
Supplement Facts

XYMOGEN
AngiNOX™
Effervescent Nitric Oxide Formula
ePV: 050862-04|062515|00001|
Net Wt. 17 oz (480 g)
Dietary Supplement

LifeExtension
NitroVasc™
Support For Nitric Oxide Production and Vascular Health
DAILY
30 Vegetarian Capsules

PUMPS* • RECOVERY* • PERFORMANCE*
CONCENTRATED NITRIC OXIDE PRECURSOR*
NITRIX 2.0
ADVANCED STRENGTH
3 L-CITRULLINE PER DAY!
3 CREATINE PER DAY!
PTEROPURE™ & RESVIDA™
DIETARY SUPPLEMENT • 90 TABLETS

irwin naturals
Plus MCTs & Beet Root
Nitric Oxide
Pre-Sport
with L-Citrulline
Pre-Workout Booster
Advanced Energy Activator for Maximum Physical Response
60 Liquid Soft-Gels
DIETARY SUPPLEMENT

FACTS

Beets do not equal nitrate

(all beets are not created equal)

Nitrate does not equal nitric oxide

(antiseptics – >200M)

(antibiotics – >200M)

(PPI's – >200M)

L-Arg/L-cit products do not work in patients with endothelial dysfunction

WHAT TO LOOK FOR IN PRODUCT TECHNOLOGY

1. Issued patents – demonstrates innovation and uniqueness
2. Published clinical trials in peer-reviewed journals on the actual product (not an ingredient)
3. Licensed from a reputable University or Institution (demonstrates research has been performed on technology)
4. Is the inventor or product developer an expert in NO biochemistry and published in the NO field (PubMed Search)

DON'T BE FOOLED BY CREATIVE MARKETING. SCIENCE AND EXPERIENCE MATTER

Let Us Do The Due Diligence For You

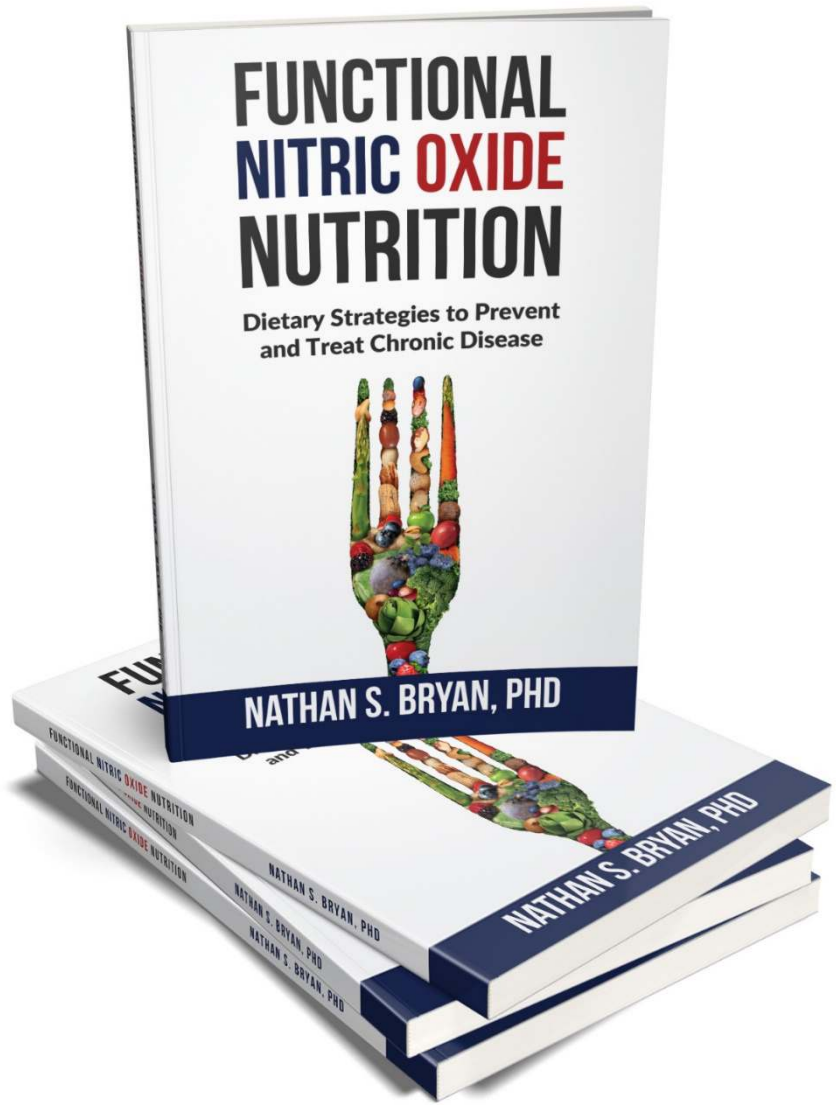
FullScript provides a credible and reliable product source for your practice. If a product is not offered on FullScript platform, then it has not met the scientific and clinical rigor

Trust the people that have actually done the research and have published in the nitric oxide field

NO THERAPEUTIC INTERVENTION

CONCLUSIONS

- Nitric oxide controls and regulates vascular structure and function.
- There is an age-related decline in NO production that asserts its effect on cardiovascular risk and age related disease.
- Restoring NO production can lead to better vascular function and better perfusion of all tissues.
- Strategies to restore NO production/homeostasis will have a profound impact on public health and on the aging process.
- Patients cannot and will not heal or get better without restoring nitric oxide based signaling.



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https://us.fullscript.com/practitioner-signup/dr-bryan

ADVANTAGES:

Your office does not have to stock products
Patients can order directly from FullScript and you get credit
You can trust the products offered are safe and reliable scientifically

www.drnathansbryan.com
drnathanbryan@gmail.com

NO THERAPEUTIC INTERVENTION