Georgia

Dr. Pat Luse


Tri-State
Physicians
Medical &
Weight Loss
Chiropractic
Physical Therapy
Massage

7 SYSTEMS PLAN

Cell

Leading Edge
Review

The

Carlos Lóp
[1]Departamer
[2]Telomeres a
[3]Max Planck
[4]Institute of
[5]Tumor Supp
[6]INSERM, U
[7]Metabolomi
[8]Centre de R
[9]Pôle de Bio
[10]Université
*Correspond
http://dx.do

Figure 1. The Hallmarks of Aging
The scheme enumerates the nine hallmarks described in this Review: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, d

er[6,7,8,9,10]
de Oviedo, Oviedo, Spain
(CNIO), Madrid, Spain

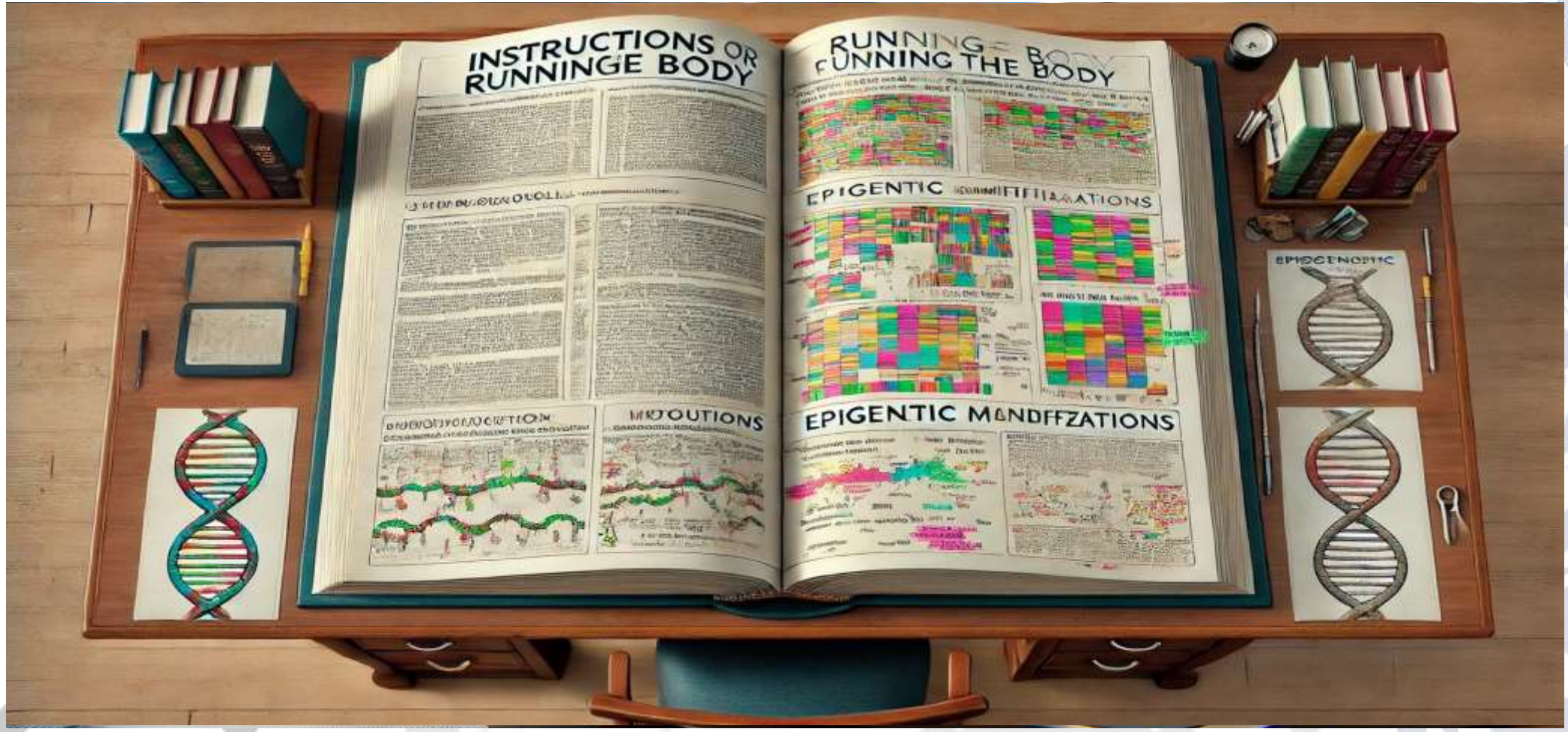
London, UK
Madrid, Spain

Aging is
to impaired function
and incre
tor for major human

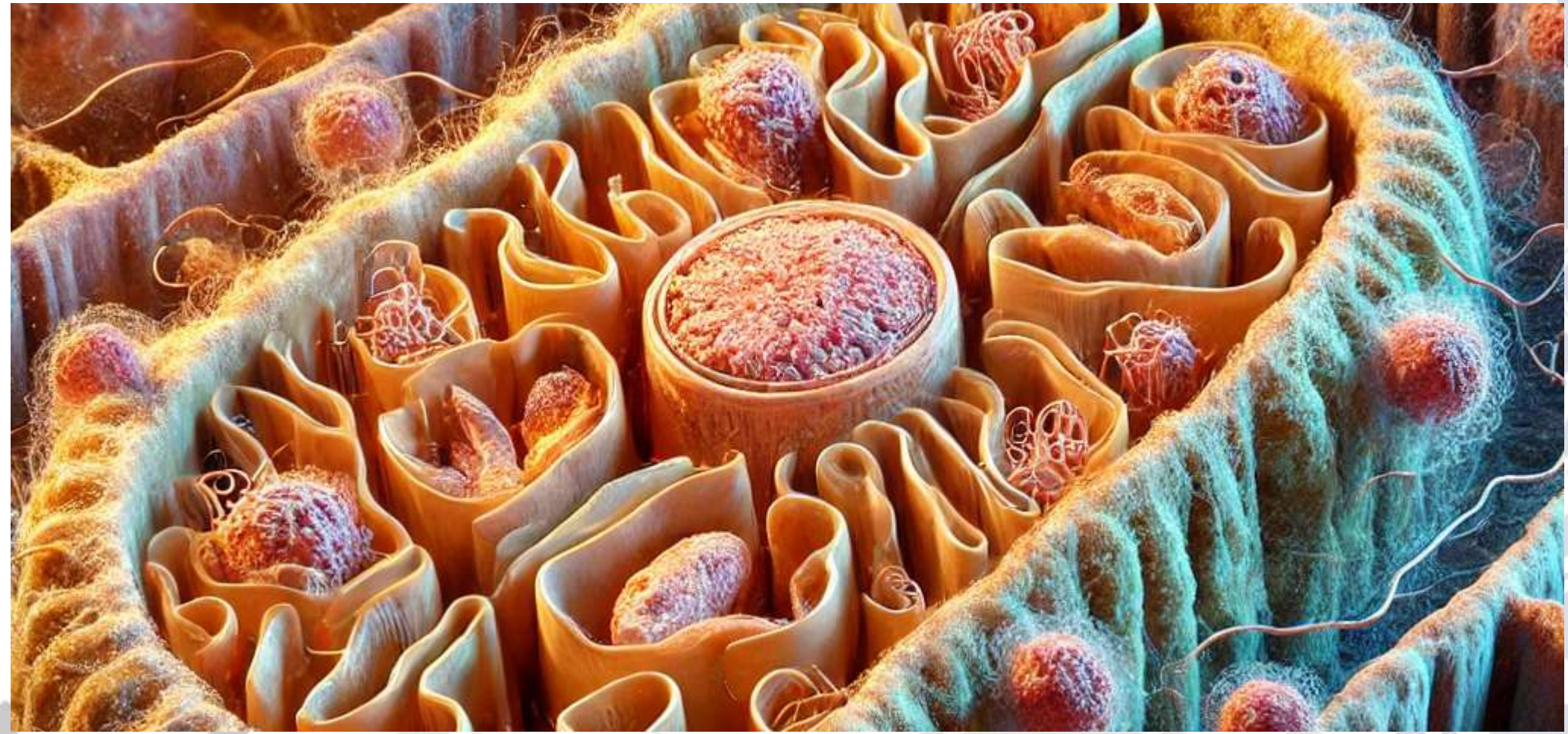
Genomic Instability

Telomere Attrition

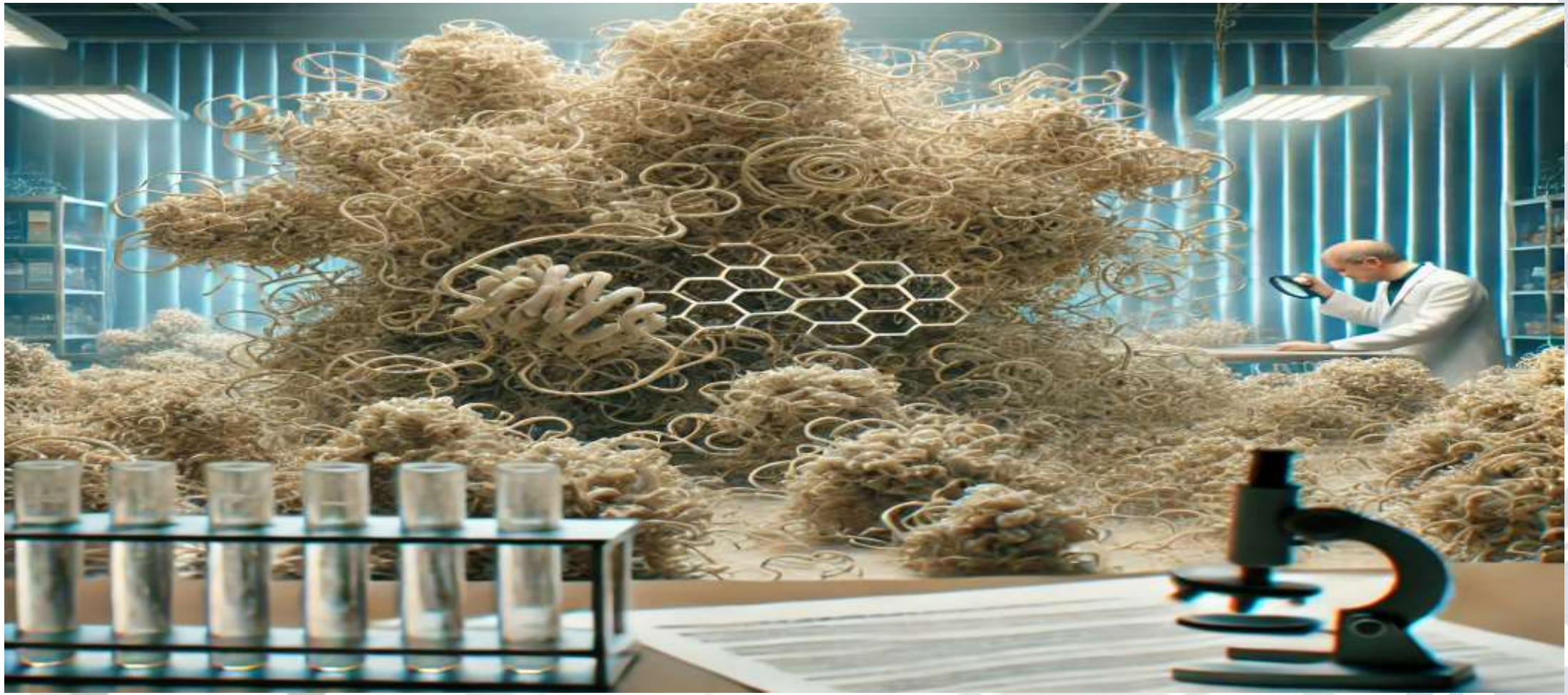
Epigenetic Alterations



Mitochondrial Dysfunction

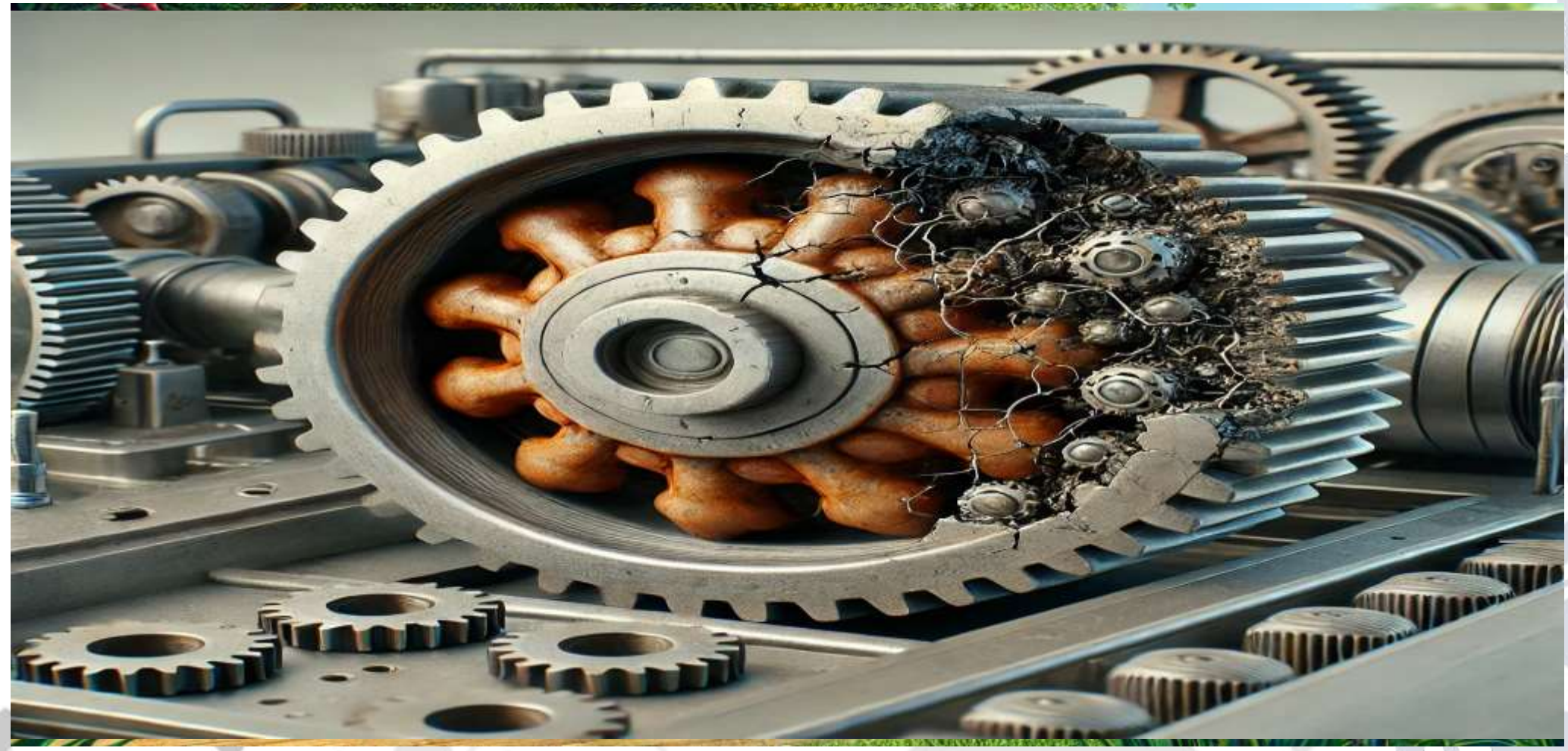


Loss of Proteostasis

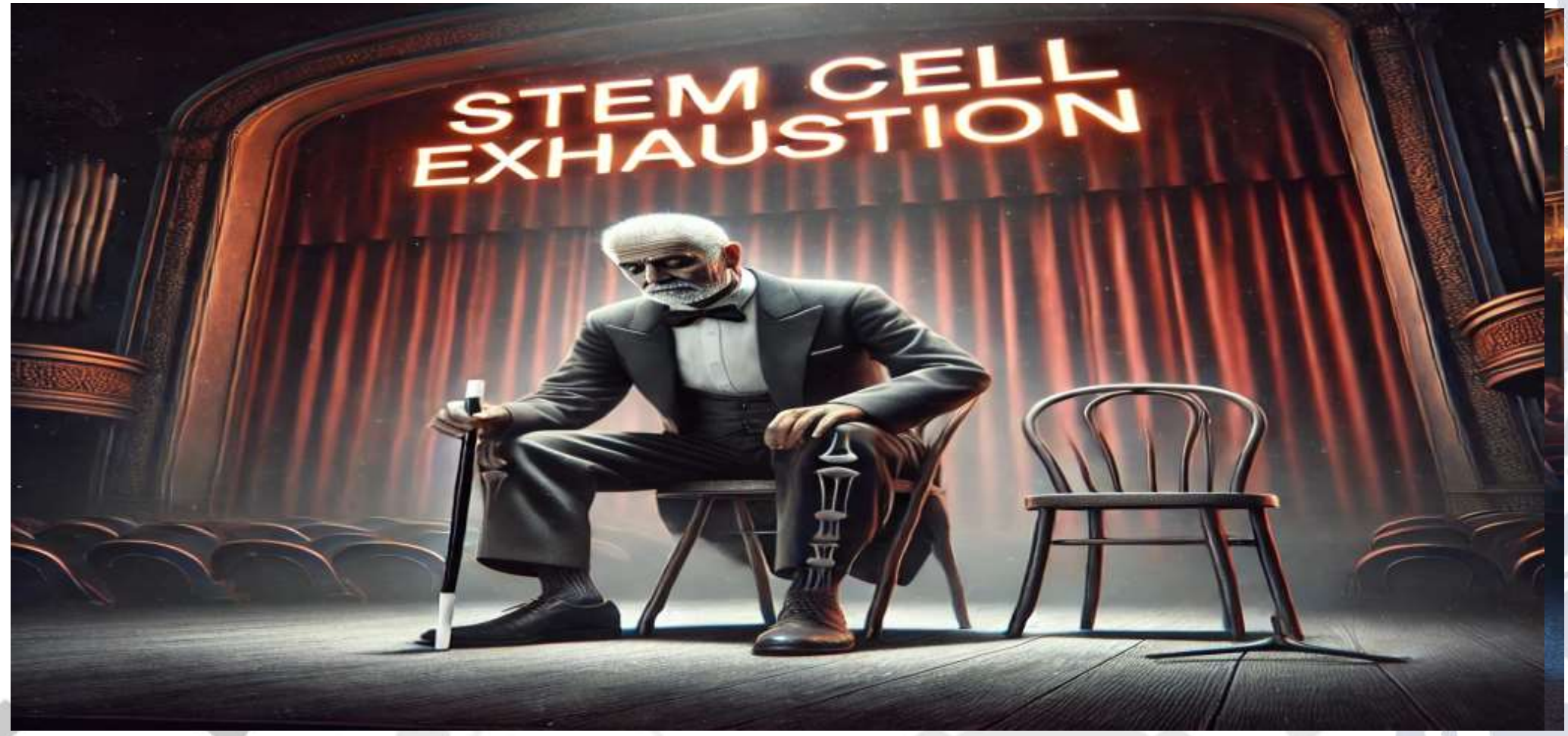


Deregulated Nutrient Sensing

Cellular Senescence



Stem Cell Exhaustion



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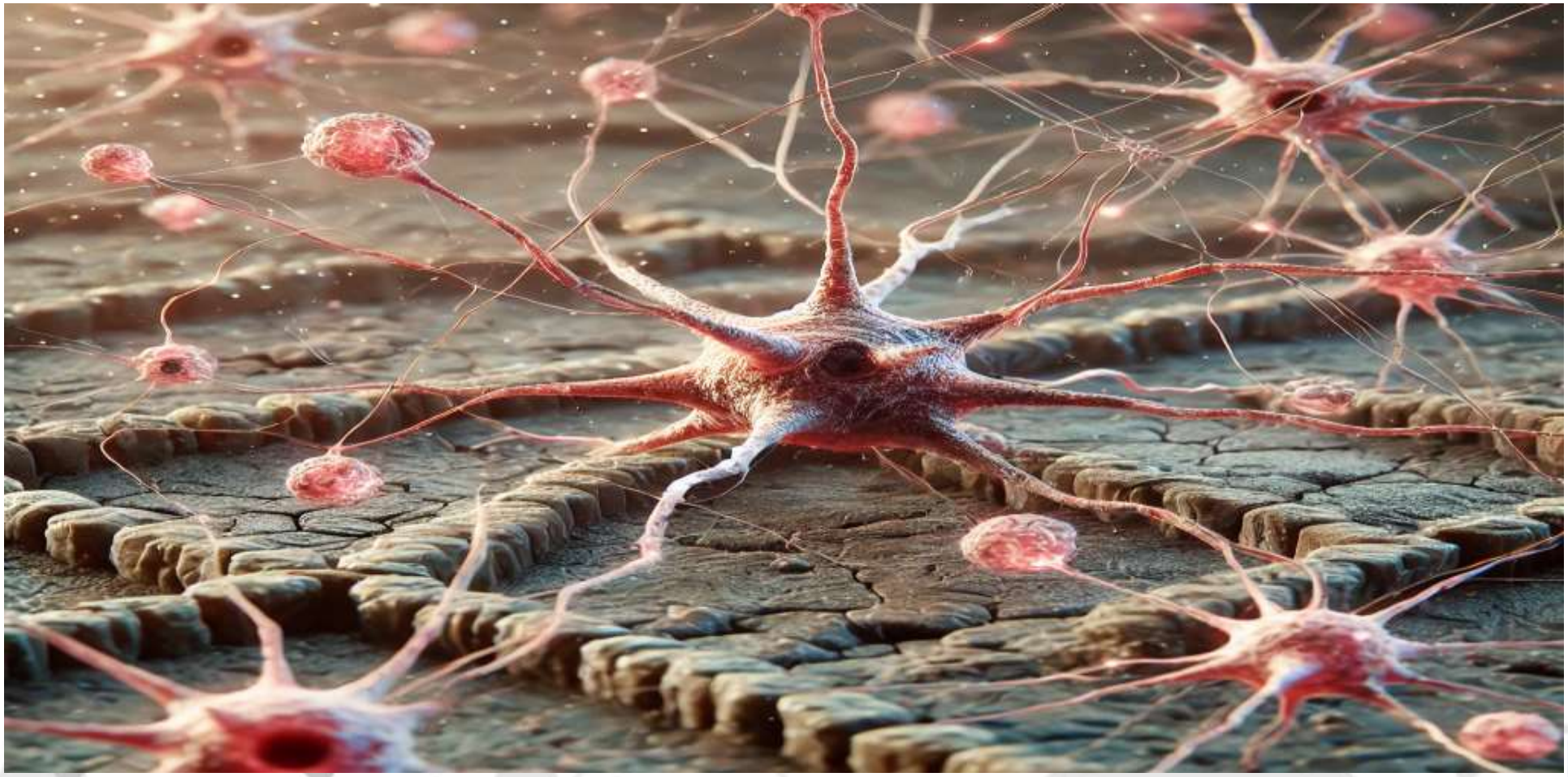
Altered Intercellular Communication



Compromised Autophagy

Gut Dysbiosis

SYSTEMS PLAN

Inflammation

Peter Lynch- 10 Bagger

- 10 x return of investment

Magellan fund

- Understand fundamentals
- Good price to earnings ratio
- Strong growth potential

7 Systems Plan

- Understand the systems
- Accessible and affordable
- Evidence based 10 baggers

A Supplement that Helps All 12?

Magnesium

- Over 50% of the population is deficient
- It plays crucial roles in over 300 enzymatic reactions and deficiency is linked to an increased risk of chronic diseases.
- A 2024 study explored magnesium's effects on the 12 hallmarks of aging found magnesium deficiency negatively impacts each of the 12.

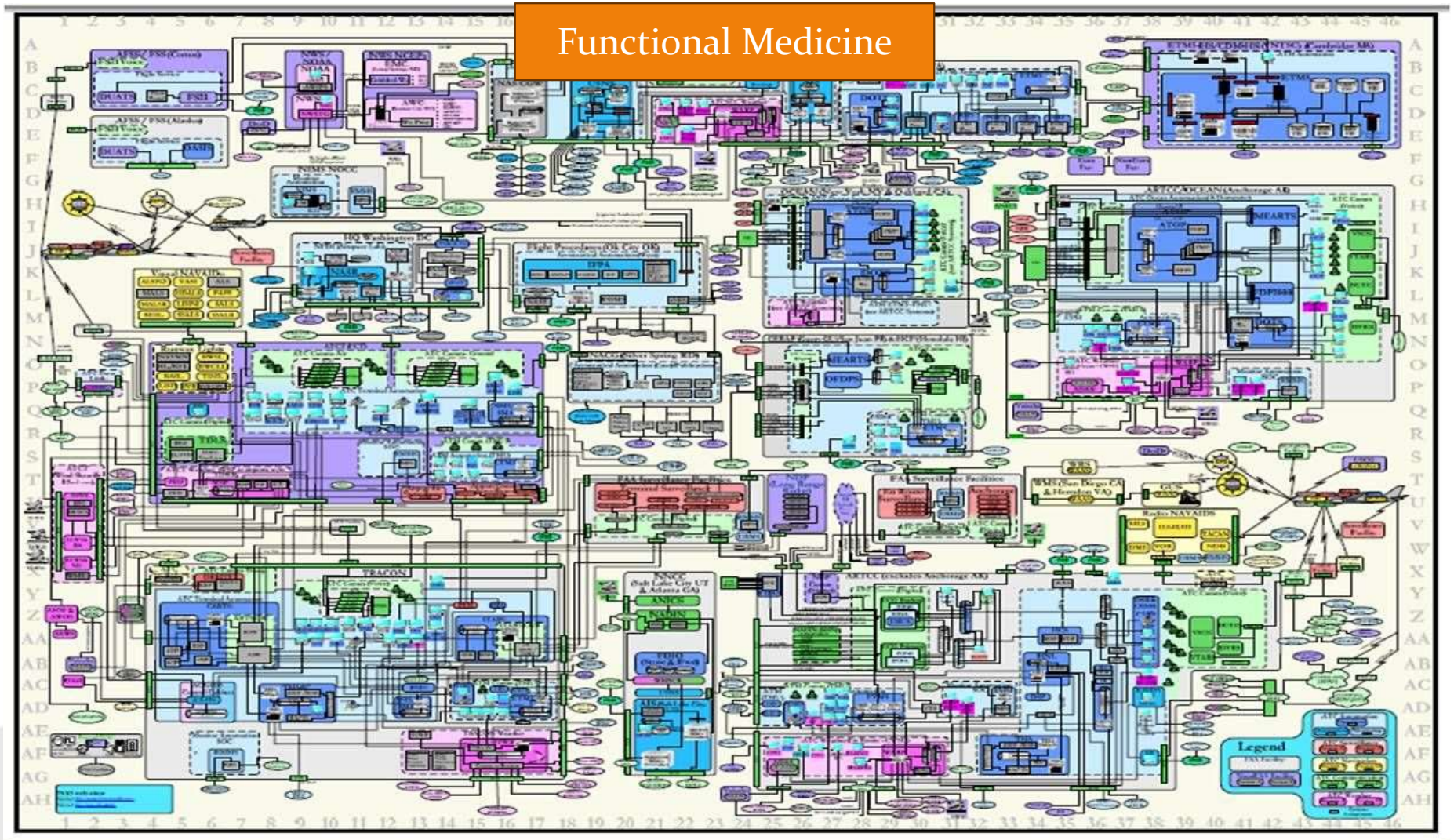
Nutrients. 2024 Feb; 16(4): 496, Magnesium and Aging

Functional Medicine Training

SYSTEMS PLAN

Understanding And Fixing Systems

Functional Medicine

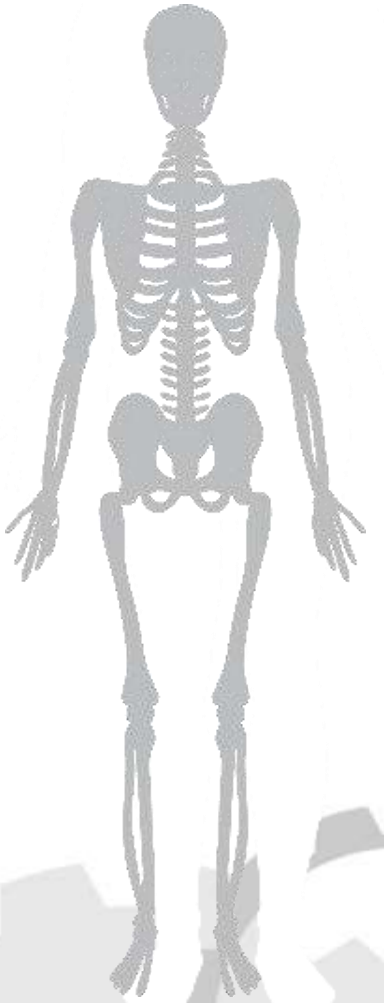


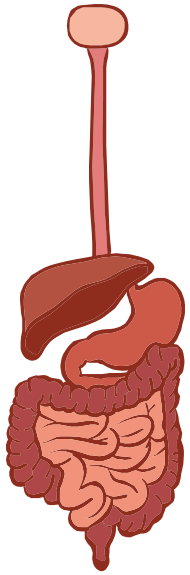
SYSTEMS PLAN

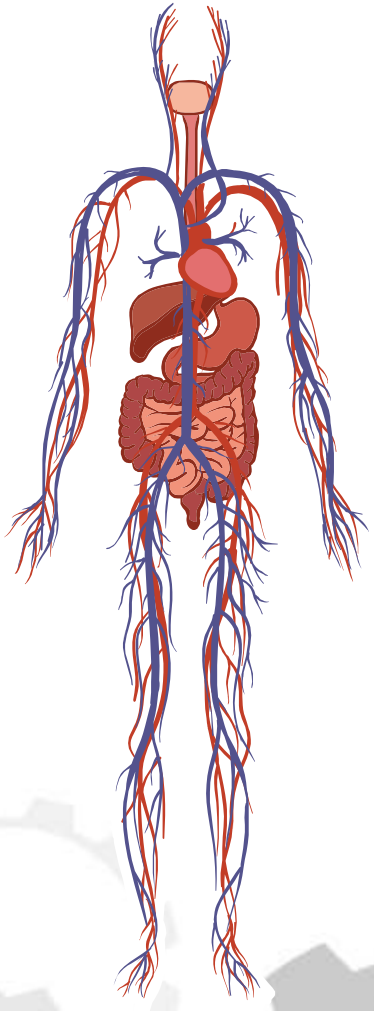
Understanding And Fixing Systems

- Can take a lot of time
- Be very complicated
- Be expensive

Eat→ Digest→ Deliver→ Energy

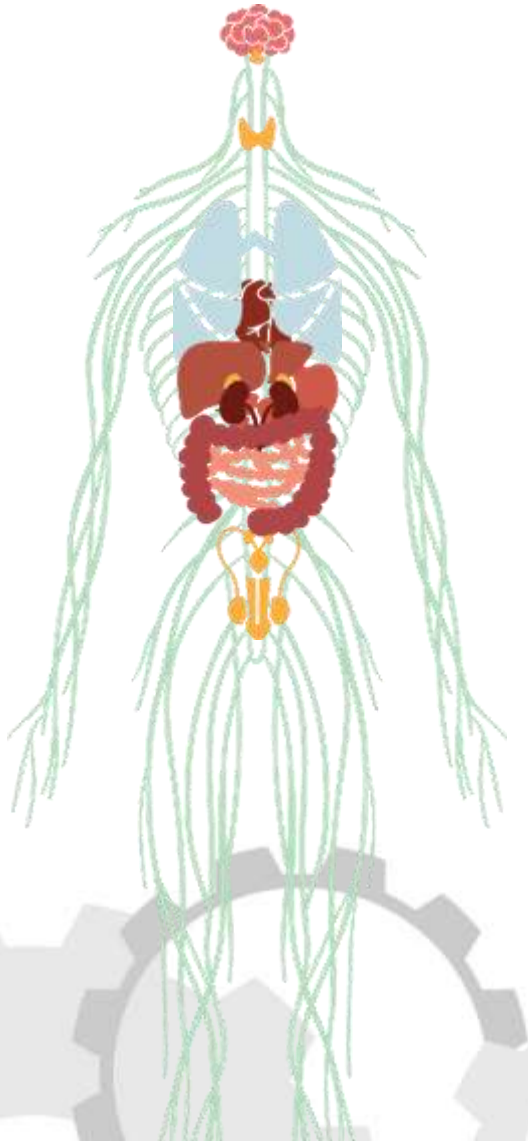






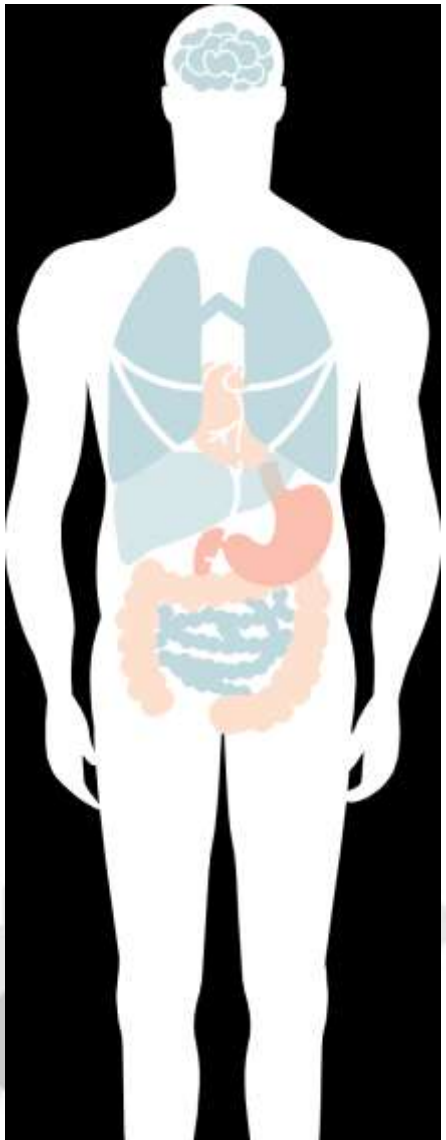
3 Support Systems

Communicate



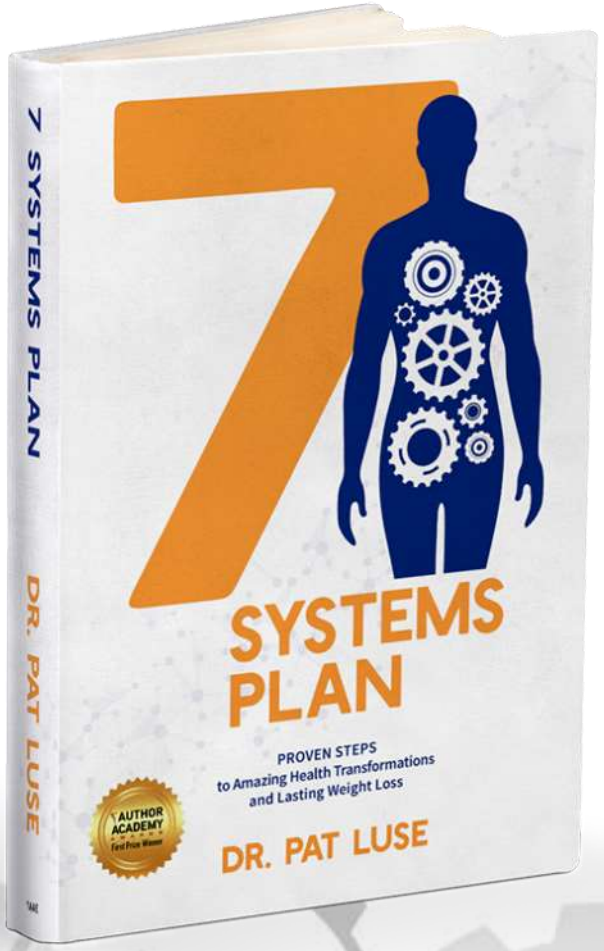
Defend

Clean up



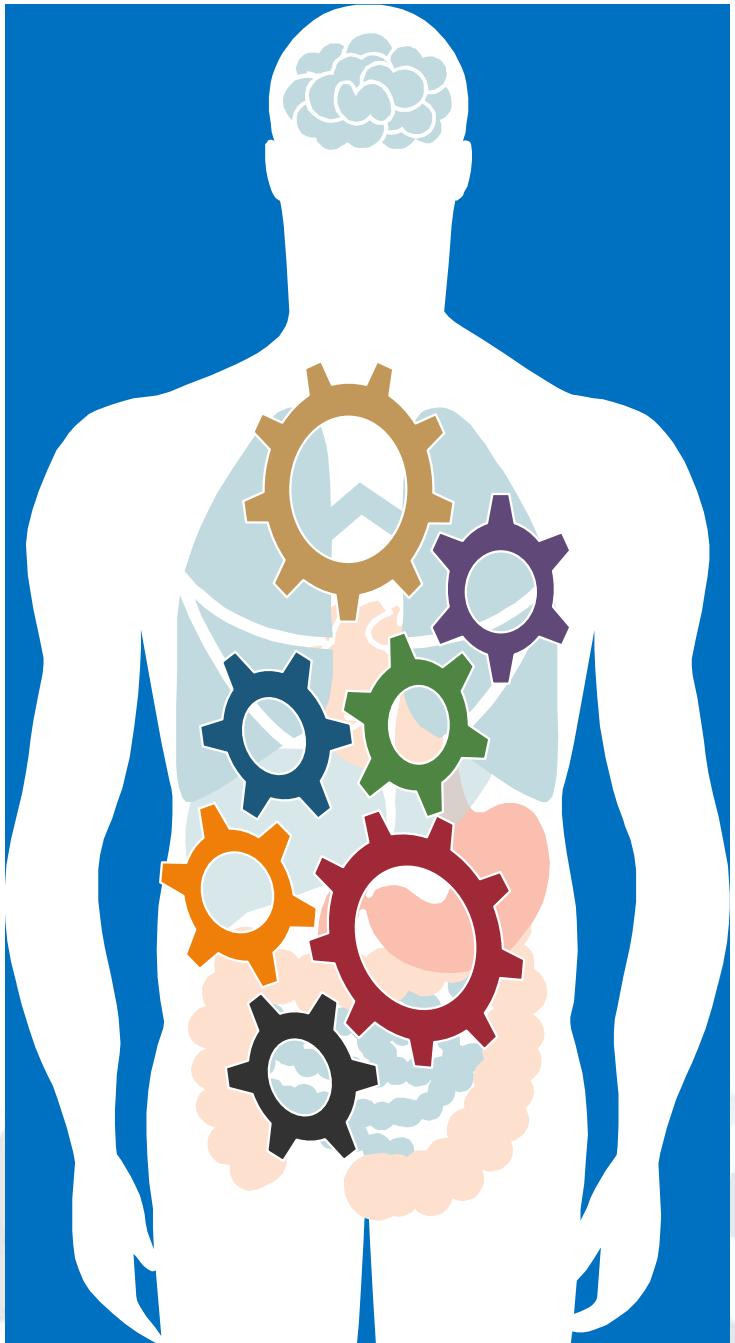
SYSTEMS PLAN

My Discovery- A Simple Way To...



1. Evaluate Your Systems
2. Identify System Malfunction
3. Optimize All Your Systems Using Simple Proven Steps

7 SYSTEMS PLAN



LONGEVITY and HEALTH

1. Structure
2. Digestive
3. Delivery
4. Energy
5. Communication
6. Defense
7. Detox

7 SYSTEMS PLAN

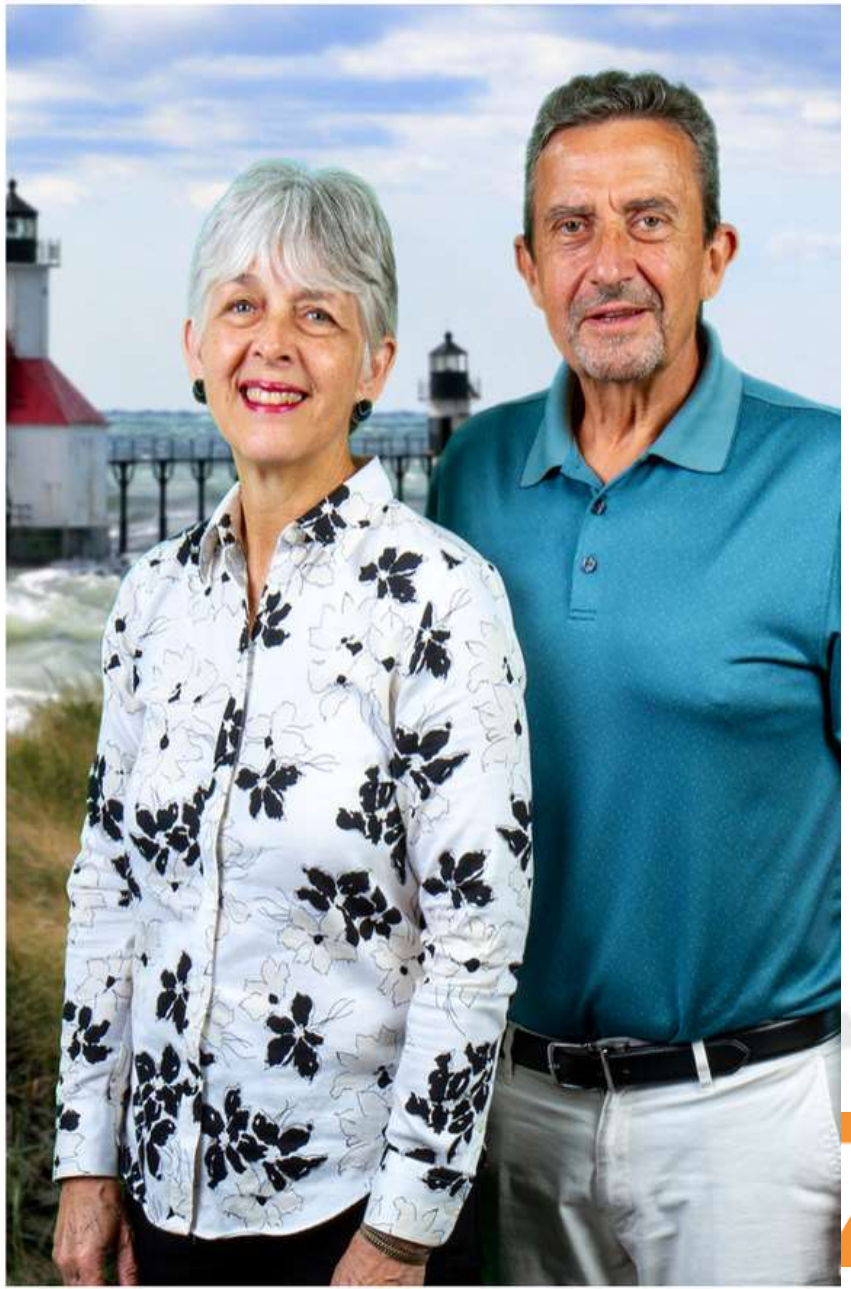
Transforming Lives

Kevin

SYSTEMS
PLAN

June 2018
242

June 2019
175



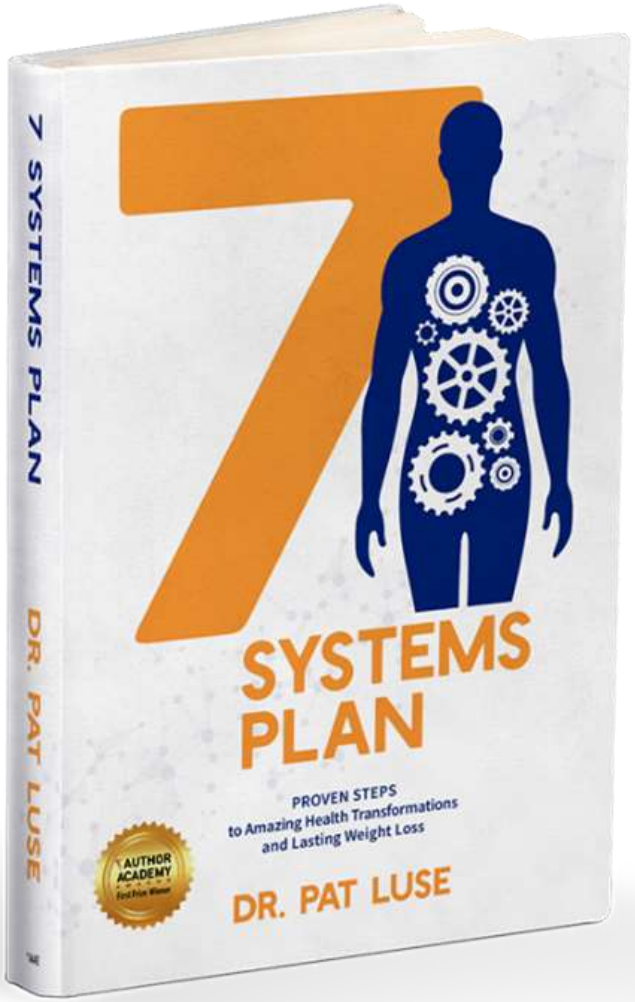
SYSTEMS PLAN

Justin

Candi

Marla- Fibromyalgia Gone

Kurt- Migraines Gone



#1 New Release
amazon

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Doctors: NE, SD, MN, ND, WI, IA, UT, OH, ND, GA, TX, OK

Who wants to live to be 100 years old?

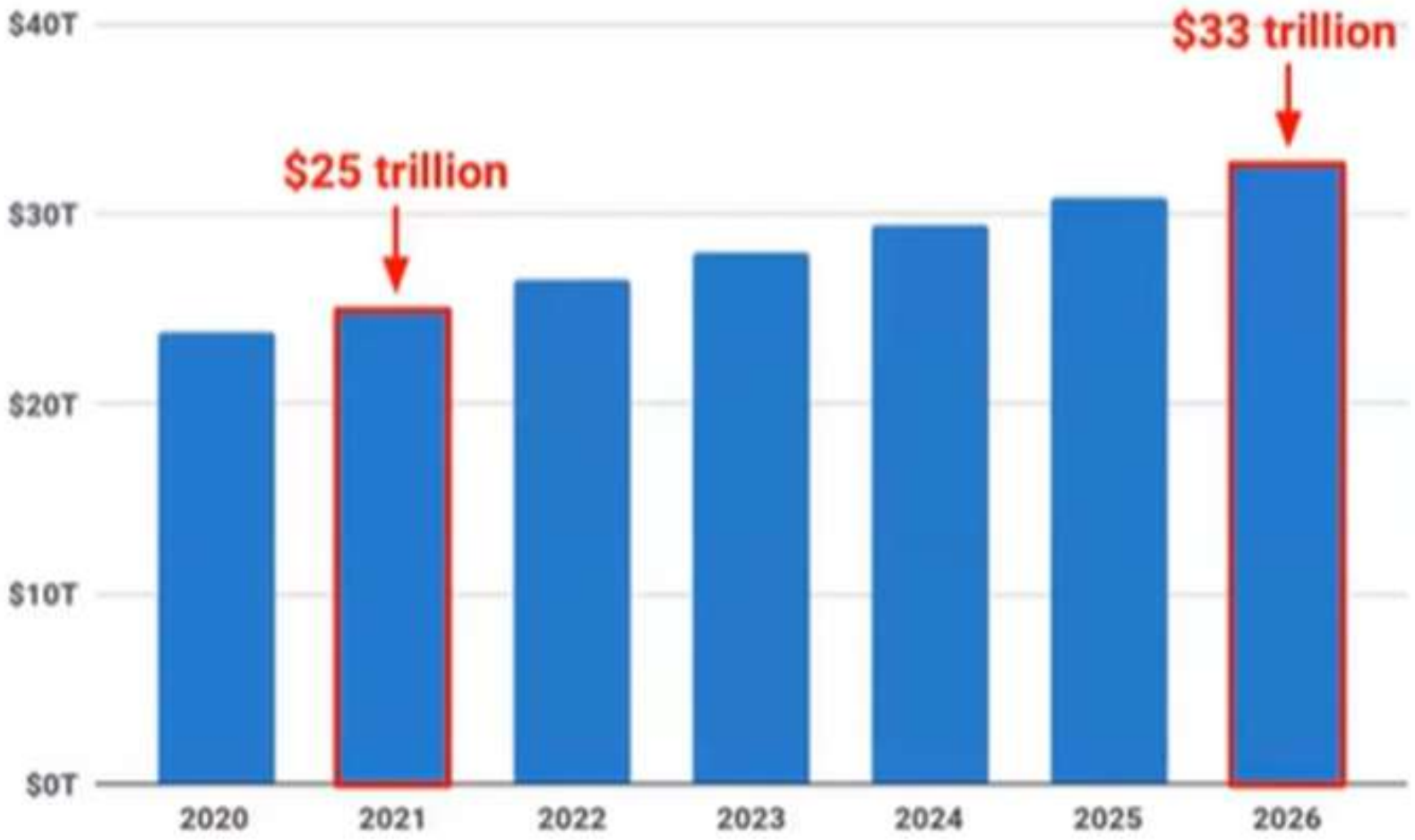
Who wants to live to be 100 years old?

Dynamic Chiropractic **Trends 2024**

Longevity / Biohacking

- Many people are looking for self-care guidance and are willing to take more control of the way they look, feel, and move so *biohacking* is trending right up there with longevity.
- Biohacking starts with empowering individuals to take ownership of their own well-being and happiness. Leading-edge doctors help people sort through misinformation and make better personalized choices in diet, sleep, exercise, breath work, balancing out the sympathetic and parasympathetic systems, etc., to establish new health habits.

The Longevity Economy: Scale Projections, Trillion USD



SYSTEMS PLAN

Life Expectancy

- 2019 78.8
- 2020 77.0
- 2021 76.4

- 2.4 year decrease

In August 2022, provisional life expectancy estimates[1,2] for 2021 were released showing Americans had lost nearly three years of life expectancy during 2020 and 2021. In December 2022, the finalized mortality report[3] confirmed these shocking data.

In 2019, the average life span of Americans of all ethnicities was 78.8 years.[4] By the end of 2020, it had dropped to 77.0 years[5] and by the end of 2021, it was 76.4.[6] As noted by the U.S. Centers for Disease Control and Prevention in its finalized mortality report for 2021,[7] "From 2020 to 2021, death rates increased for each age group 1 year and over

John Alfred Tinniswood, 111, is now the world's oldest man. (Guinness World Records via AP)

Legendary sumo wrestler Akebono Taro dead at 54 from heart failure.


" I sure feel my age, I ache all over."
"I feel like a newborn, no hair, no teeth, and I just peed my pants!"

Review Article

Dietary Interventions to Extend Life Span and Health Span Based on Calorie Restriction

AS the quincentennial of the 1513 launch of Ponce de Leon's famously futile quest for the fountain of youth draws near, efforts of gerontologists over the past several

www.aging-us.com AGING 2020, Vol. 12, No. 1

Editorial

Lifestyle vs. pharmacological interventions for healthy aging

Nagula Parrar and Christoph Handschin

The fountain of youth, the elixir of life, the Philosopher's stone, or an analogous mythical object to remedy the scourges of aging, has been sought after throughout the history of humankind, up to the present day. In modern times, inventing a drug that prevents the beneficial outcome of caloric restriction in non-human primates is due to a reduction of numerous diseases observed in control-fed primates (whatever control levels mean in a laboratory context for these animals), or if true "anti-aging" effects were achieved

The fountain of youth, the elixir of life, the Philosopher's stone, or an analogous mythical object to remedy the scourges of aging, has been sought after throughout the history of humankind, up to the present day. In modern times, inventing a drug that prevents the

Figure 1. How to age in a healthy manner. Examples of behaviors and lifestyle aspects that reduce the risk for developing chronic diseases, help in mitigating pathological events, and decrease morbidity and mortality, thus collectively contributing to healthy aging. At the moment, it is unclear how a single or even multiple pharmacological agents can elicit a similar broad and complex response.

You Need a Plan

Life and Health Lessons from Running with the Bulls

Pamplona Spain

"Some of the finest and most sustained writing that this generation has produced."
—The New York World

THE SUN ALSO RISES

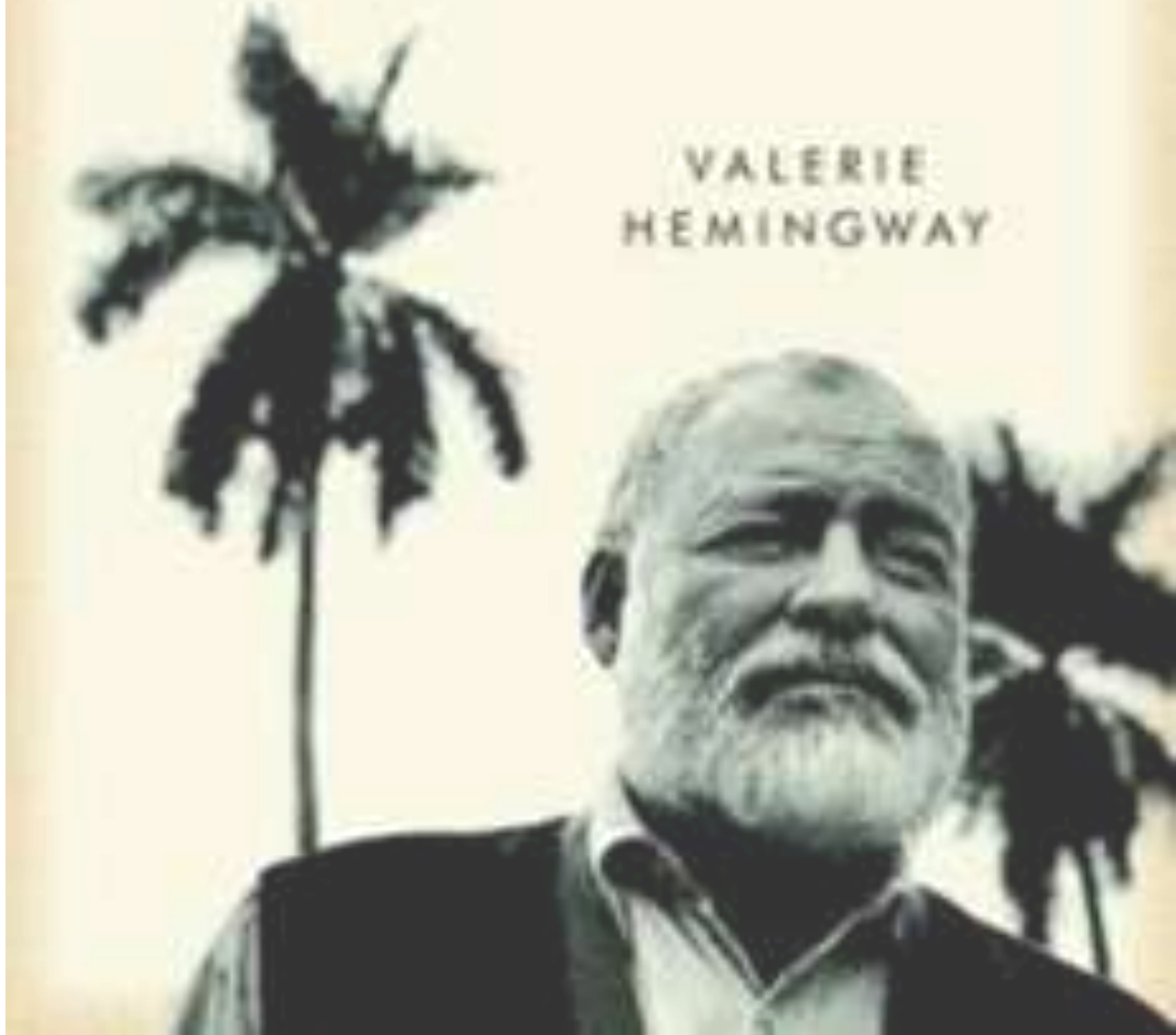
THE HEMINGWAY LIBRARY EDITION

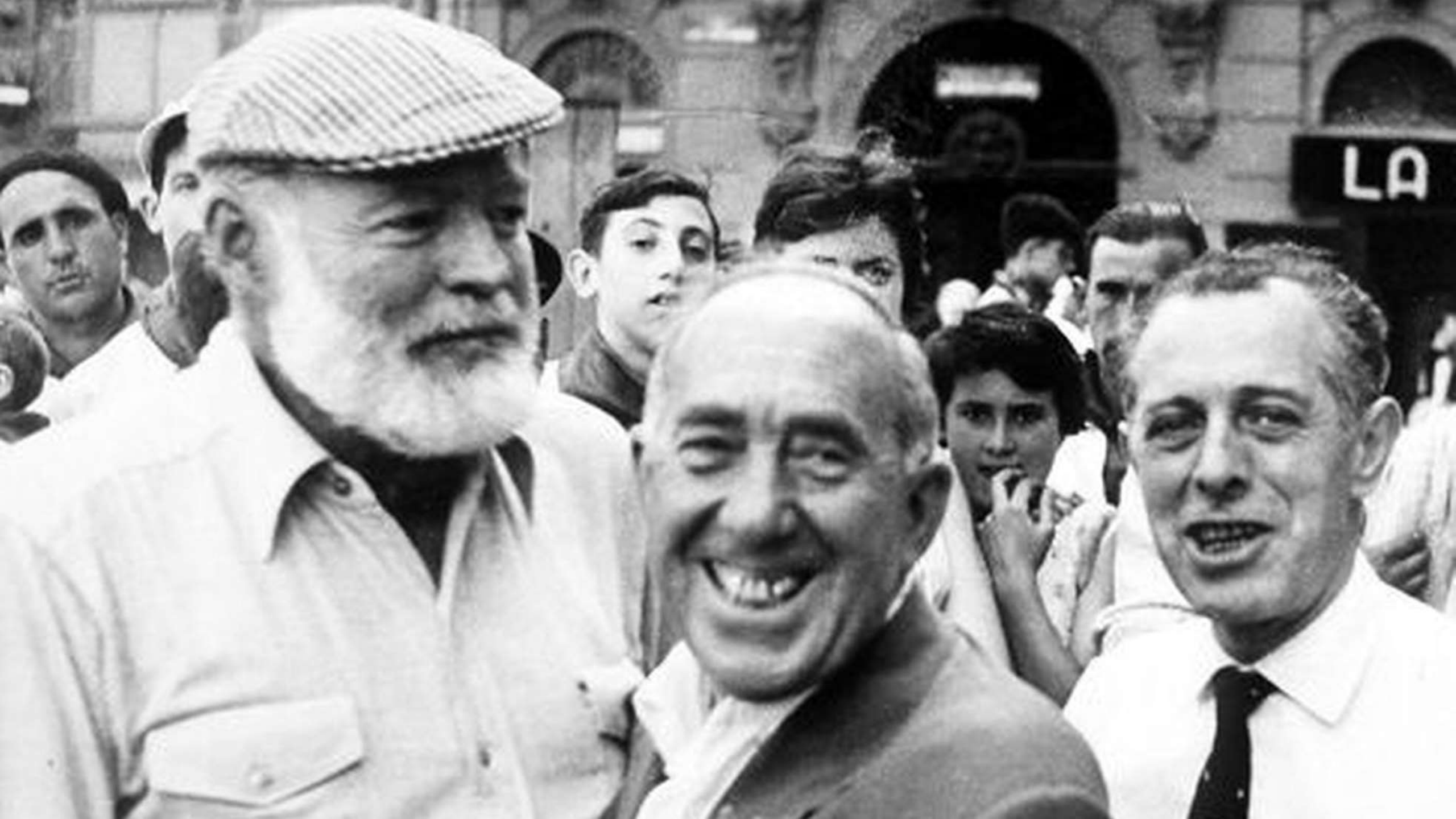
SUPPLEMENTED WITH EARLY DRAFTS AND DELETED CHAPTERS

My Years with the

HEMINGWAYS

VALERIE HEMINGWAY




LA


AGENCIA ELIZARI INMOBILIARIA


AGENCIA ELIZARI INMOBILIARIA


ELIZARI
BAR MOL
RESERVADO RESERVED

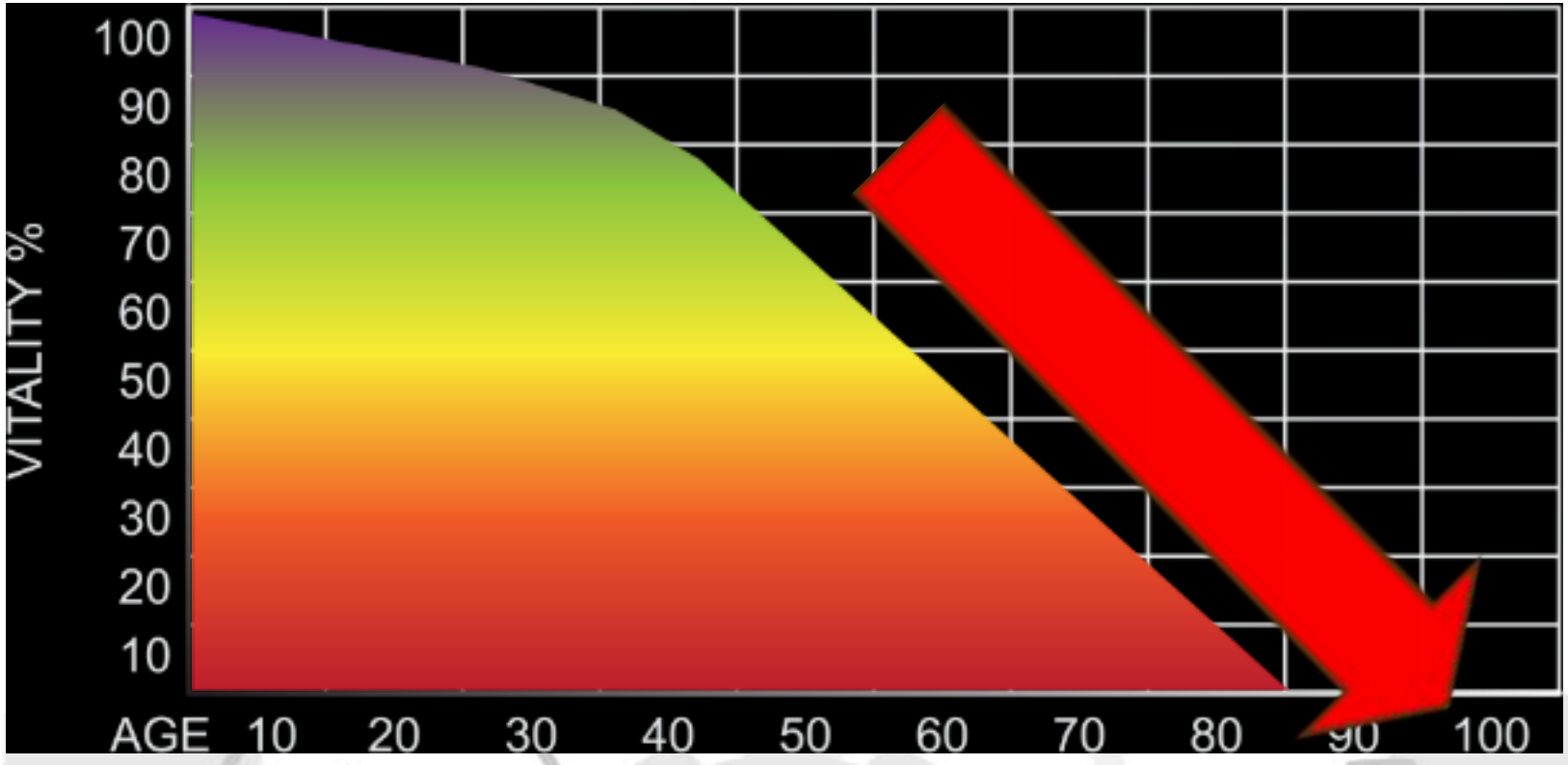
We are all in the Run

- The running of the bulls
- The run of life
- 10 Life and Health Lessons

1. Having a Plan can Save Your Life


Aldapa Kalea
Calle Navarrería
Calle de Curia
Calle Dormitalería
Parque de Tererca
San Fermin
1
Burgoen Plaza
2
Ayuntamiento de Pamplona
Calle Mayor
Calderería Kalea
Calle de la Merced
Cafe Iruña
LA PERLA
3
Plaza del Castillo
Calle de San Agustín
Bajada de Labrit
Lezo
Palacio Guendulain
Iglesia de San Nicolás
San Fermin
Av. Carlos III
Tellería Kalea
4
Plaza de Toros

Running the Race of Life without a Plan



- Optimal Lifeline
- Typical Lifeline
- Optimal Health & Vitality
- Declining Health
- Poor Health
- Disease, Medications and Disability

Fries, J. *NEJM*. 1980; 303:130-135. | Vita, AJ *et al*. *NEJM*. 1998;338:1035-1041.

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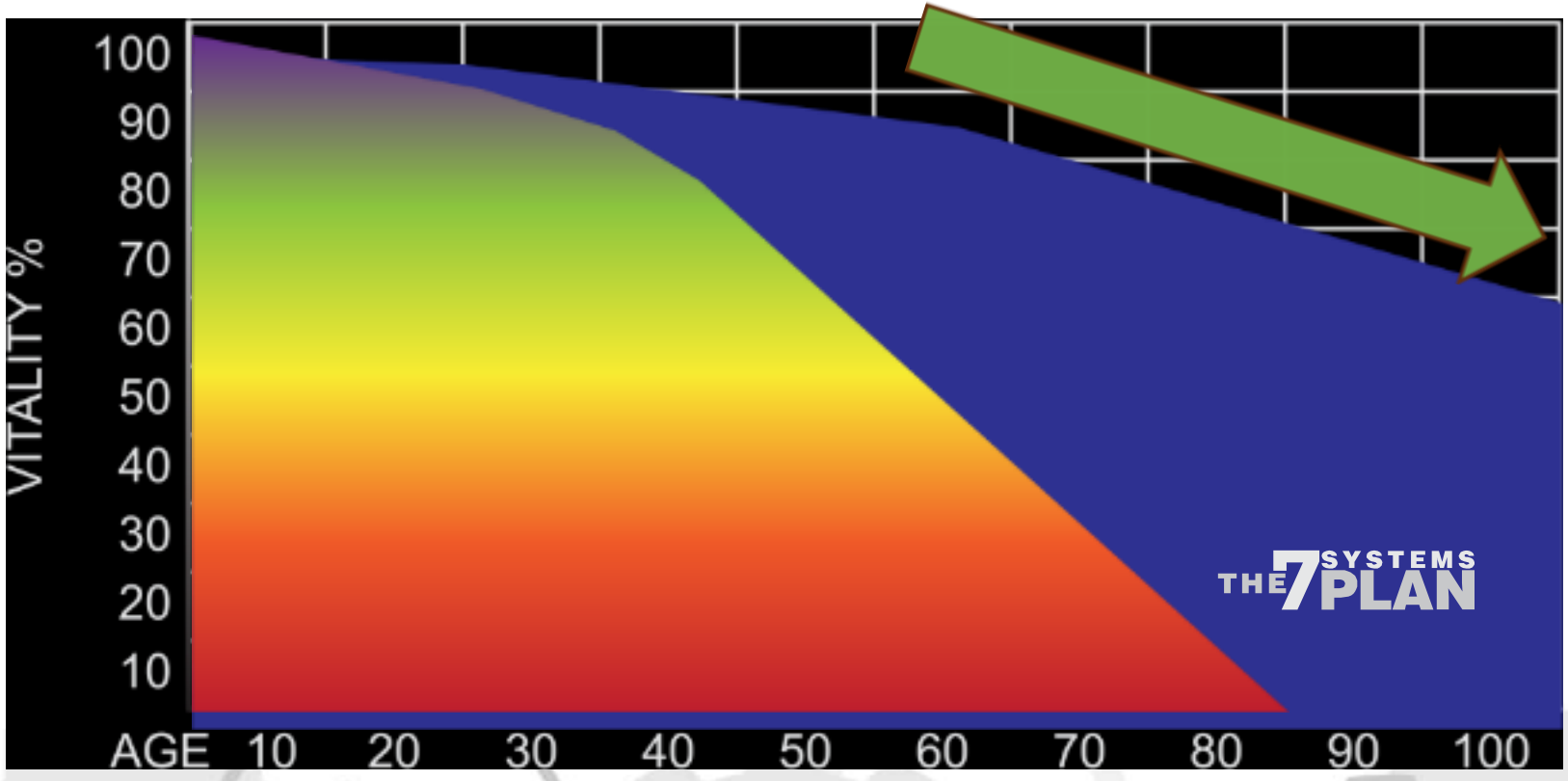
No Plan

- 33% will end up in a **nursing home**
- 70% of people 65 and over will need **long term care**
- 90% of older adults take **one medication**
- 20% take **10 medications**
- 50% of adults have **multiple morbid conditions**

Running the Race of Life with a Plan



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Fries, J. *NEJM*. 1980; 303:130-135. | Vita, AJ *et al*. *NEJM*. 1998;338:1035-1041.

7 SYSTEMS PLAN

Run with a Plan!

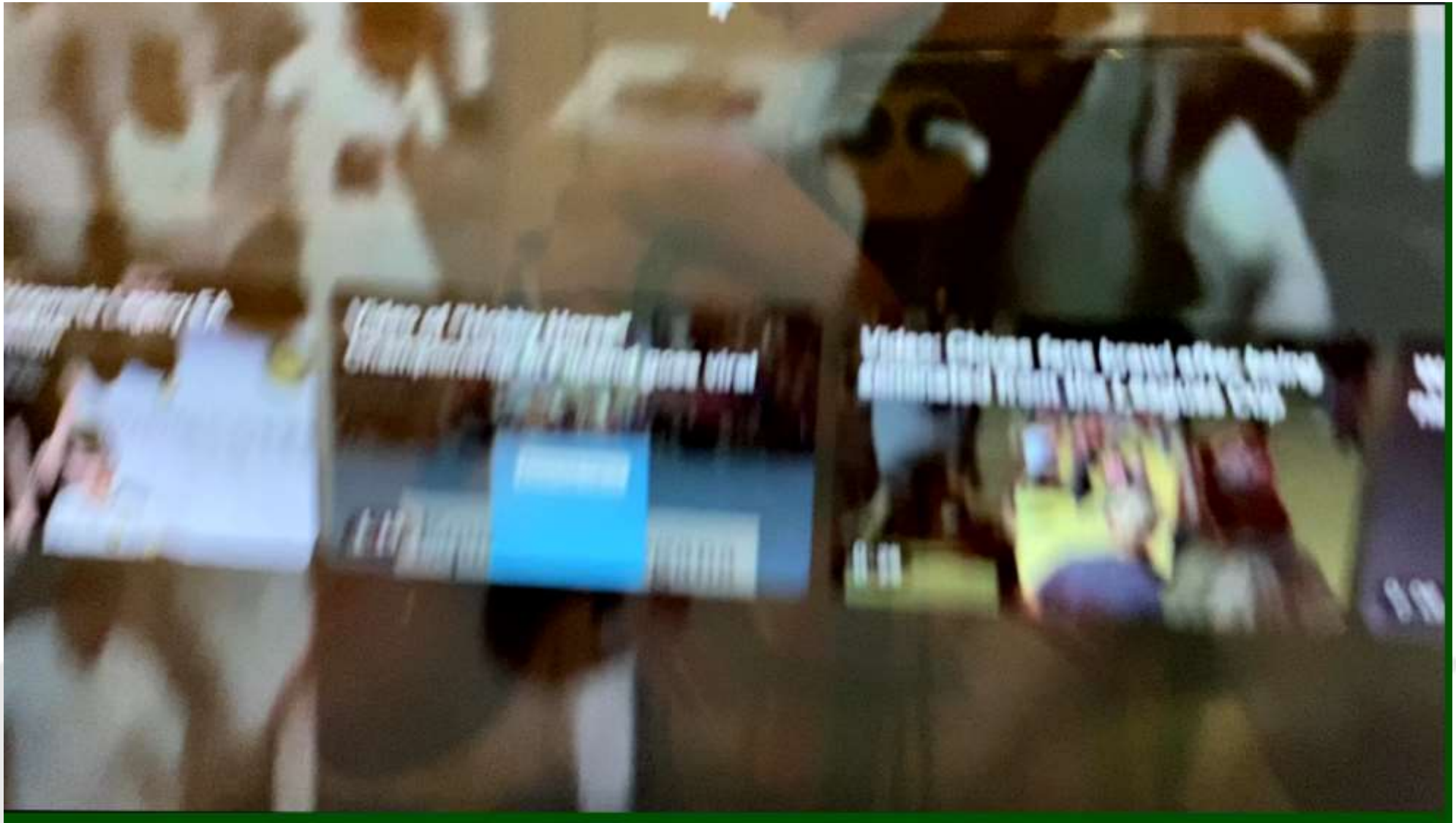
- Optimal Lifeline
- Typical Lifeline
- Optimal Health & Vitality
- Declining Health
- Poor Health
- Disease, Medication and Disability

Fries, J. *NEJM*. 1980; 303:130-135. | Vita, AJ *et al*. *NEJM*. 1998;338:1035-1041.

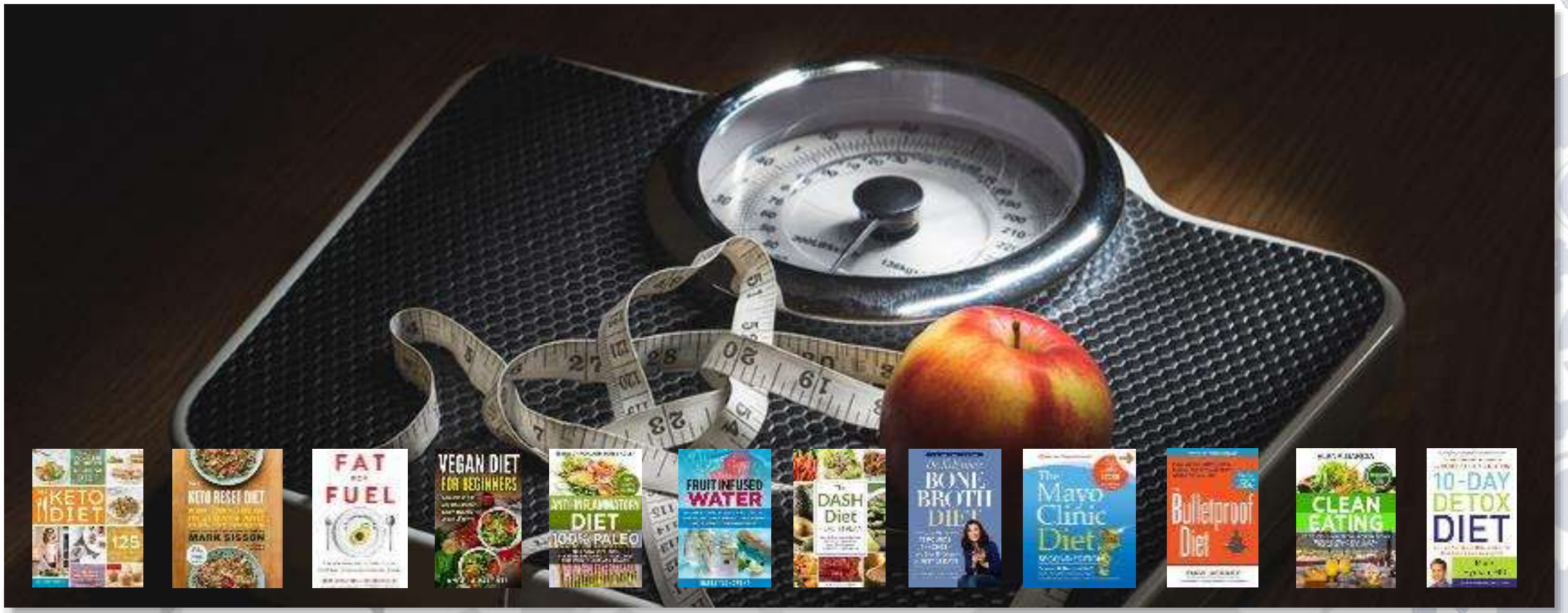
7 SYSTEMS PLAN

2. You Must Choose a Good Plan

Danger if You have the Wrong Plan

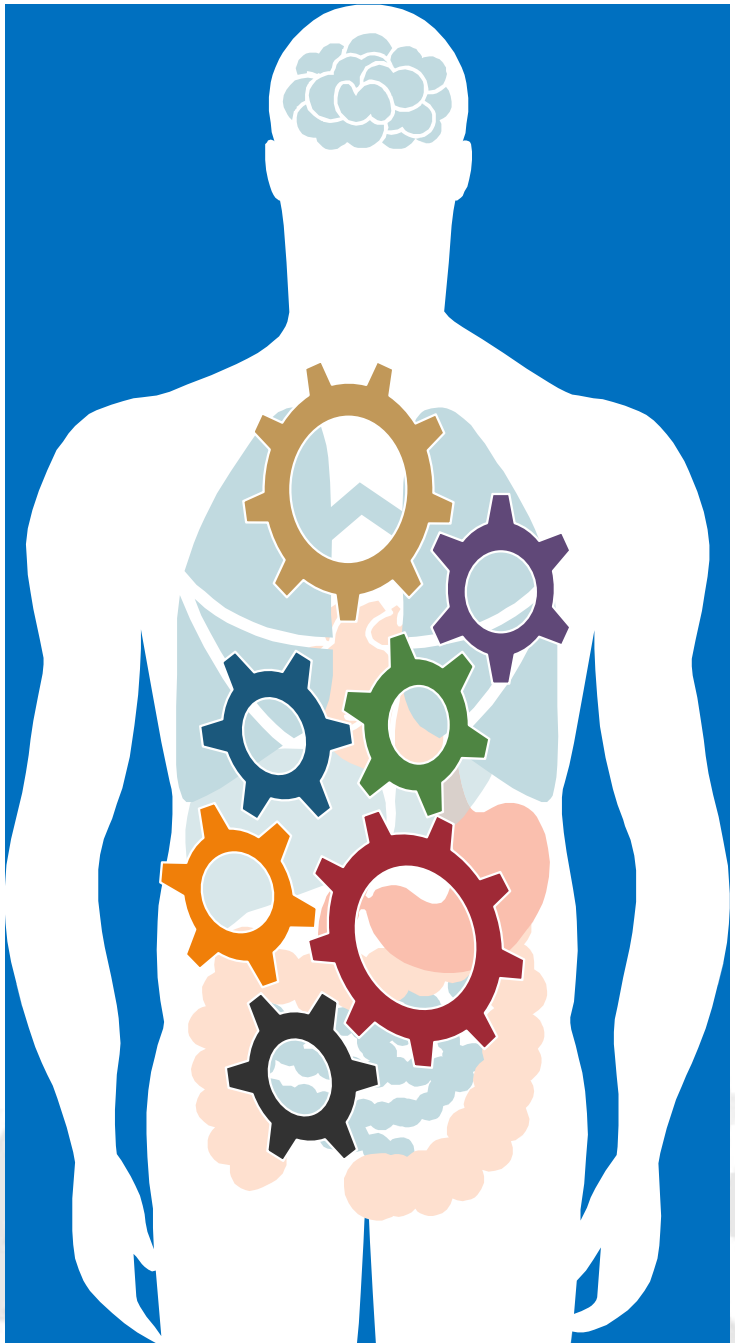


Which Plan do You Choose?



7 SYSTEMS PLAN

7 SYSTEMS PLAN



1. Structure-weight
2. Digestive-microbiome
3. Delivery-healthy diet
4. Energy- mitochondria
5. Communication-hormones
6. Defense-inflammation
7. Detox- avoid toxins

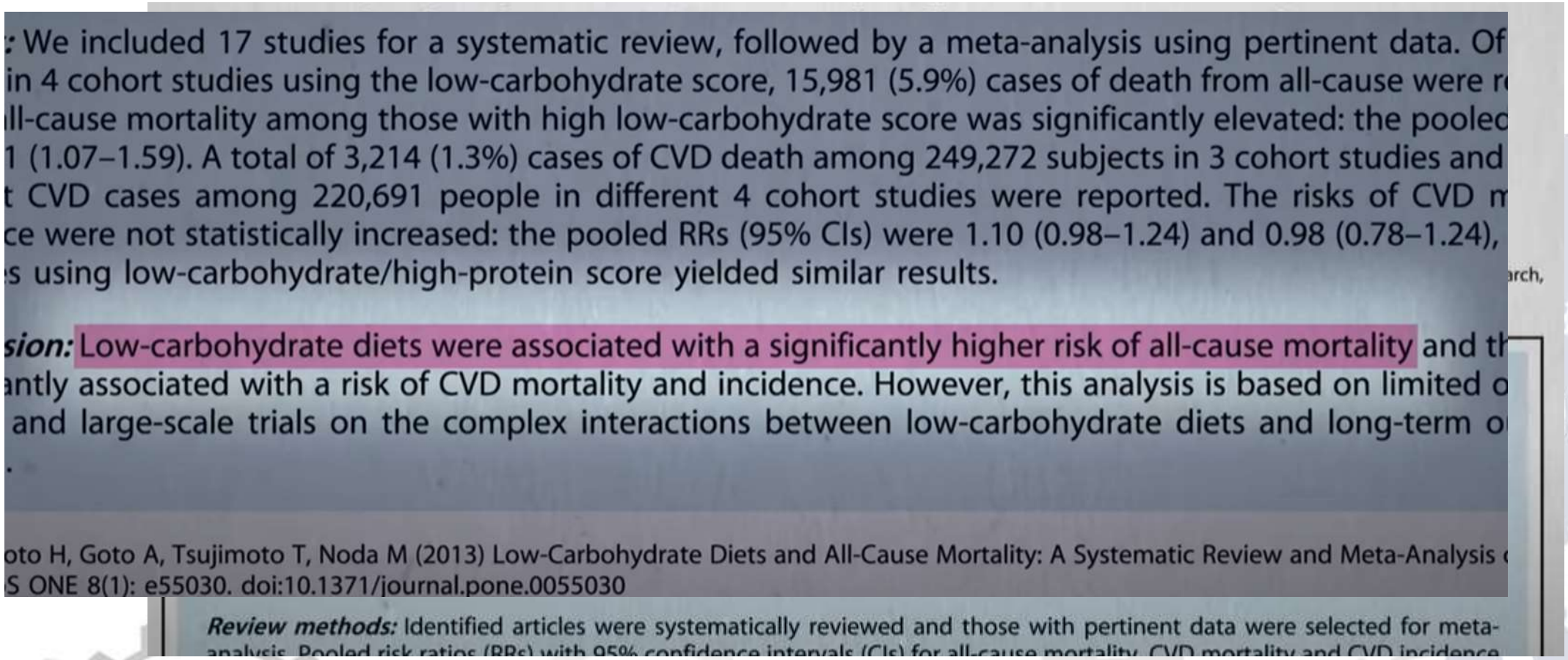
7 SYSTEMS PLAN

3. Some Plans Look Good but are Not

Ultra-Processed Food

PNG

Low Carb-
Significantly Higher Risk of Mortality



: We included 17 studies for a systematic review, followed by a meta-analysis using pertinent data. Of
in 4 cohort studies using the low-carbohydrate score, 15,981 (5.9%) cases of death from all-cause were r
ll-cause mortality among those with high low-carbohydrate score was significantly elevated: the pooled
1 (1.07–1.59). A total of 3,214 (1.3%) cases of CVD death among 249,272 subjects in 3 cohort studies and
t CVD cases among 220,691 people in different 4 cohort studies were reported. The risks of CVD m
ce were not statistically increased: the pooled RRs (95% CIs) were 1.10 (0.98–1.24) and 0.98 (0.78–1.24),
s using low-carbohydrate/high-protein score yielded similar results.

sion: Low-carbohydrate diets were associated with a significantly higher risk of all-cause mortality and th
antly associated with a risk of CVD mortality and incidence. However, this analysis is based on limited o
and large-scale trials on the complex interactions between low-carbohydrate diets and long-term o

oto H, Goto A, Tsujimoto T, Noda M (2013) Low-Carbohydrate Diets and All-Cause Mortality: A Systematic Review and Meta-Analysis
S ONE 8(1): e55030. doi:10.1371/journal.pone.0055030

Review methods: Identified articles were systematically reviewed and those with pertinent data were selected for meta-
analysis. Pooled risk ratios (RRs) with 95% confidence intervals (CIs) for all-cause mortality, CVD mortality and CVD incidence

Animal Fats Worse than Plant Fats- 50% Higher Mortality Risk

Background—The healthiest dietary pattern for myocardial infarction (MI) survivors is not known. Specific long-term benefits of a low-carbohydrate diet (LCD) are unknown, whether from animal or vegetable sources. There is a need to examine the associations between post-MI adherence to an LCD and all-cause and cardiovascular mortality.

Methods and Results—We included 2258 women from the Nurses' Health Study and 1840 men from the Health Professional Follow-Up Study who had survived a first MI during follow-up and provided a pre-MI and at least 1 post-MI food frequency questionnaire. Adherence to an LCD high in animal sources of protein and fat was associated with higher all-cause and cardiovascular mortality (hazard ratios of 1.33 [95% CI: 1.06 to 1.65] for all-cause mortality and 1.51 [95% CI: 1.09 to 2.07] for cardiovascular mortality comparing extreme quintiles). An increase in adherence to an animal-based LCD prospectively assessed from the pre- to post-MI period was associated with higher all-cause mortality and cardiovascular mortality (hazard ratios of 1.30 [95% CI: 1.03 to 1.65] for all-cause mortality and 1.53 [95% CI: 1.10 to 2.13] for cardiovascular mortality comparing extreme quintiles). An increase in adherence to a plant-based LCD was not associated with lower all-cause or cardiovascular mortality.

Conclusions—Greater adherence to an LCD high in animal sources of fat and protein was associated with higher all-cause and cardiovascular mortality post-MI. We did not find a health benefit from greater adherence to an LCD overall after MI. **(*J Am Heart Assoc.* 2014;3:e001169 doi: 10.1161/JAHA.114.001169)**

Key Words: low-carbohydrate diet • mortality • myocardial infarction • secondary prevention

SYSTEMS PLAN

Second Study-
Higher Mortality with Keto After MI

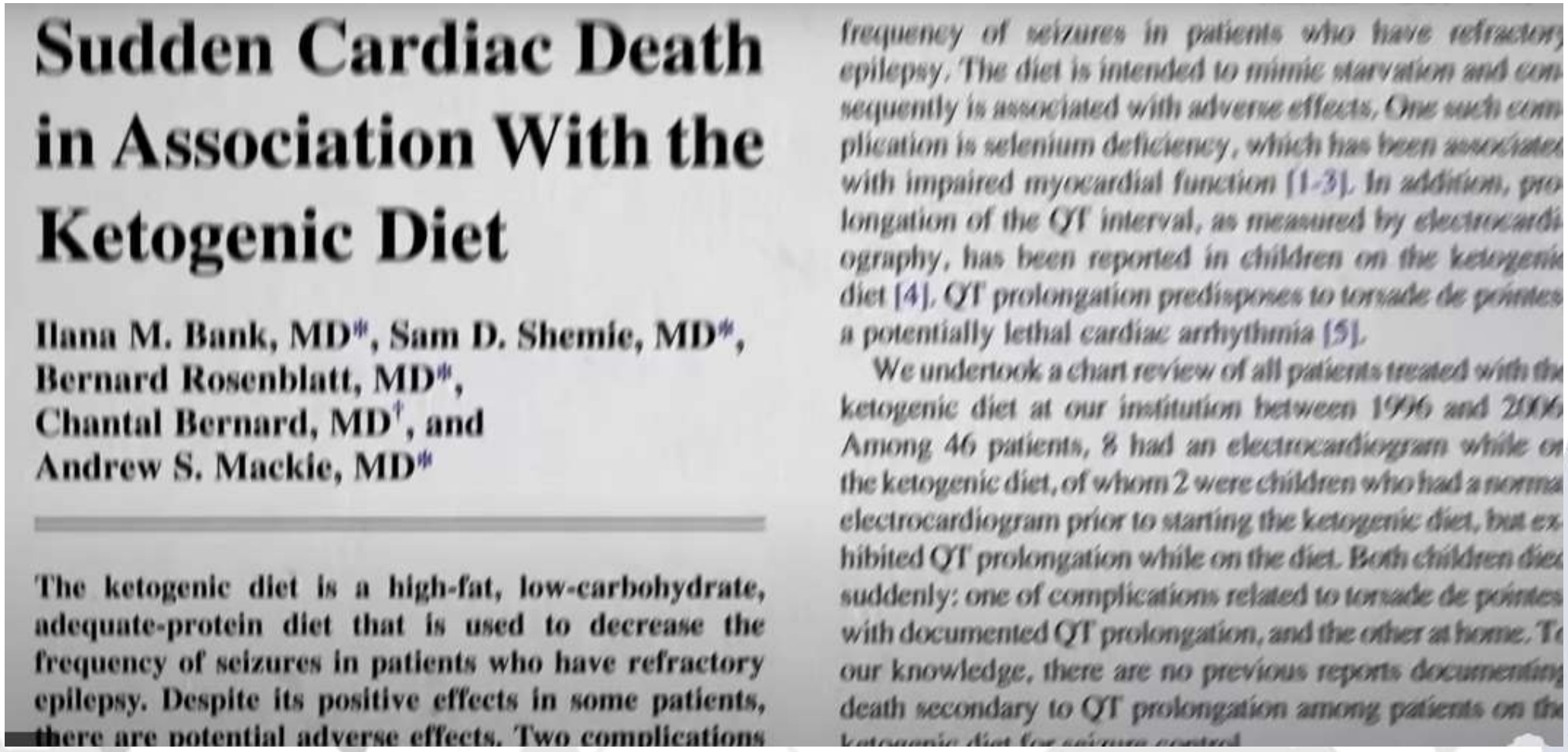
a percentage of 50–55% energy from carbohydrate was associated with the lowest risk of mortality. In the meta-analysis of all cohorts (432 179 participants), both low carbohydrate consumption (<40%) and high carbohydrate consumption (>70%) conferred greater mortality risk than did moderate intake, which was consistent with a U-shaped association (pooled hazard ratio 1·20, 95% CI 1·09–1·32 for low carbohydrate consumption; 1·23, 1·11–1·36 for high carbohydrate consumption). However, results varied by the source of macronutrients: mortality increased when carbohydrates were exchanged for animal-derived fat or protein (1·18, 1·08–1·29) and mortality decreased when the substitutions were plant-based (0·82, 0·78–0·87).

Interpretation Both high and low percentages of carbohydrate diets were associated with increased mortality, with minimal risk observed at 50–55% carbohydrate intake. Low carbohydrate dietary patterns favouring animal-derived protein and fat sources, from sources such as lamb, beef, pork, and chicken, were associated with higher mortality, whereas those that favoured plant-derived protein and fat intake, from sources such as vegetables, nuts, peanut butter, and whole-grain breads, were associated with lower mortality, suggesting that the source of food notably modifies the association between carbohydrate intake and mortality.

Funding National Institutes of Health.

SYSTEMS PLAN

Sudden Cardiac Death



Sudden Cardiac Death in Association With the Ketogenic Diet

Ilana M. Bank, MD*, Sam D. Shemie, MD*, Bernard Rosenblatt, MD*, Chantal Bernard, MD†, and Andrew S. Mackie, MD*

The ketogenic diet is a high-fat, low-carbohydrate, adequate-protein diet that is used to decrease the frequency of seizures in patients who have refractory epilepsy. Despite its positive effects in some patients, there are potential adverse effects. Two complications

frequency of seizures in patients who have refractory epilepsy. The diet is intended to mimic starvation and consequently is associated with adverse effects. One such complication is selenium deficiency, which has been associated with impaired myocardial function [1-3]. In addition, prolongation of the QT interval, as measured by electrocardiography, has been reported in children on the ketogenic diet [4]. QT prolongation predisposes to torsade de pointes, a potentially lethal cardiac arrhythmia [5].

We undertook a chart review of all patients treated with the ketogenic diet at our institution between 1996 and 2006. Among 46 patients, 8 had an electrocardiogram while on the ketogenic diet, of whom 2 were children who had a normal electrocardiogram prior to starting the ketogenic diet, but exhibited QT prolongation while on the diet. Both children died suddenly: one of complications related to torsade de pointes with documented QT prolongation, and the other at home. To our knowledge, there are no previous reports documenting death secondary to QT prolongation among patients on the ketogenic diet for seizure control

Lancet 2018

- This study examined the relationship between low-carbohydrate diets, all-cause death, deaths from coronary heart disease, and cancer in 24,825 people. **Compared to those in the highest carbohydrate group, those who ate the lowest carbohydrates had a 32 percent higher risk of all-cause death over six years. In addition, risks of death from heart disease and cancer were increased by 51 percent and 35 percent, respectively.**

Wrong Plan

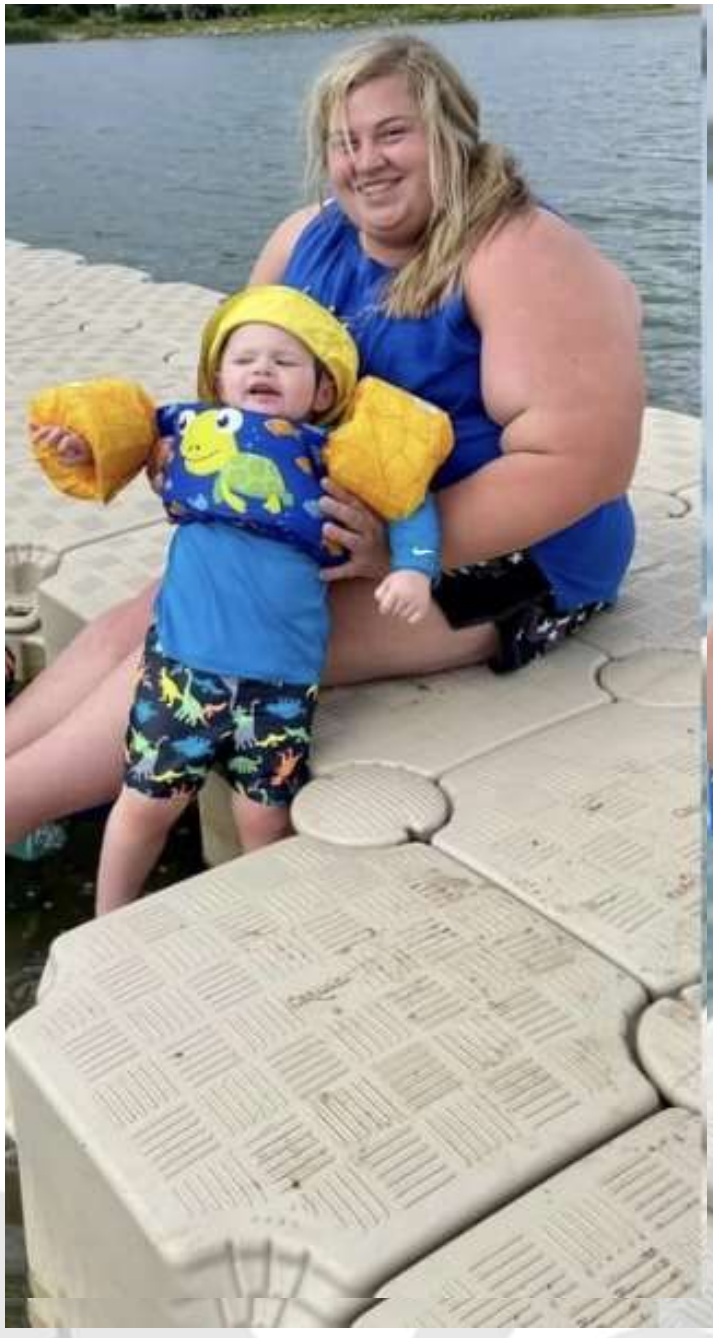
- Diabetes will shorten your life 6 years
- Multiple meds to control diabetes results in shorter life
- Overweight (40+ BMI) may take as much as 10 years off your life

Life expectancy decreases with each additional chronic condition

- A 67-year-old individual with no chronic conditions will live on average to be 89.6
- A 67-year-old individual 10 chronic conditions will live on average to be 72

Larry- Wrong Plan

4. Having a Coach can be Very Valuable



SYSTEMS PLAN

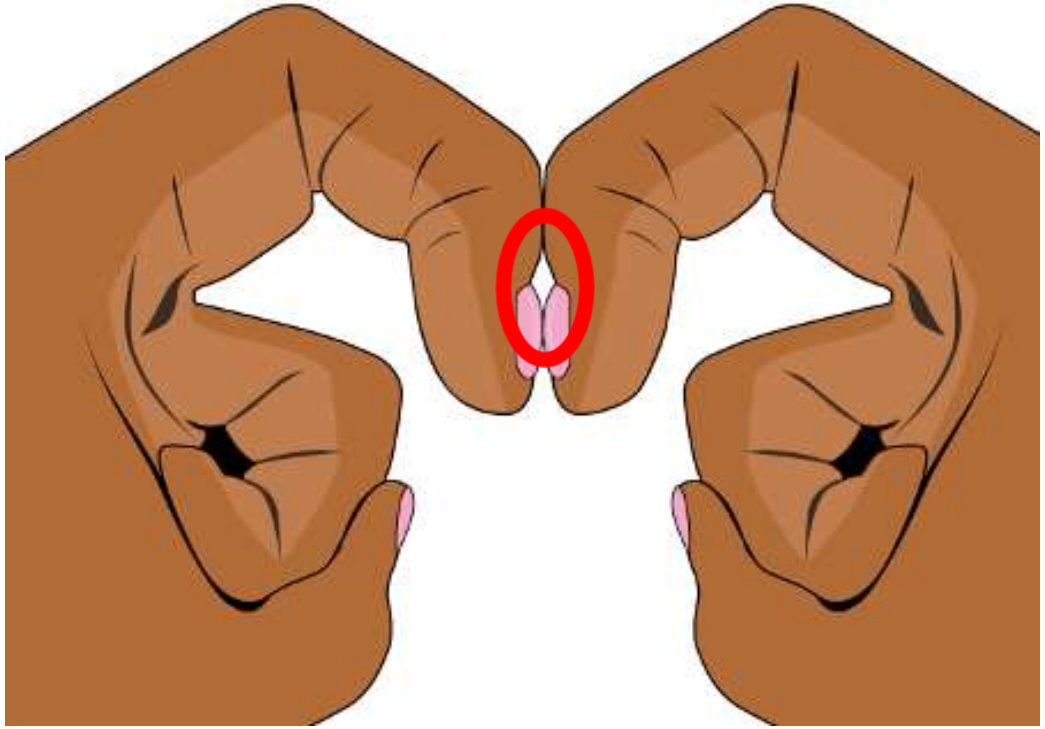
5. Danger Signs can be Seen

Ear Lobe Crease
Frank's Sign

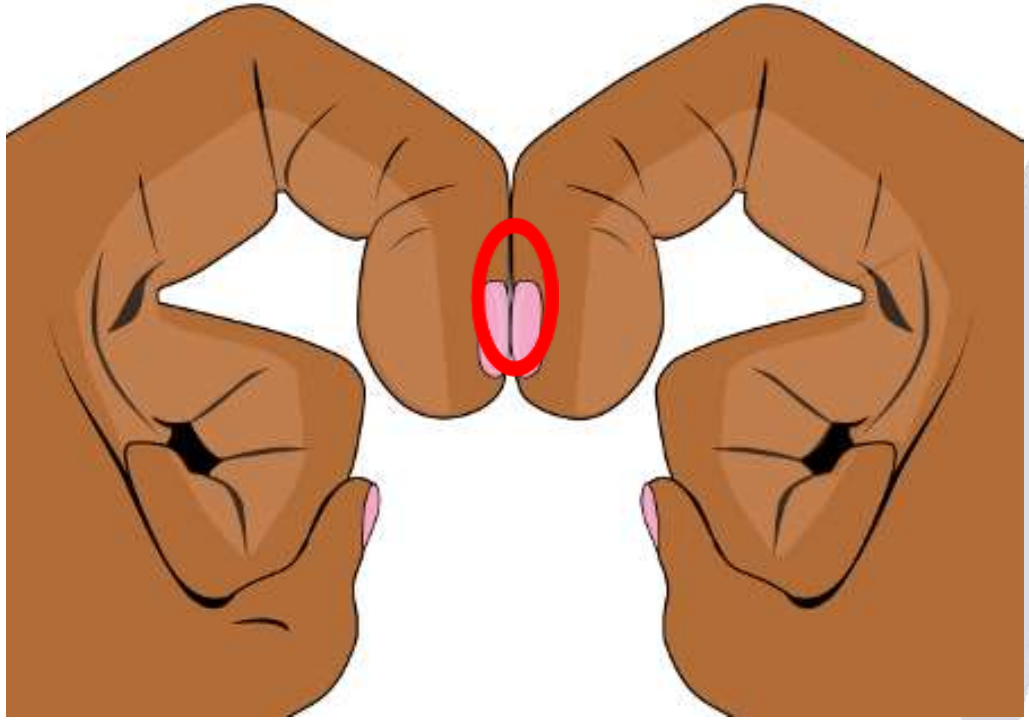
SYSTEMS PLAN

Schamroth Window Test-Lung Cancer

Normal Finger



Clubbing finger



Acanthosis Nigricans (AN),

- This Skin Condition can be a **Sign of Diabetes**
- **Darkening of the skin, at the nape of the neck, could be an early indication of insulin resistance and diabetes.**
- The condition, is marked by the **darkening and thickening of the skin on the sides or back of the neck, the armpits, under the breast, and groin.**
- Acanthosis Nigricans is a skin condition that **signals high insulin** levels in the body.

High Insulin

1. Blood test for fasting insulin – less than 5
2. Pinch test

Eyebrow Sign

Warning Signs

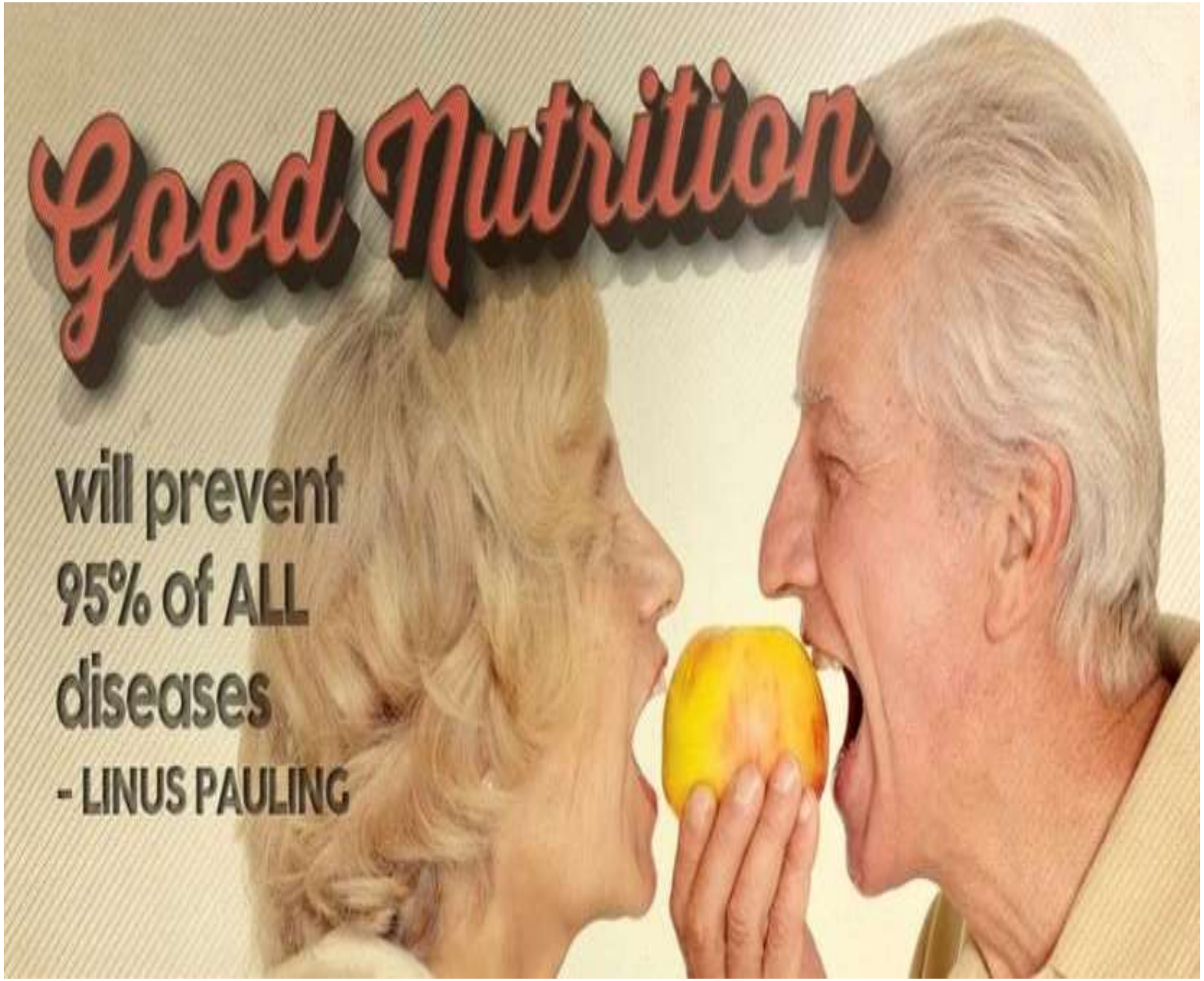
- Physical signs
- BMI over 28
- High BP or BP medications
- Pulse over 65
- A1C over 6
- Multiple meds

Roy

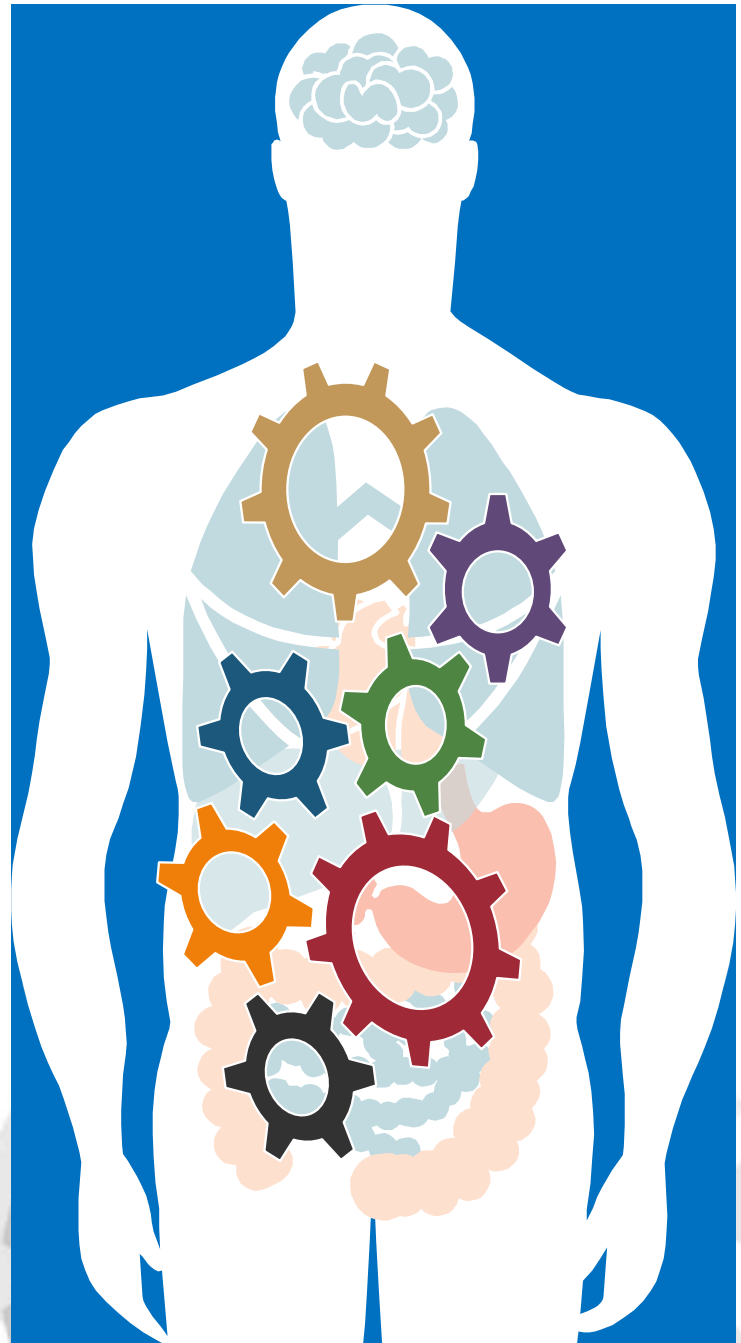
Delivery System

6. Avoid Things that will Kill You

Leading causes of death in the US



7 SYSTEMS PLAN



1. Structure-weight
2. Digestive-microbiome
3. Delivery-healthy diet
4. Energy-exercise
5. Communication-hormones
6. Defense-inflammation
7. Detox- avoid toxins

7 SYSTEMS PLAN

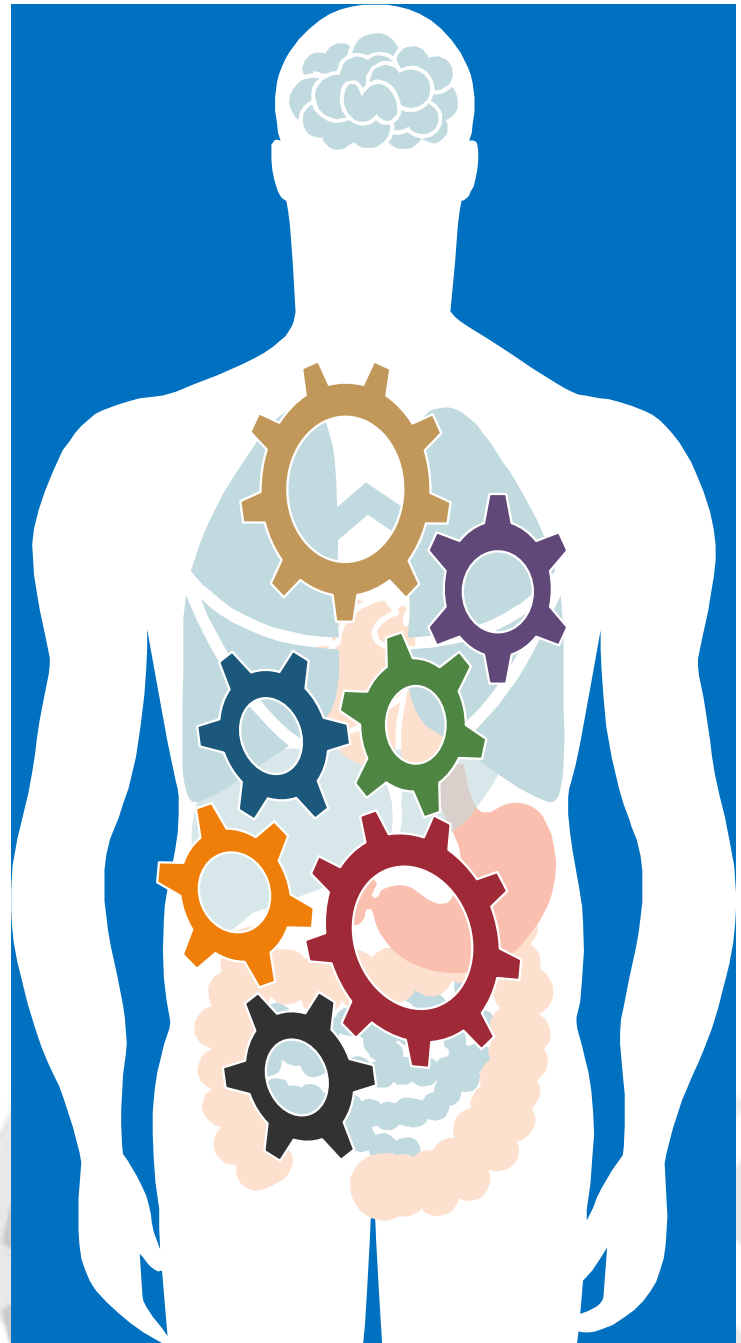
7. People Can Trip You Up or Help You

People Can

- Get you off track
- Give you bad advice
- Make it harder to stay on track
- Help you meet your health goals

8. Do the Right Thing When You Get Knocked Down

7 SYSTEMS PLAN



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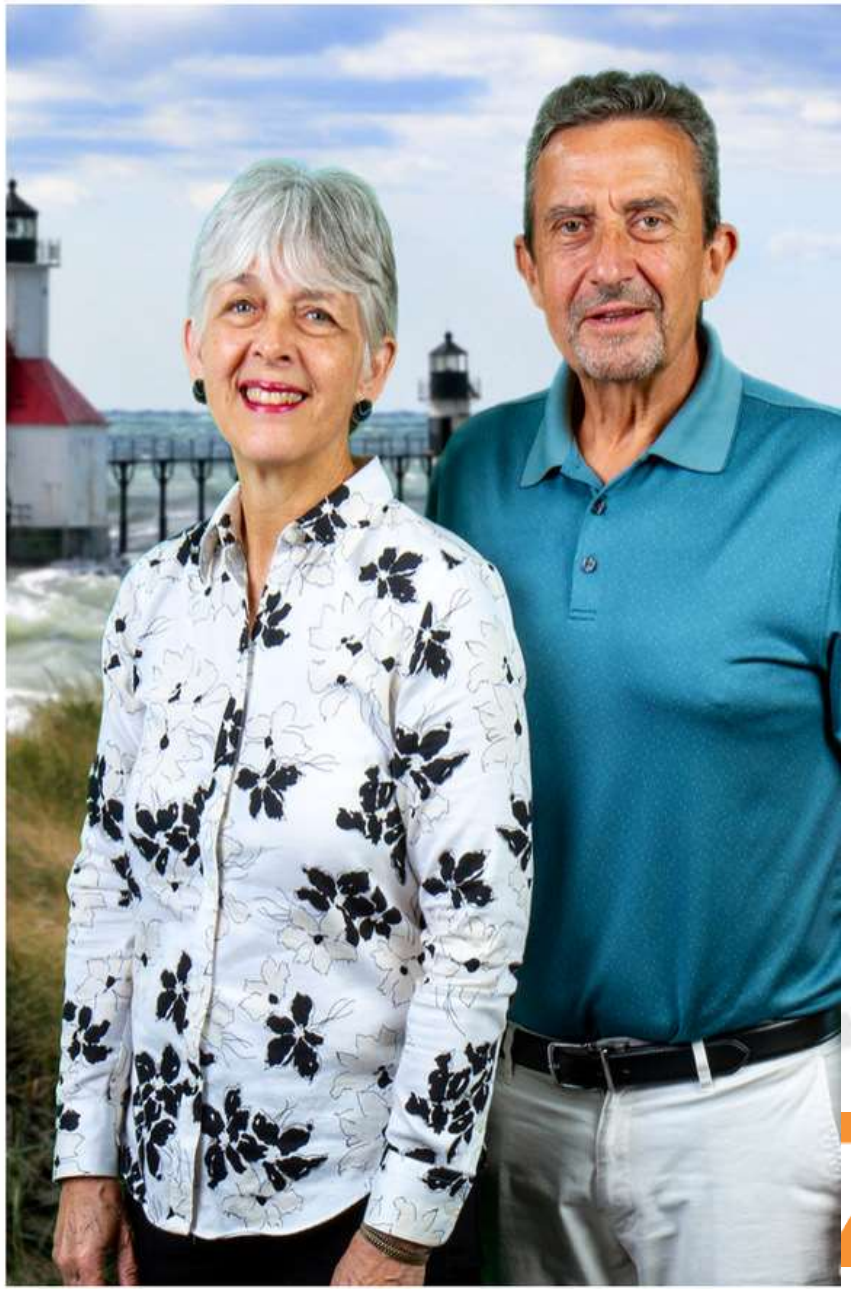
7 SYSTEMS PLAN

June 2018
242

June 2019
175



SYSTEMS PLAN

Brandon A1C 9.7 to 5.7 in 90 Days

9. Sometimes Bad Things Happen

Ron

Run the Race with Successful Runners

- Don’t do it on your own
- Join a support group

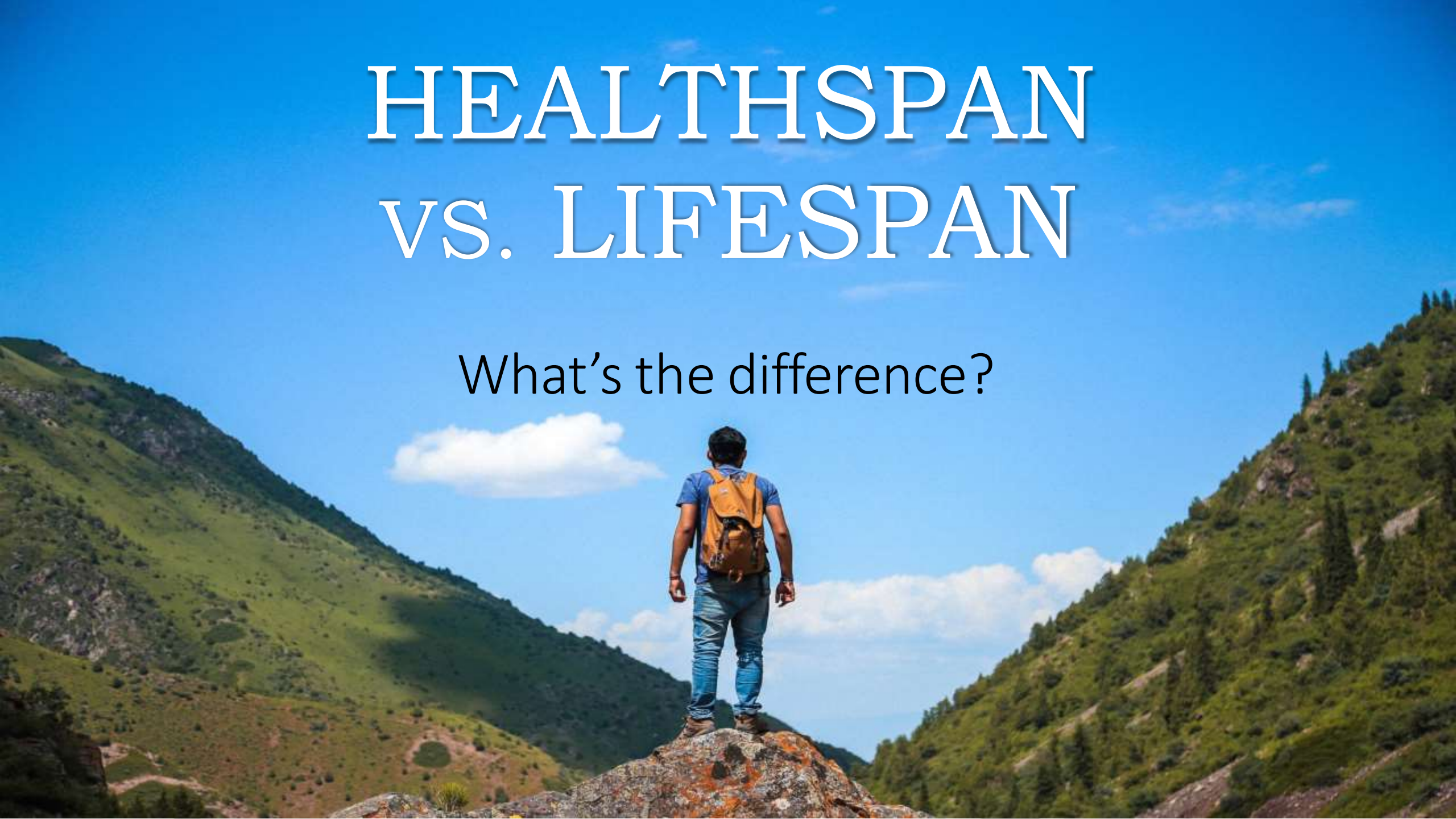
Run the Race Well

10. Run to Win

Hackman was surprised with 105 Fireball shooters in celebration of her big day. (Fireball)

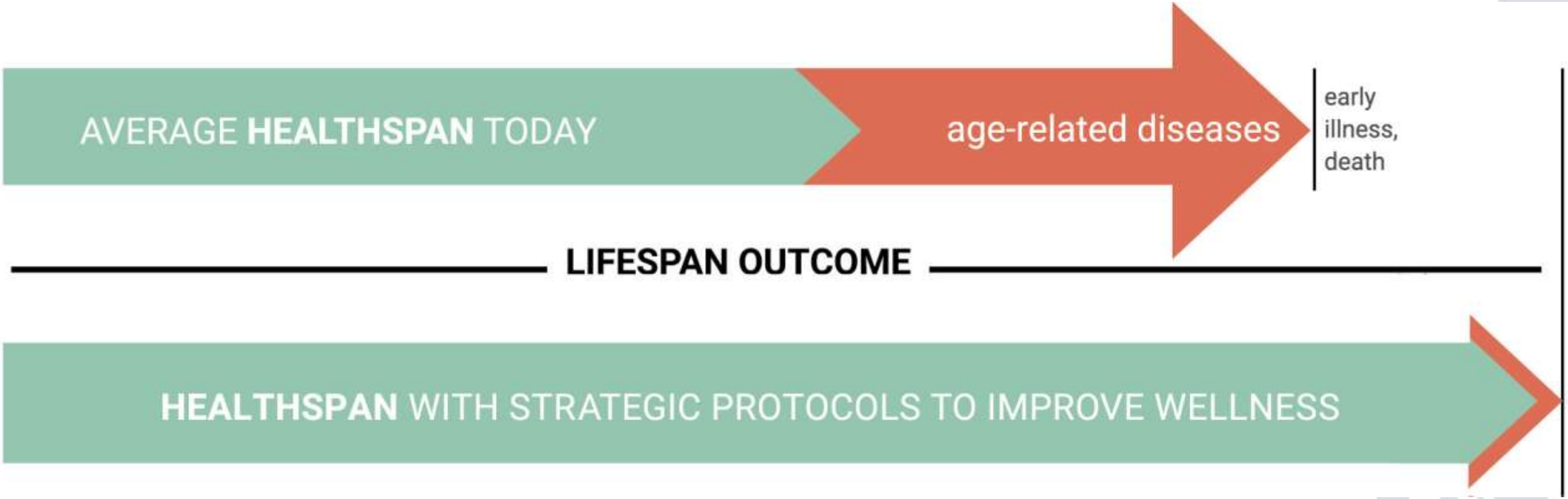
HEALTHSPAN VS. LIFESPAN

What's the difference?



Healthspan vs. Lifespan

Healthspan vs. Lifespan



SYSTEMS PLAN

HEALTHSPAN WITH STRATEGIC PROTOCOLS TO IMPROVE WELLNESS

Wayne Down 110 Pounds!

Candi

SYSTEMS PLAN

Make 4 Simple Lifestyle Changes

Begin at age 50, prolong life by:

- 14 years for females
- 12.2 years for males

Circulation

ORIGINAL RESEARCH ARTICLE

Impact of Healthy Lifestyle Factors on Life Expectancies in the US Population

BACKGROUND: Americans have a shorter life expectancy compared with residents of almost all other high-income countries. We aim to estimate the impact of lifestyle factors on premature mortality and life expectancy in the US population.

Yanping Li, MD, PhD*
An Pan, PhD*
Dong D. Wang, MD, ScD
Xiaoran Liu, PhD

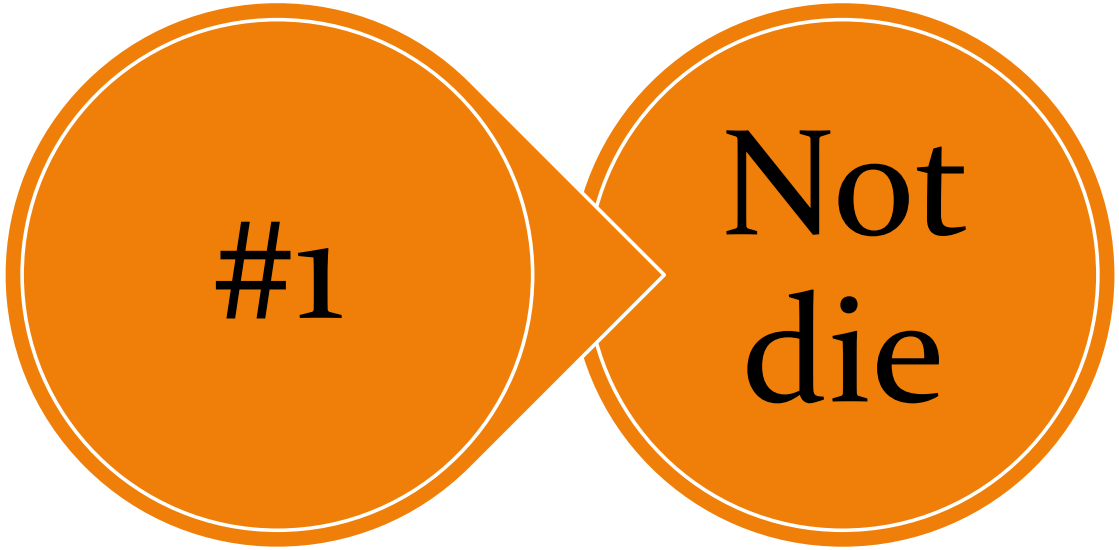
We estimate that adherence to a low-risk lifestyle could prolong life expectancy at age 50 years by 14.0 and 12.2 years in female and male US adults compared with individuals without any of the low-risk lifestyle factors.

7 SYSTEMS PLAN

Who wants to live to be 100 years old?

The #1 Thing to Live to be 100

#1 Thing to do to Live Longer?



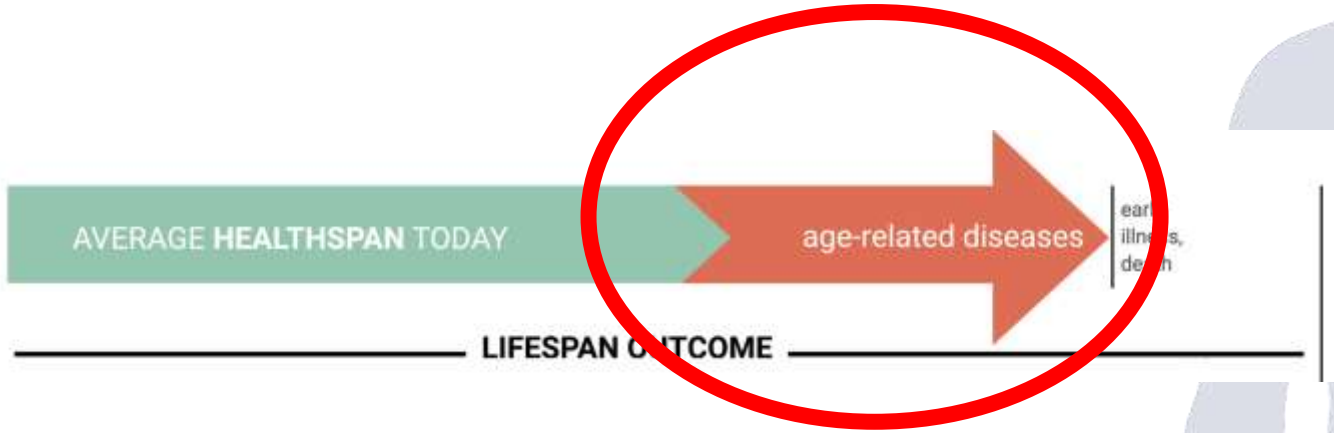
Why do Centenarians Die?

The top five causes of death in 2000 were:

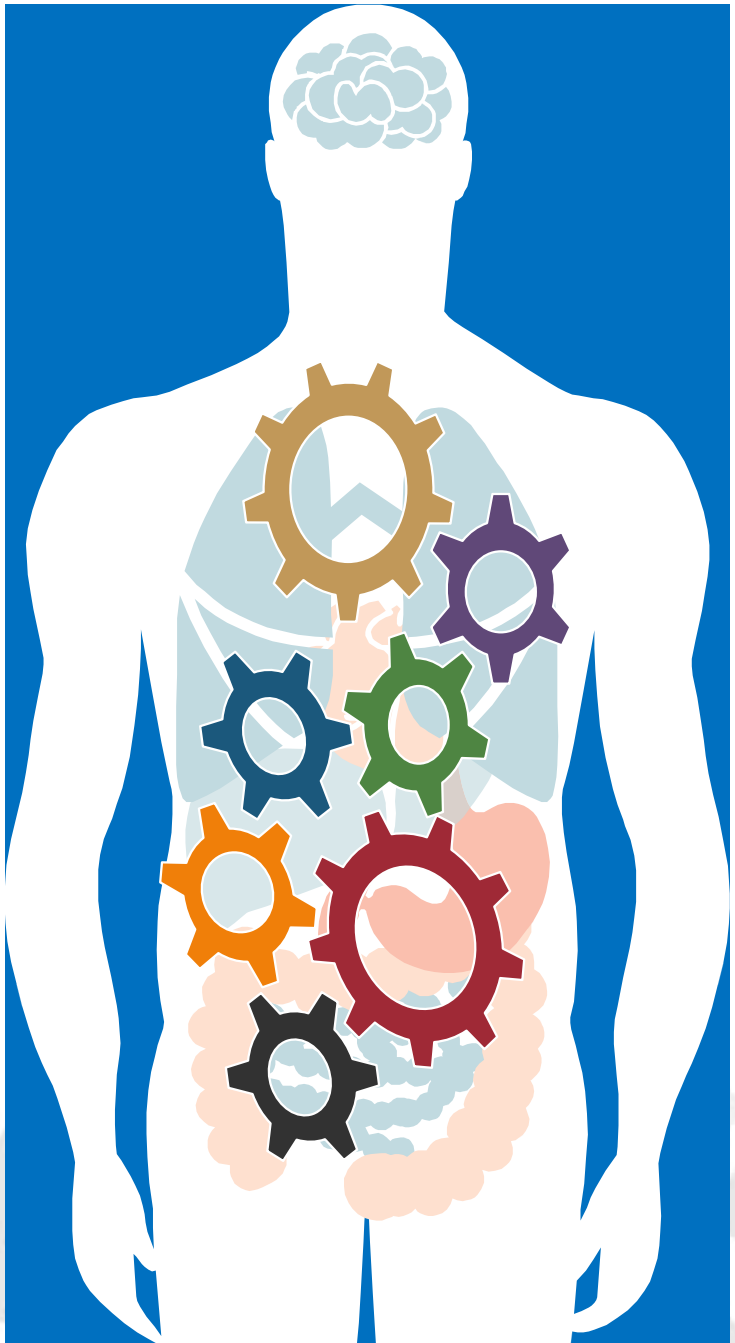
- heart disease
- stroke
- influenza and pneumonia
- cancer
- Alzheimer's disease

Leading Causes of Death

1. Heart disease
2. Cancer
3. Unintentional injuries
4. Chronic lower respiratory disease
5. Stroke and cerebrovascular diseases
6. Alzheimer's disease
7. Diabetes
8. Influenza and pneumonia
9. Kidney disease
10. Suicide



SYSTEMS PLAN



LONGEVITY and HEALTH

1. Structure
2. Digestive
3. Delivery
4. Energy
5. Communication
6. Defense
7. Detox

7 SYSTEMS PLAN

Leading Causes of Death

1. Heart disease
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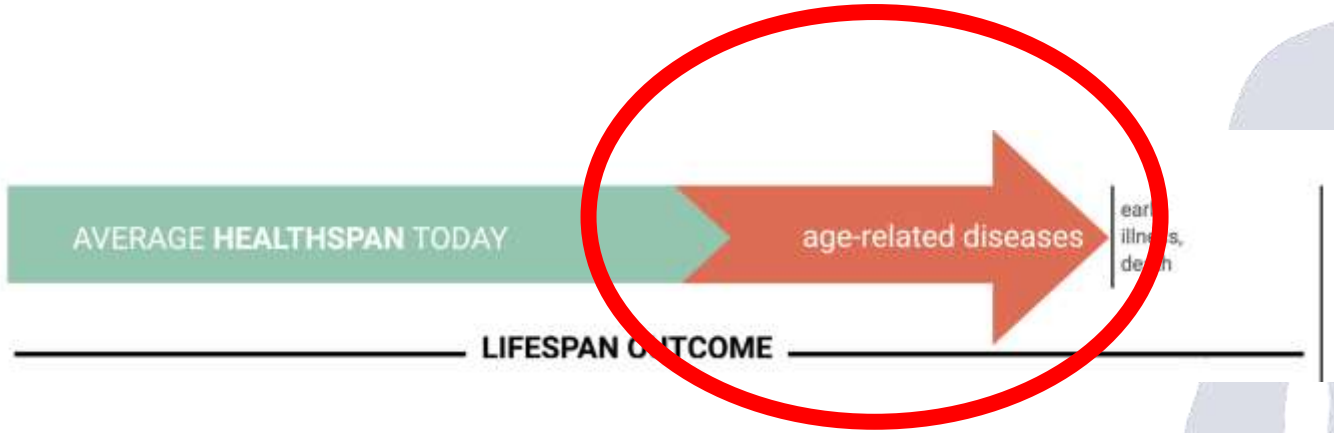
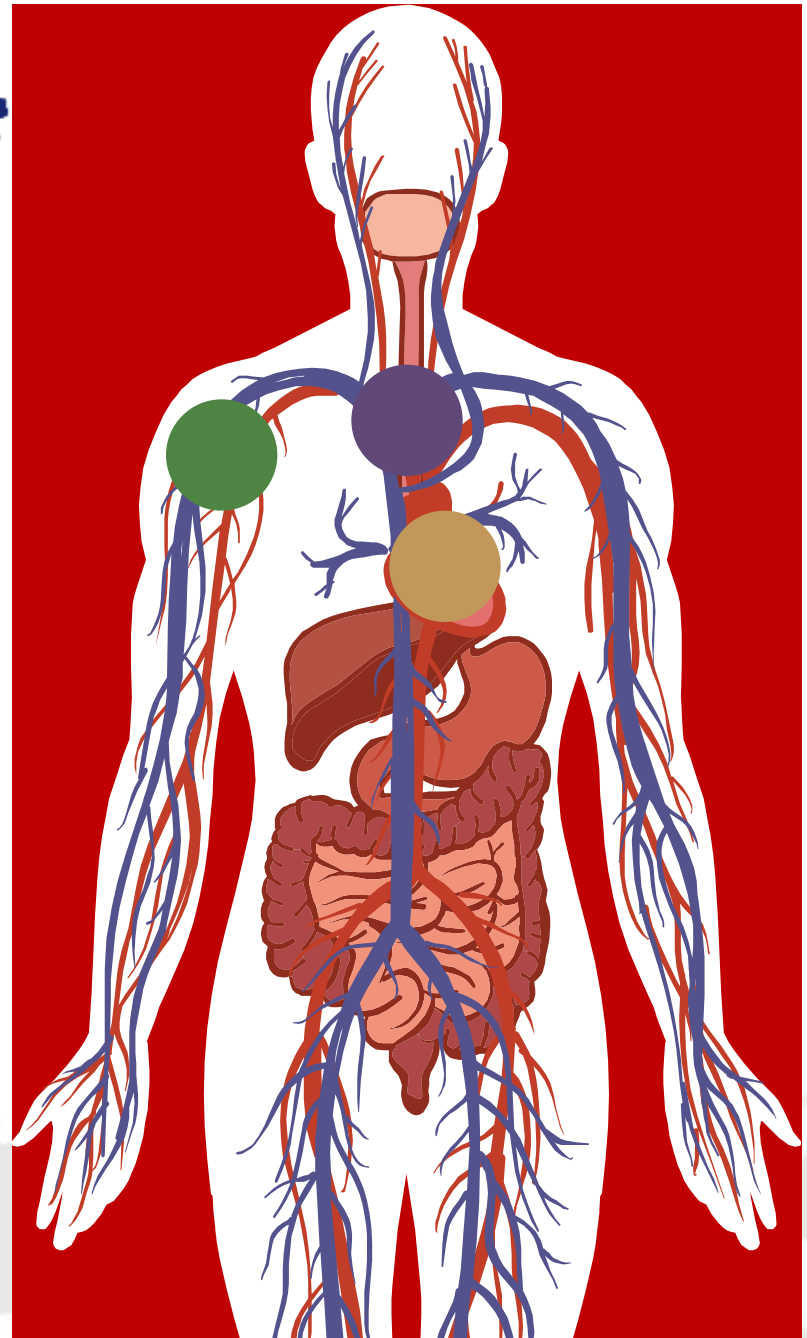


SYSTEMS PLAN

“ A person is as old as their Arteries”

Thomas Sydenham, English Physician

DELIVERY SYSTEM



1. Heart
2. Blood vessels
3. Nutrient Transport-
   LDL, VLDL, Albumin…

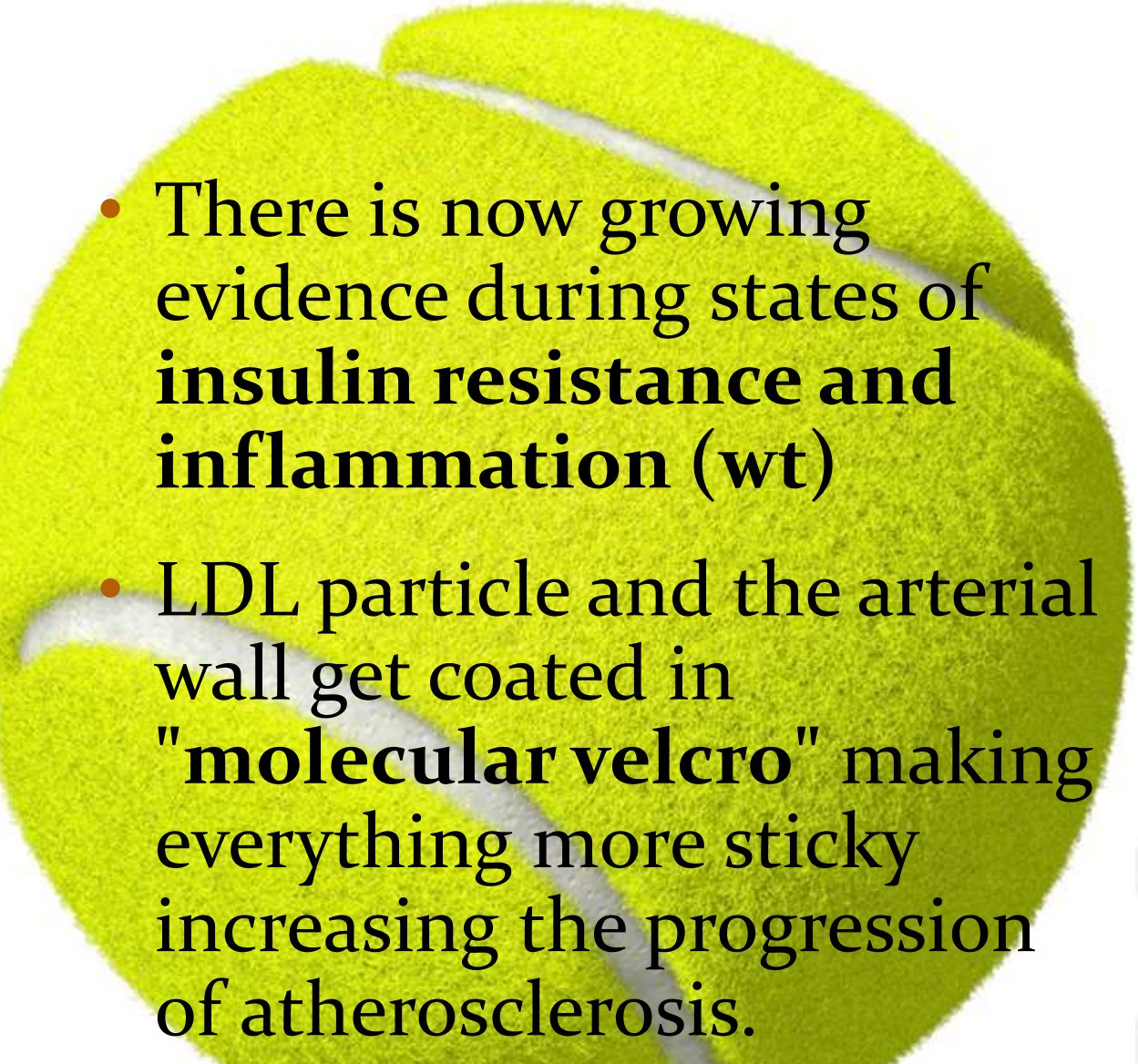
A Sign of Heart Disease?

Roy (1990)

Delivery System

- Obese
- Blocked coronary artery
  - high LDL cholesterol
  - angina- nitroglycerin
  - in need of bypass
- Deconditioned
- Poor diet

LDL Cholesterol

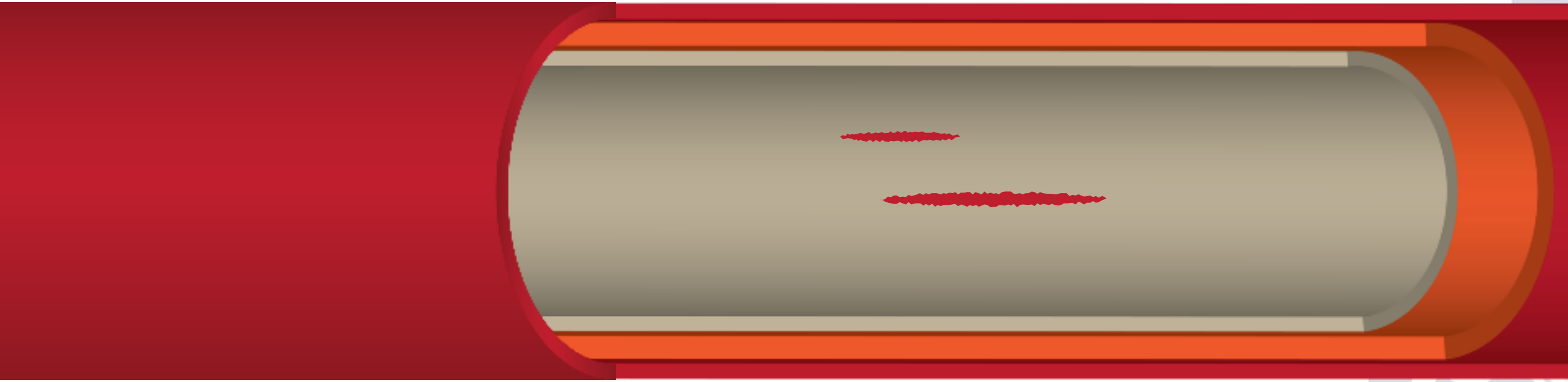


- There is now growing evidence during states of **insulin resistance and inflammation (wt)**
- LDL particle and the arterial wall get coated in "**molecular velcro**" making everything more sticky increasing the progression of atherosclerosis.

- https://academic.oup.com/qjmed/article/96/12/927/1533176
- https://pubmed.ncbi.nlm.nih.gov/14631060/
- https://www.bmj.com/content/368/bmj.m1182/rr-21
- https://pubmed.ncbi.nlm.nih.gov/7729918/
- https://www.sciencedirect.com/science/article/pii/S0022227520333630
- Fat controversy
- https://pubmed.ncbi.nlm.nih.gov/7772105/
- https://pubmed.ncbi.nlm.nih.gov/11259144/
- https://diabetes.diabetesjournals.org/content/50/9/2126
- https://pubmed.ncbi.nlm.nih.gov/18489581/
- https://pubmed.ncbi.nlm.nih.gov/10978261/
- https://link.springer.com/article/10.1007/BF00400234
- https://www.liebertpub.com/doi/10.1089/met.2018.0105

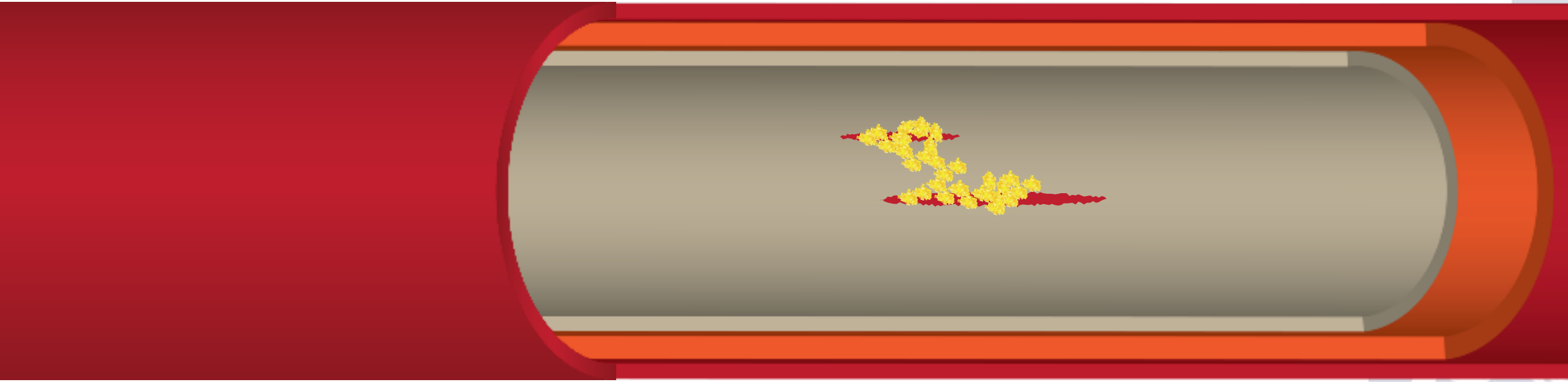
7 SYSTEMS PLAN

Overweight
Insulin Resistance and Inflammation

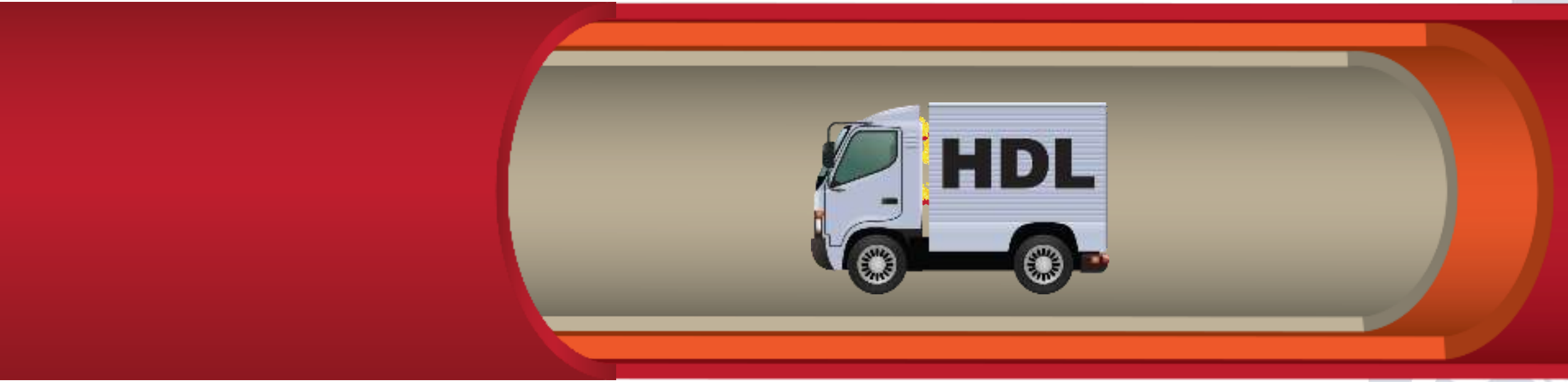


SYSTEMS PLAN

Sticky LDL Deposits Cholesterol in the Injury



HDL Picks up the Cholesterol

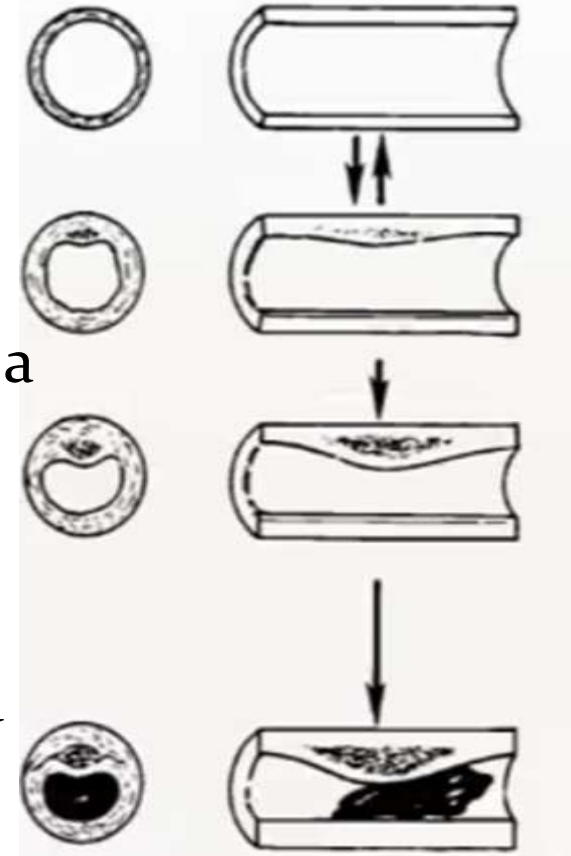


Roy

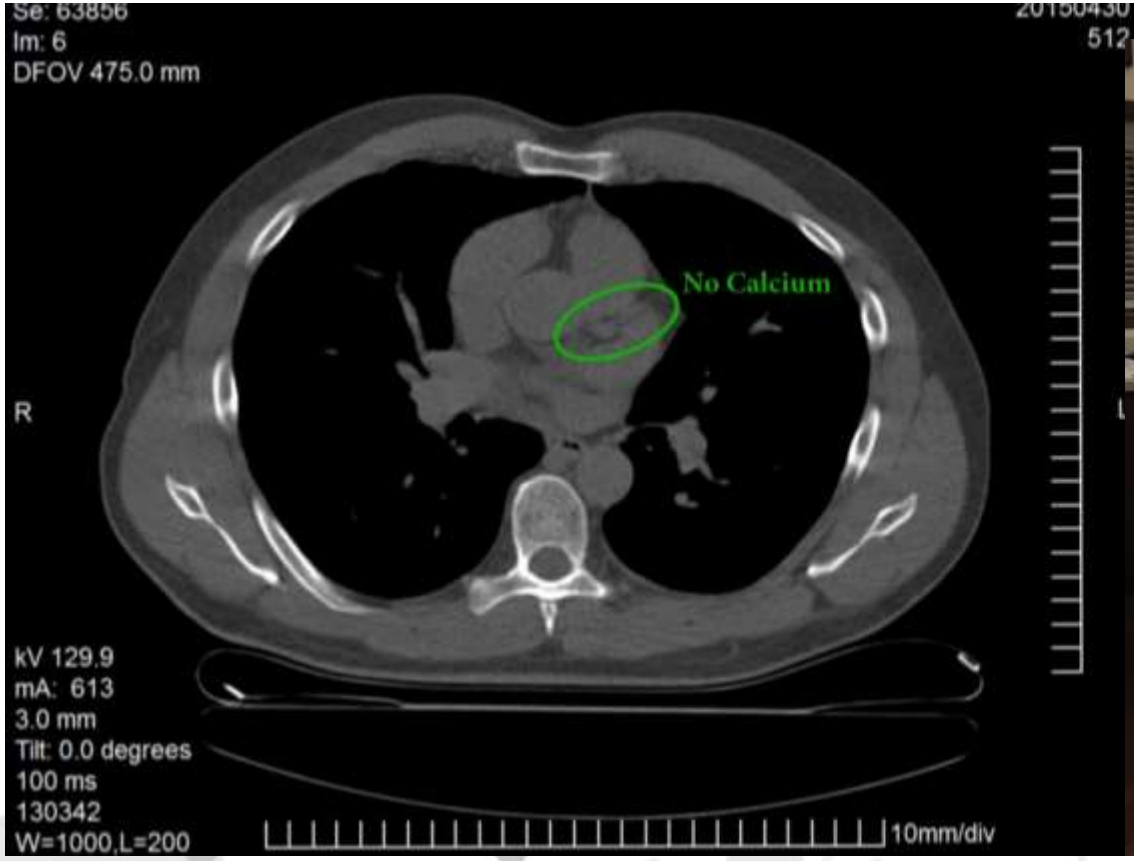
Delivery System

Coronary Artery Calcium (CAC) Score.

- **Zero — No plaque with a low risk of a heart attack.**
- 1-10 — Small amount of plaque and less than 10% chance of heart disease.
- 11-100 — Some plaque with mild heart disease and a moderate risk of a heart attack.
- 101-400 — Moderate amount of plaque that may block a coronary artery, with a moderate to high risk of a heart attack.
- **400+ — Large amount of calcified plaque** is found in the coronary arteries with more than a **90% chance it is blocking an artery**.



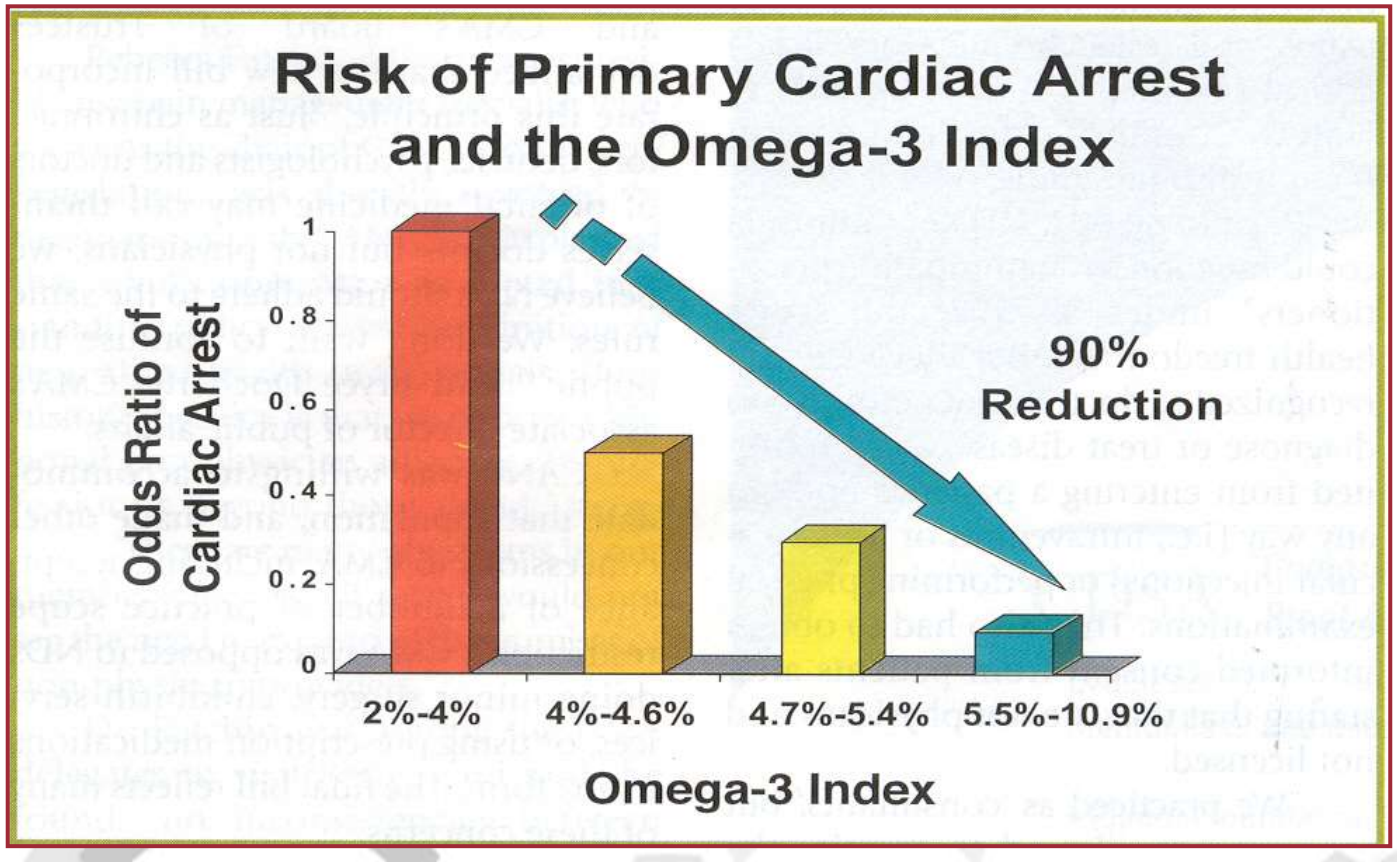
My Heart



High Risk Patient

SYSTEMS PLAN

Omega-3s Reduce the Risk of Heart Attacks by up to 90%



Adapted from Siscovich et al. *JAMA*. 1995;274:1363-1367.

SYSTEMS PLAN

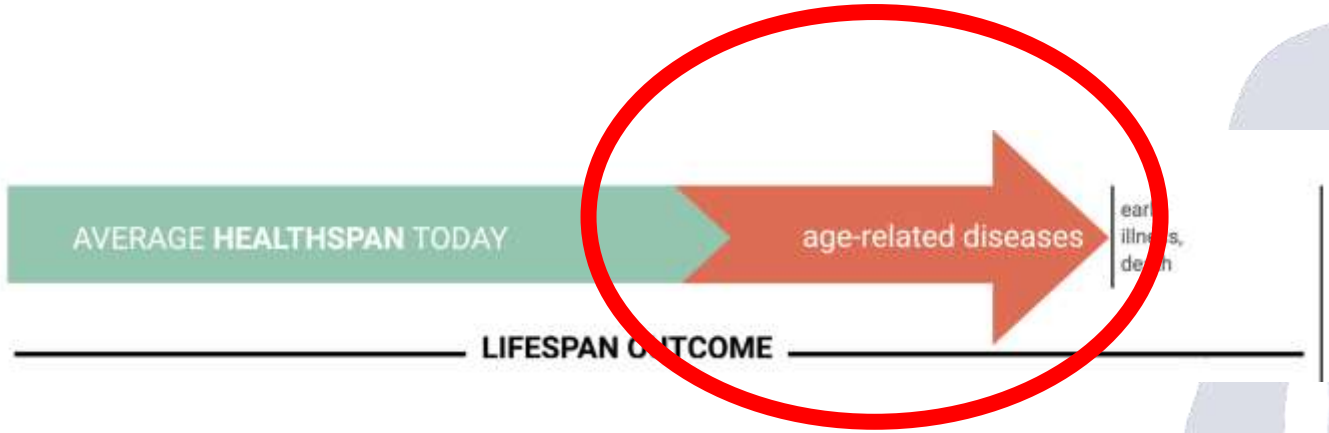
Help Your Patients

- Maintain a healthy diet
- Lose **weight**
- Decrease **inflammation**
- Improve **insulin sensitivity**
- Take supplements
- Test: Franks Sign, pulse (65)

7 SYSTEMS PLAN

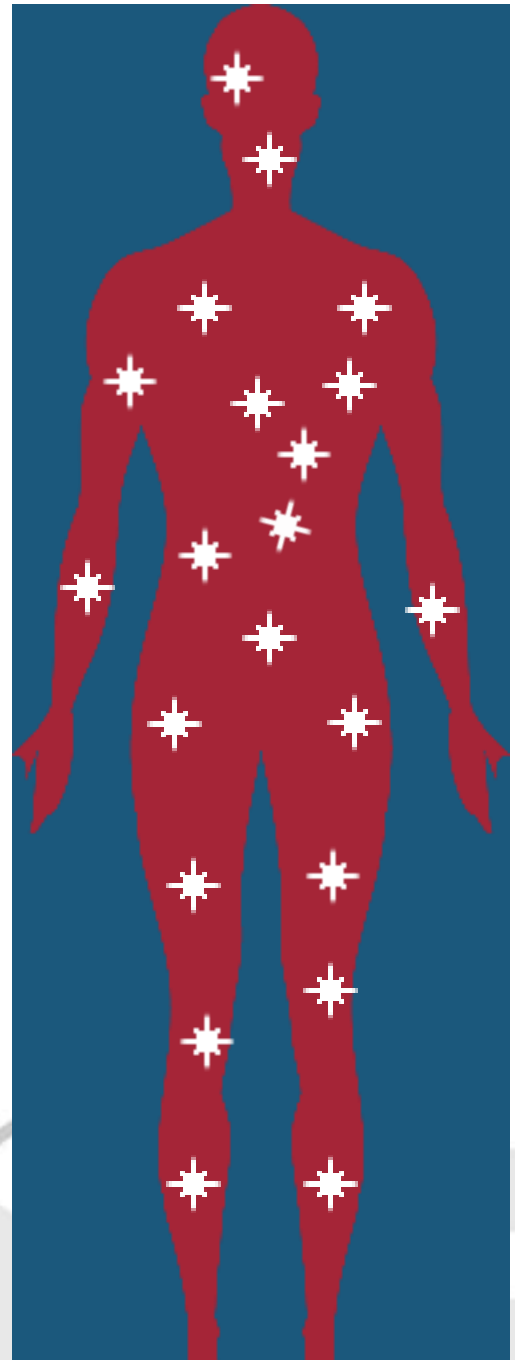
Leading Causes of Death

1. Heart disease
2. Cancer
3. Unintentional injuries
4. Chronic lower respiratory disease
5. Stroke and cerebrovascular diseases
6. Alzheimer's disease
7. Diabetes
8. Influenza and pneumonia
9. Kidney disease
10. Suicide



SYSTEMS PLAN

Energy System



1 Mitochondria

By Age 50 You May Have Lost ½ Your Mitochondria

PLoS One. 2014 Dec 22;9(12):e115433. doi: 10.1371/journal.pone.0115433. eCollection 2014.

Age-related mitochondrial DNA depletion and the impact on pancreatic Beta cell function.

Nile DL[1], Brown AE[1], Kumaheri MA[1], Blair HR[1], Heggie A[1], Miwa S[2], Cree LM[3], Payne B[4], Chinnery PF[4], Brown L[5], Gunn DA[5], Walker M[1].

Author information

Open/close author information list

Abstract

Type 2 diabetes is characterised by an age-related decline in insulin secretion. We previously identified a 50% age-related decline in mitochondrial DNA (mtDNA) copy number in isolated human islets. The purpose of this study was to mimic this degree of mtDNA depletion in MIN6 cells to determine whether there is a direct impact on insulin secretion. Transcriptional silencing of mitochondrial transcription factor A, TFAM, decreased mtDNA levels by 40% in MIN6 cells. This level of mtDNA depletion significantly decreased mtDNA gene transcription and translation, resulting in reduced mitochondrial respiratory capacity and ATP production. Glucose-stimulated insulin secretion was impaired following partial mtDNA depletion, but was normalised following treatment with glibenclamide. This confirms that the deficit in the insulin secretory pathway precedes K+ channel closure, indicating that the impact of mtDNA depletion is at the level of mitochondrial respiration. In conclusion, partial mtDNA depletion to a degree comparable to that seen in aged human islets impaired mitochondrial function and directly decreased insulin secretion. Using our model of partial mtDNA depletion following targeted gene silencing of TFAM, we have managed to mimic the degree of mtDNA depletion observed in aged human islets, and have shown how this correlates with impaired insulin secretion. We therefore predict that the age-related mtDNA depletion in human islets is not simply a biomarker of the aging process, but will contribute to the age-related risk of type 2 diabetes.

PMID: 25532126 PMCID: PMC4274008 DOI: 10.1371/journal.pone.0115433

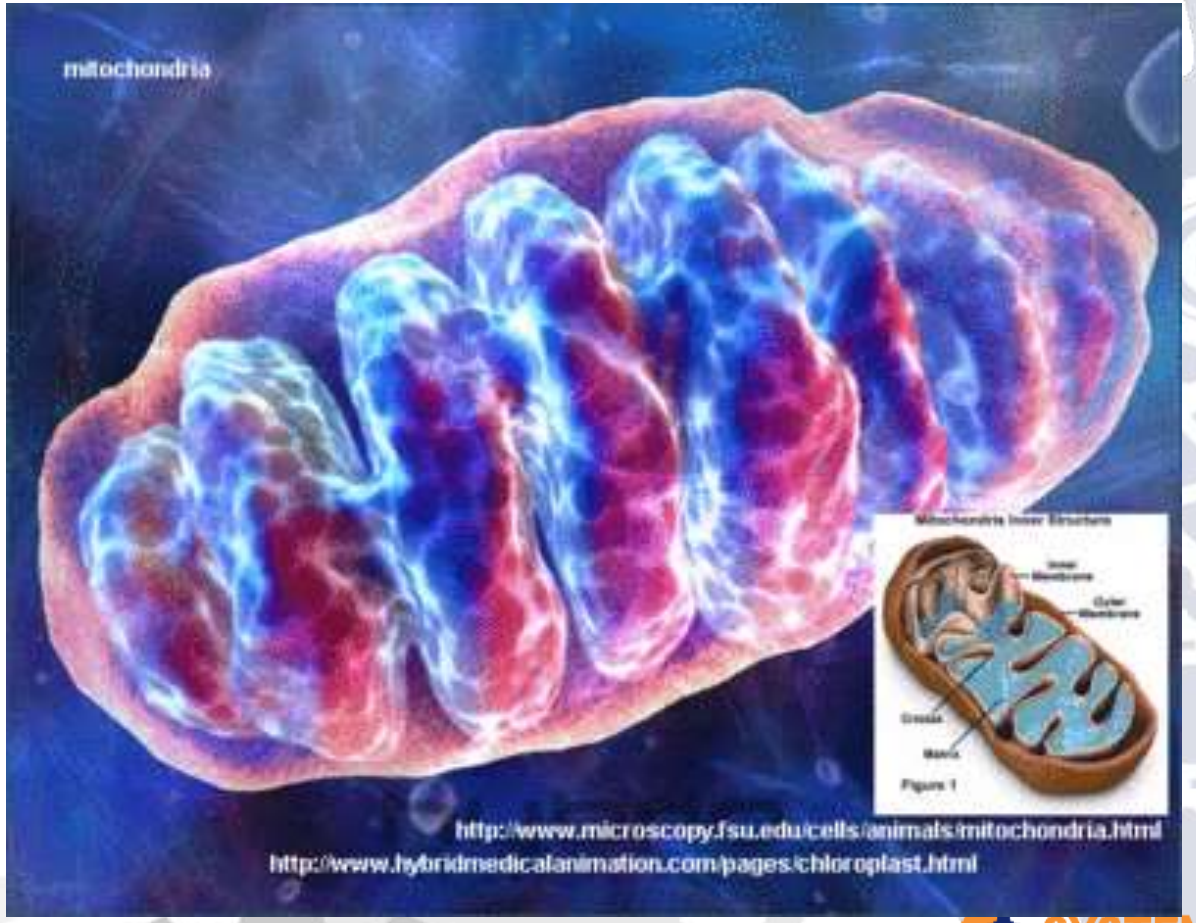
[Indexed for MEDLINE] **Free PMC Article**

SYSTEMS PLAN

Mitochondria- More than Just Energy

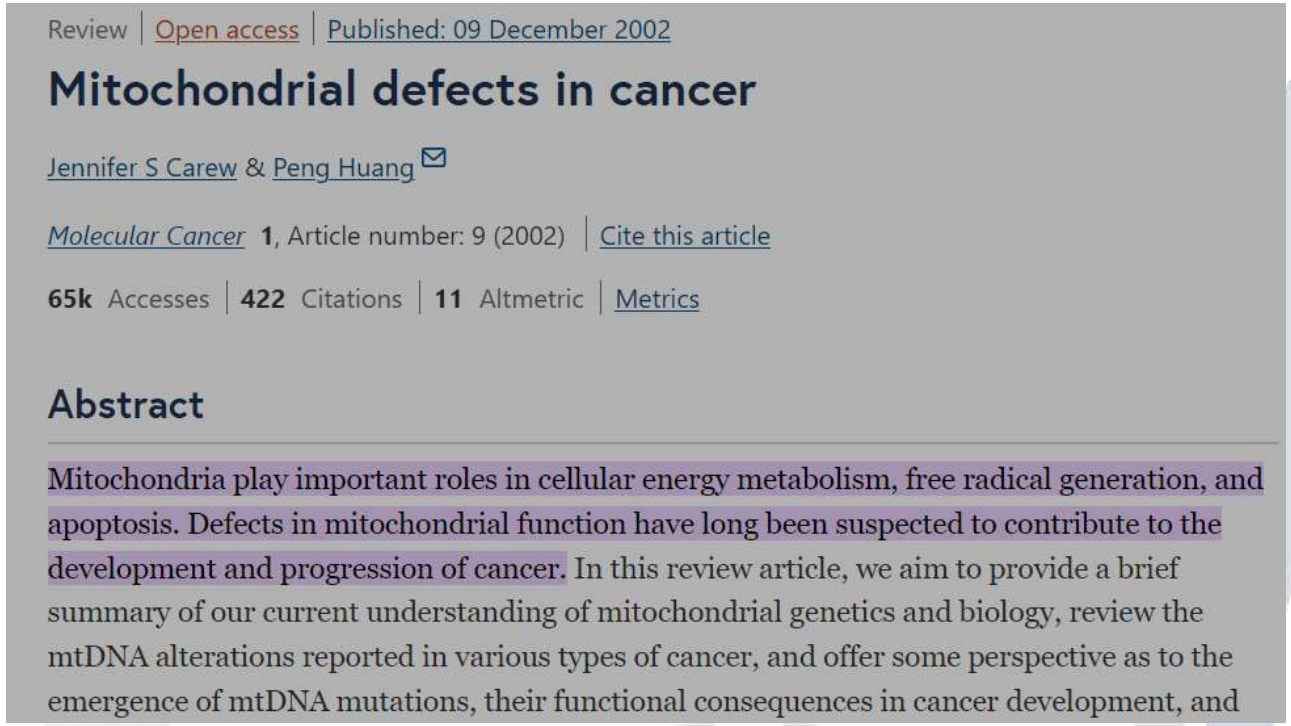
Cellular

- Energy production
- Nutrient intake
- Toxin elimination
- Repair
- **Handle problems**



Mitochondrial and Cancer

Defects in mitochondria function have long been suspected to contribute to the development and progression of cancer



Review | Open access | Published: 09 December 2002

Mitochondrial defects in cancer

Jennifer S Carew & Peng Huang

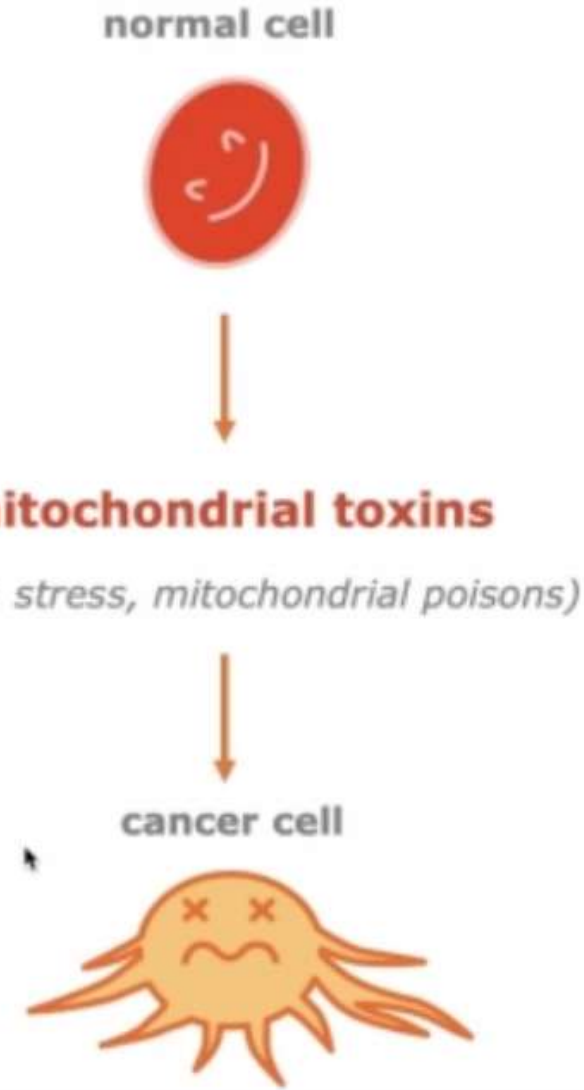
Molecular Cancer **1**, Article number: 9 (2002) | Cite this article

65k Accesses | **422** Citations | **11** Altmetric | Metrics

Abstract

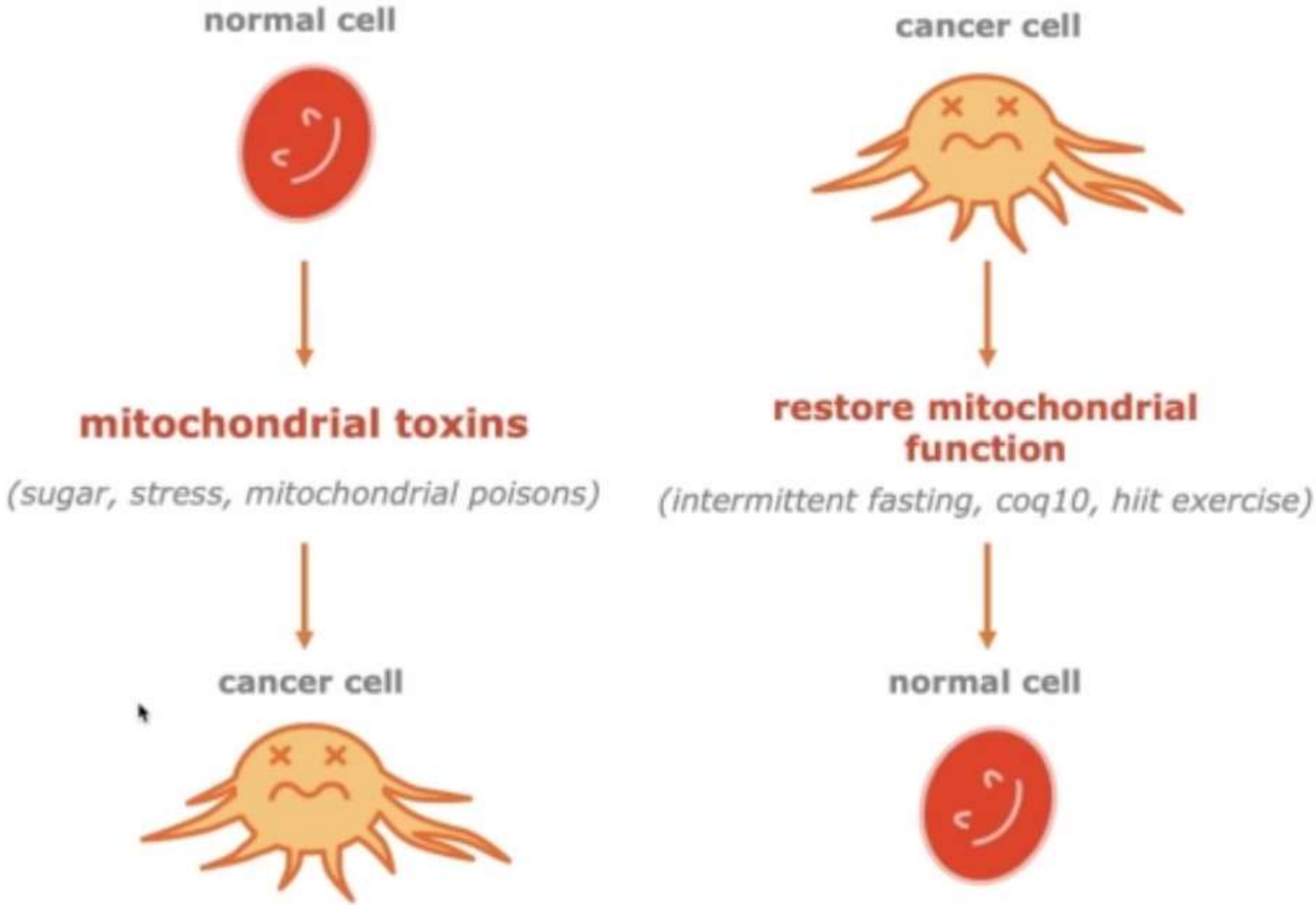
Mitochondria play important roles in cellular energy metabolism, free radical generation, and apoptosis. Defects in mitochondrial function have long been suspected to contribute to the development and progression of cancer. In this review article, we aim to provide a brief summary of our current understanding of mitochondrial genetics and biology, review the mtDNA alterations reported in various types of cancer, and offer some perspective as to the emergence of mtDNA mutations, their functional consequences in cancer development, and

cancer stem cells



SYSTEMS PLAN

cancer stem cells



SYSTEMS PLAN

Vitamin to Decrease Cancer Risk

- 83% lower risk of breast cancer
  - European Journal of Cancer 2005 May;41(8):1164-9
- 55% lower colorectal cancer
  - Cancer Prev Res (Phila). 2015 Aug;8(8):675-82
- 67% less cancer in general at levels >40
  - PLOS ONE 2016; 11 (4): e0152441
  - PR Web April 6, 2016
  - UC San Diego Health April 6, 2016
  - Science World Report April 13, 2016
  - Oncology Nurse Advisor April 22, 2016
  - Tech Times April 11, 2016
  - Chrisbeatcancer.com, Vitamin D
  - •https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5510119/

7 SYSTEMS PLAN

Disease Incidence Prevention by Serum 25(OH)D Level

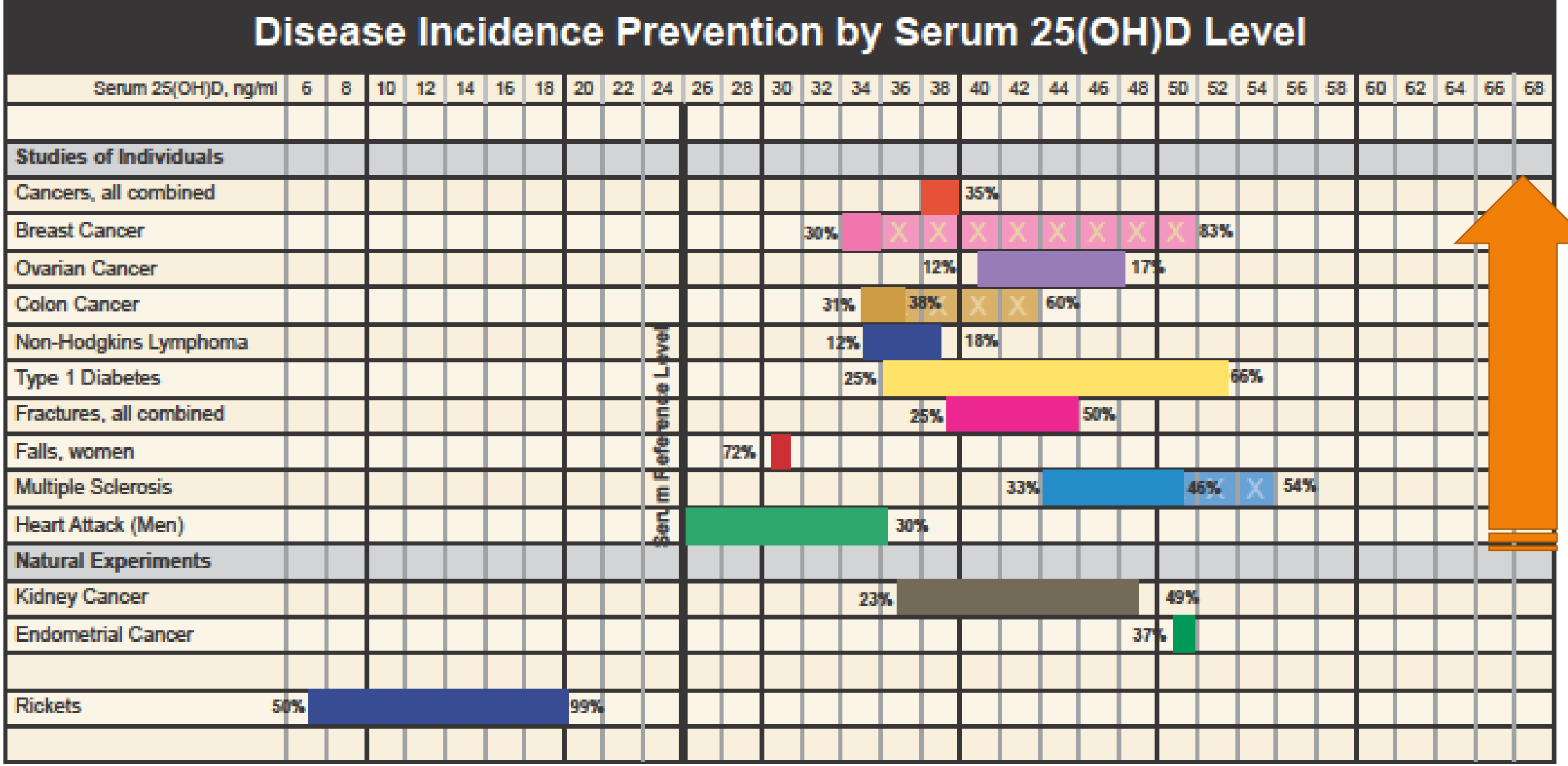


Chart prepared by: Garland CF, Baggerly CA

Legend:
All percentages reference a common baseline of 25 ng/ml as shown on the chart.
%'s reflect the disease prevention % at the beginning and ending of available data. Example: Breast cancer incidence is reduced by 30% when the serum level is 34 ng/ml vs the baseline of 25 ng/ml. There is an 83% reduction in incidence when the serum level is 50 ng/ml vs the baseline of 25 ng/ml.
The x's in the bars indicate 'reasonable extrapolations' from the data but are beyond existing data.

References:
All Cancers: Lappe JM, et al. Am J Clin Nutr. 2007;85:1586-91. Breast: Garland CF, Gorham ED, Mohr SB, Grant WB, Garland FC. Breast cancer risk according

Alice
Energy System

600% More Energy

7 SYSTEMS PLAN

Help Your Patients

- Double their mitochondria (exercise)
- Maintain mitochondrial health
- Take vitamin D3 with K2
- Test: grip strength, D test

7 SYSTEMS PLAN

Study BMJ

- This study has shown that grip strength is strongly and inversely associated with:
  - all cause mortality
  - mortality from cardiovascular disease
  - respiratory disease
  - chronic obstructive pulmonary disease
  - **all cancer**, and subtypes of cancer, including colorectal, lung, and breast cancer, with associations being modestly stronger in the younger age groups.

Leading Causes of Death

1. Heart disease
2. Cancer
3. Unintentional injuries
4. Chronic lower respiratory disease
5. Stroke and cerebrovascular diseases
6. Alzheimer's disease
7. Diabetes
8. Influenza and pneumonia
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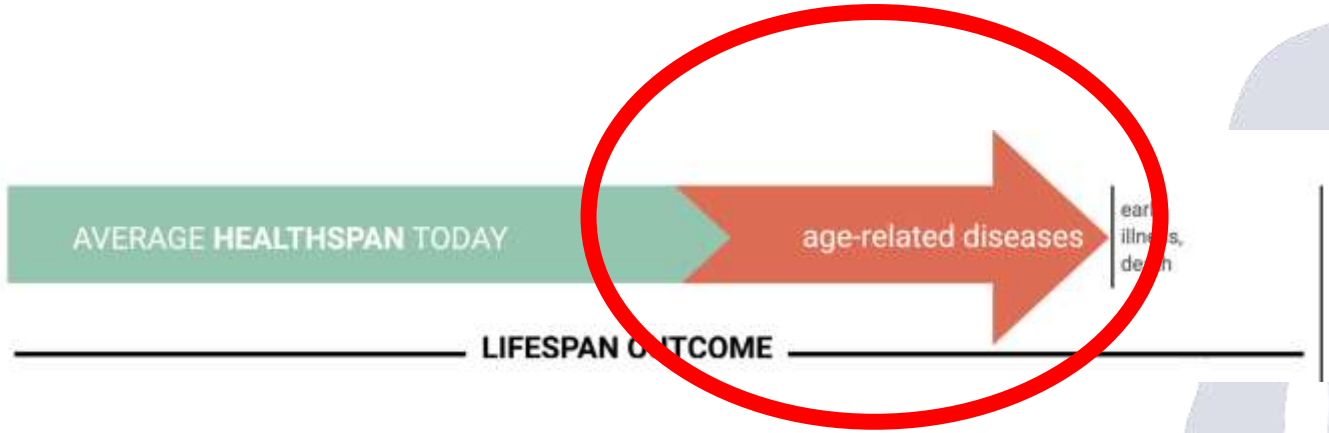
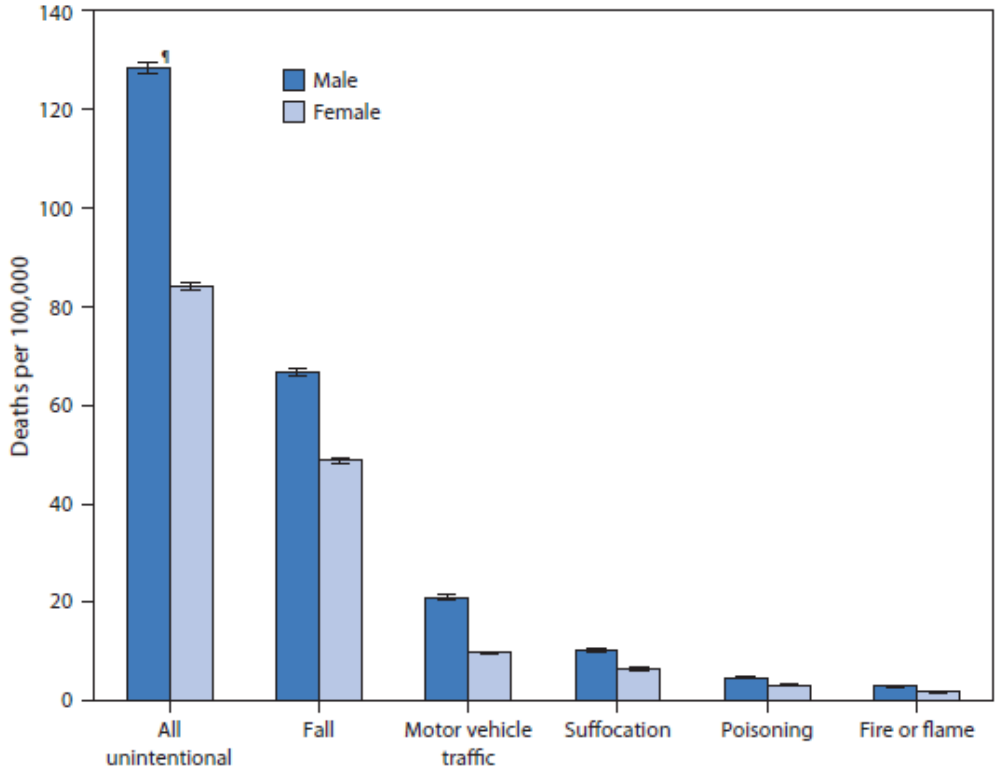


SYSTEMS PLAN

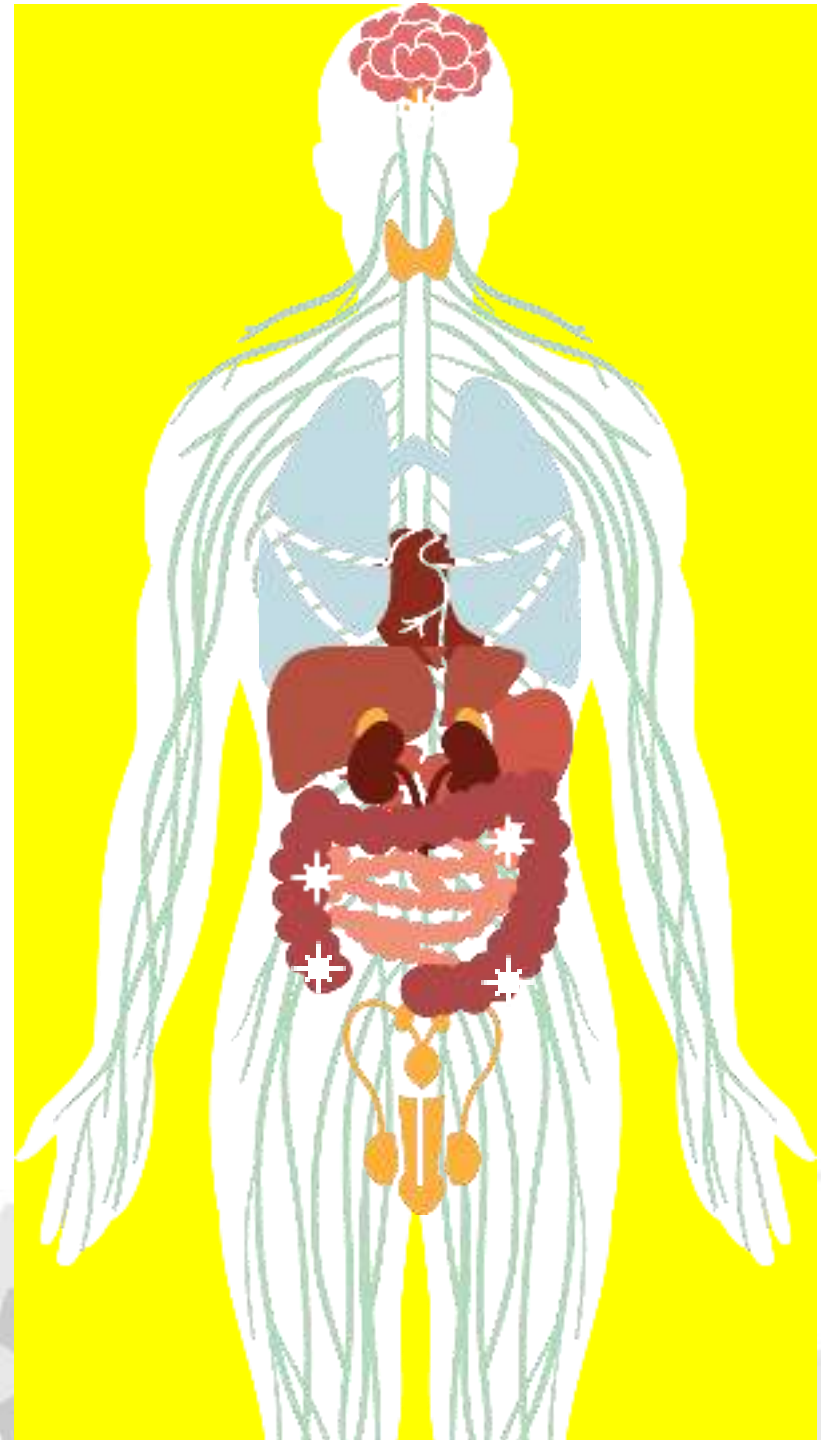
Who Has the Most Unintentional Injuries?

Who has the Most Unintentional Injuries?

- Males accounted for 67% of the 224,935 preventable injury-related deaths in 2021.



Communication System



1. Hormones
2. Nerves
3. **Neurotransmitters**

Neurotransmitters

Dopamine

Reward

Positive Affect

Extraversion

Wacker J. Psychophysiology. 2017 Mar 17. doi: 10.1111/psyp.12727.

SYSTEMS PLAN

Help Your Patients

- Not be too stupid

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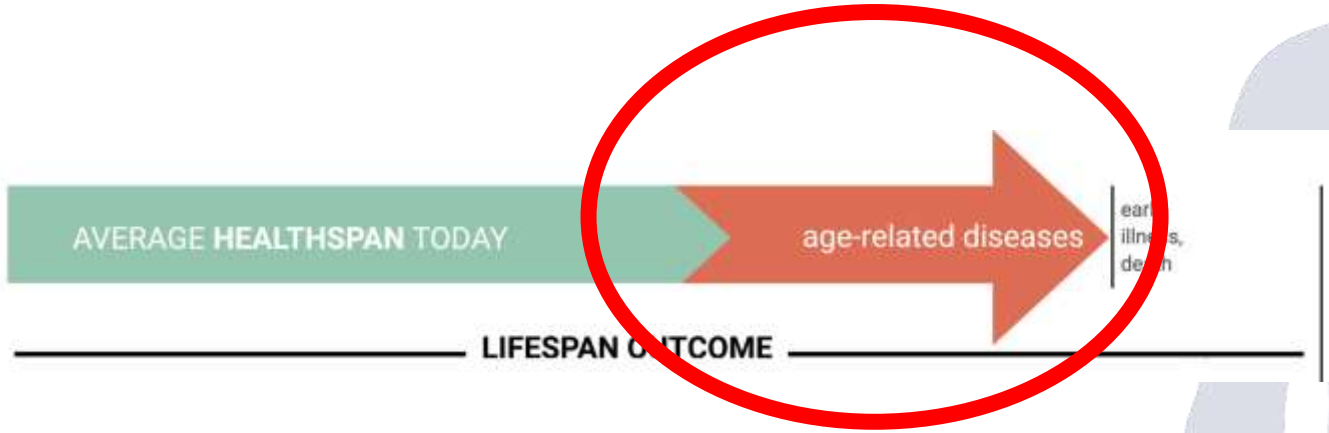
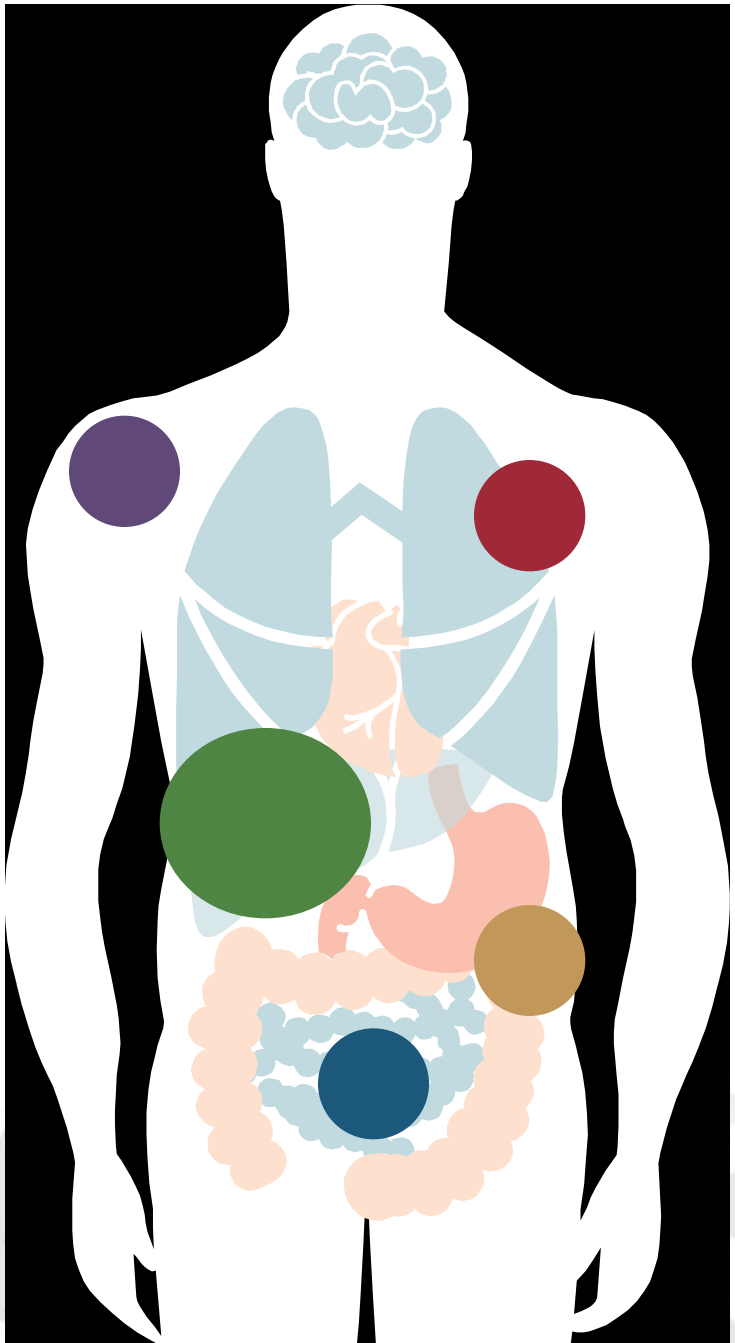


SYSTEMS PLAN

DETOX SYSTEMS



1. Kidneys
2. Skin
3. Liver
4. Colon
5. **Lungs**

7 SYSTEMS PLAN

Chronic Respiratory Diseases (CRDs)

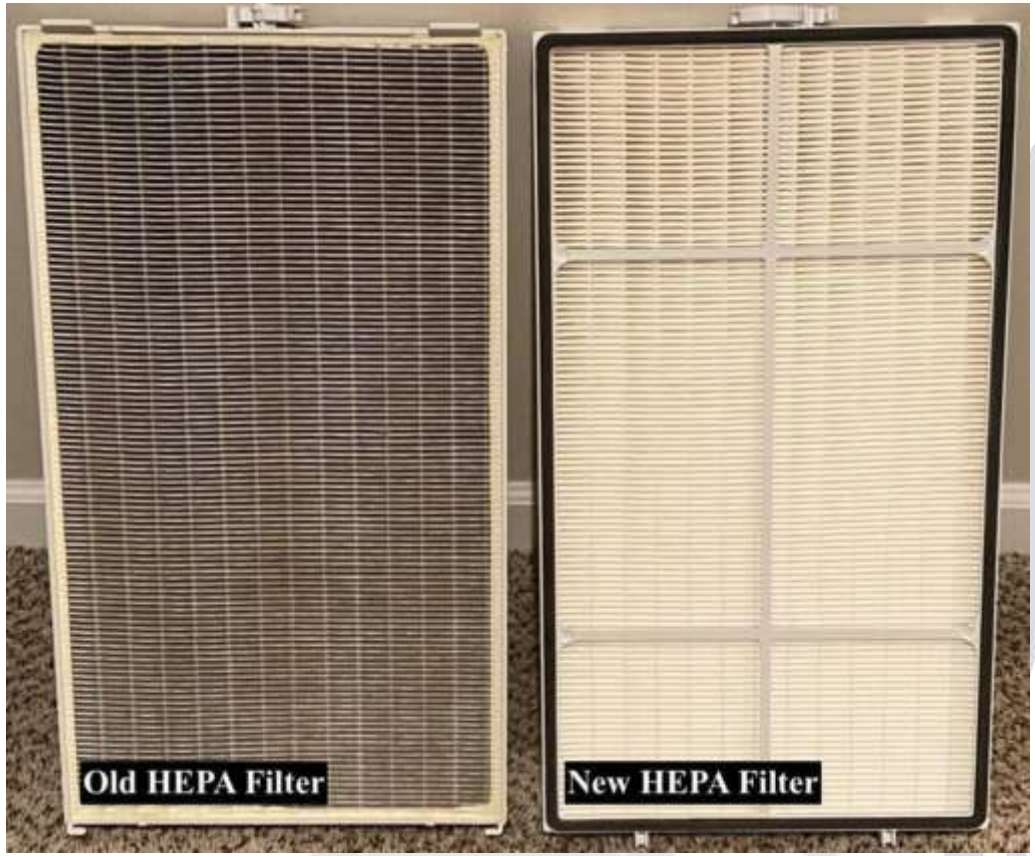
- Some of the most common are:
  - chronic obstructive pulmonary disease (COPD)
  - asthma
  - occupational lung diseases
  - pulmonary hypertension
- Risk factors:
  - tobacco smoke
  - **air pollution**
  - occupational chemical
  - **dusts**
  - and frequent lower respiratory infections during childhood
  - **Low vitamin D**

Study by Queen Mary University of London

- Data from 10,933 participants
- Upping your vitamin D can decrease respiratory infections up to 50%

Indoor Air

- According to the EPA, the levels of indoor air pollutants are often **2 to 5 times higher** than outdoor levels, and in some cases these levels can **exceed 100 times** that of outdoor levels of the same pollutants.



Help Your Patients

- Have good indoor air quality
- Not smoke
- Increase vitamin D
- Keep the Detox System working correctly
- Test: breaths/minute

7 SYSTEMS PLAN

Leading Causes of Death

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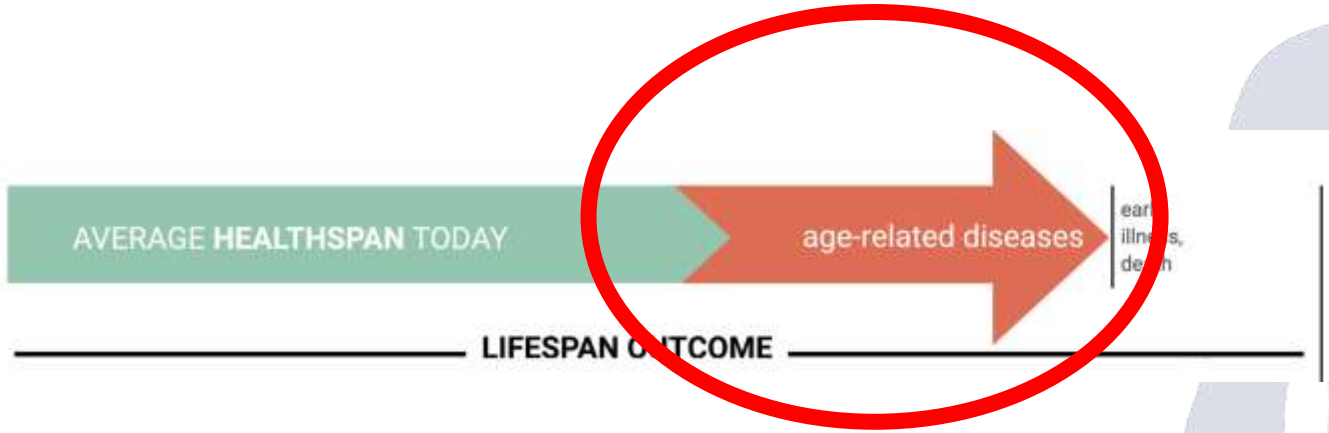
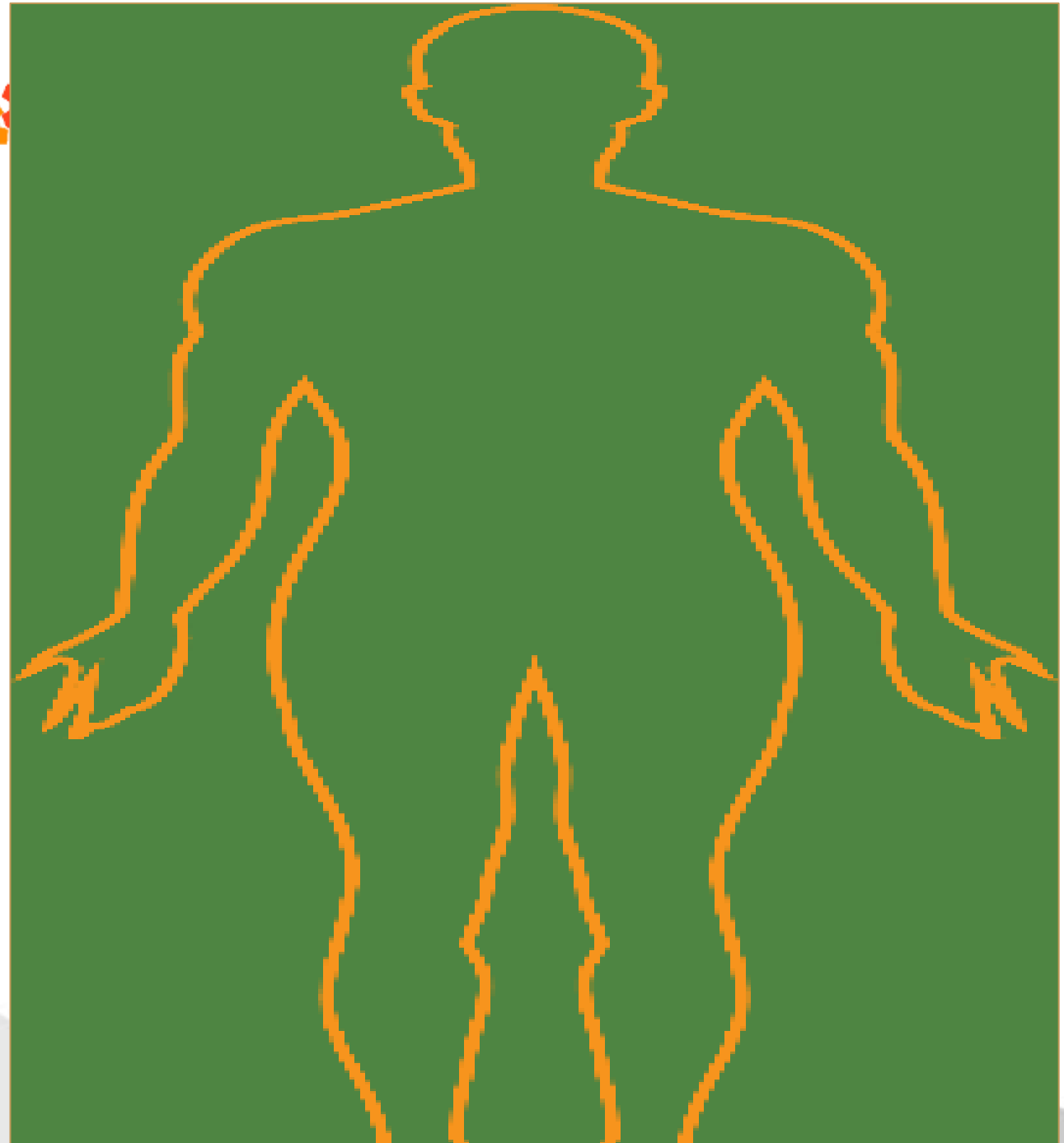


SYSTEMS PLAN



STRUCTURAL SYSTEM

1. Bone
2. Muscle
3. Fat

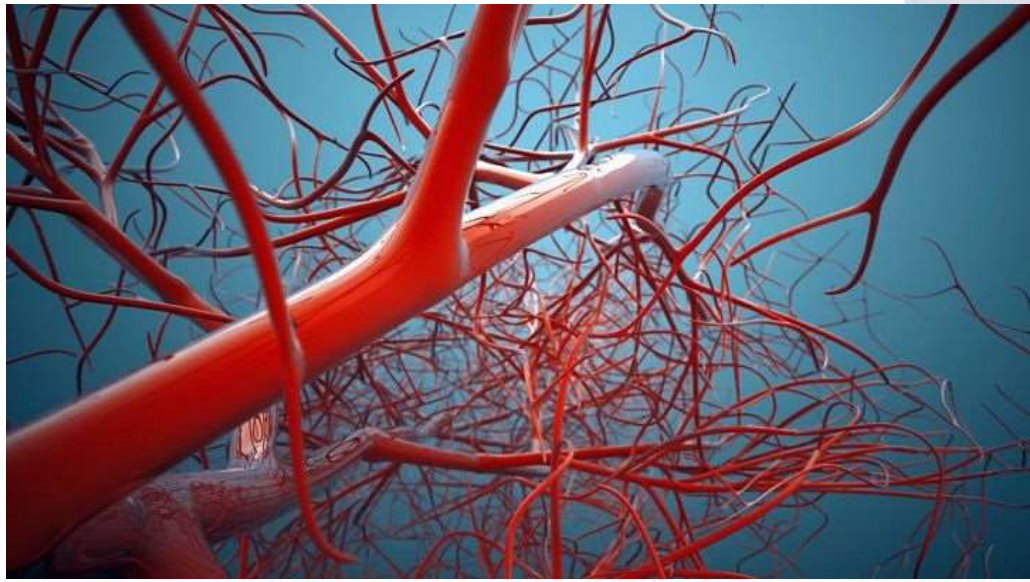
Does Excess Body Fat Increase BP?

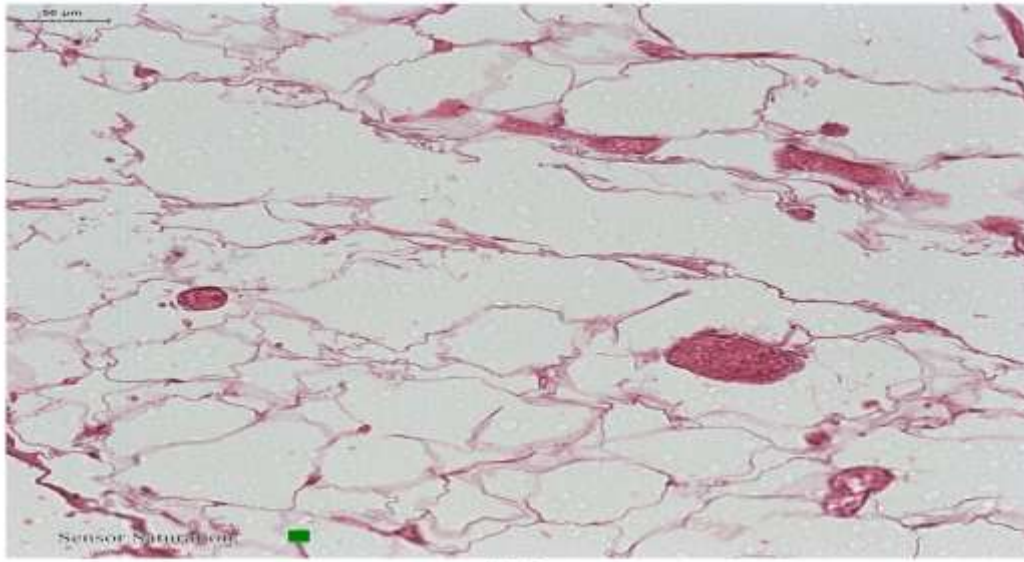
- Obesity accounts for 65-78% of cases of primary hypertension
- BMI 29 = 200-600% greater prevalence of hypertension
- **Lose 5 pounds** lowers BP
- **Lose 20 pounds** → decrease BP 10 points

SYSTEMS PLAN

Extra Fat Makes the Heart Work Harder

- Every pound of extra weight adds **5 miles** of blood vessels.
- 50 pounds of weight gain = **250 miles** of additional blood vessels.





Mayo Clinic, Dr. Kopecky

SYSTEMS PLAN

Kevin

SYSTEMS
PLAN

Dustin and Sara

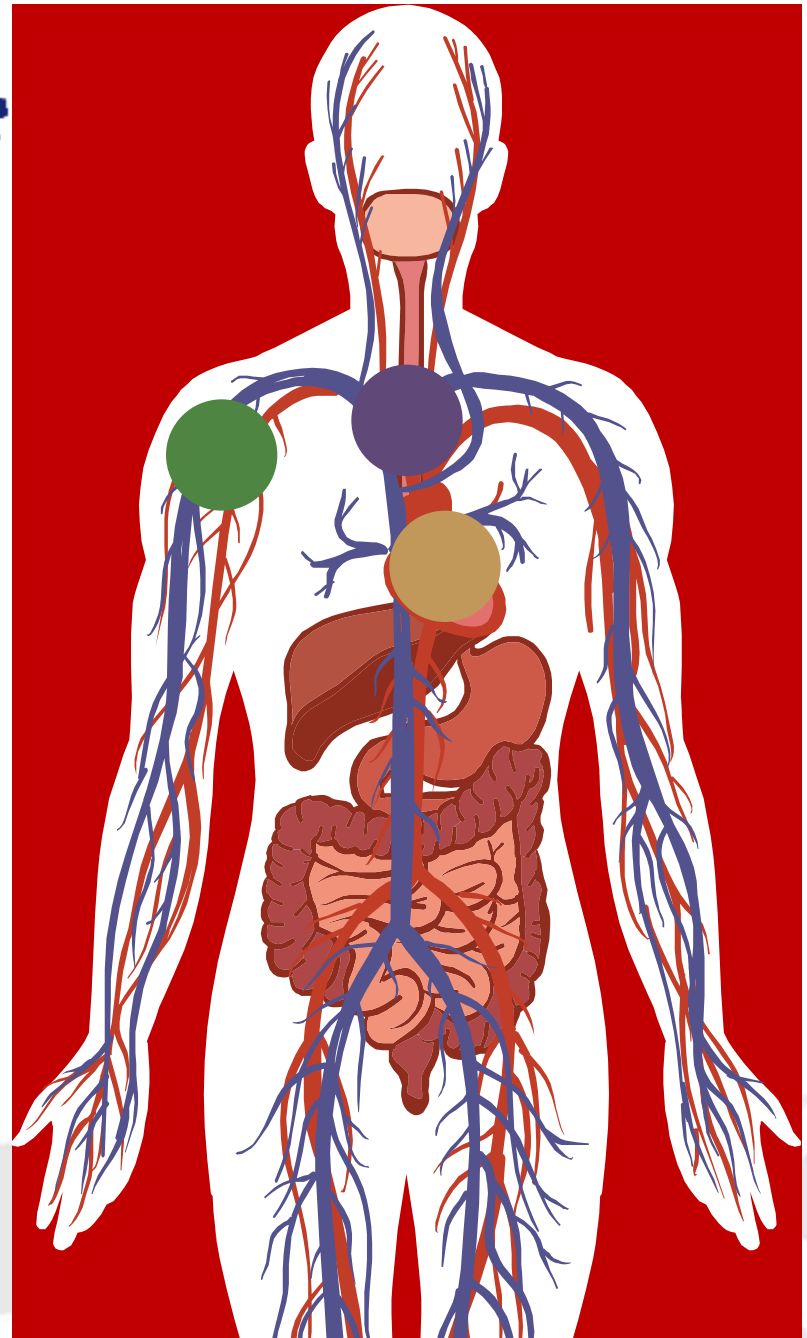
Denny- High Blood Pressure Gone

Average Reduction in Blood Pressure with Medications:

- 1. Beta Blockers - 10 mmHg (SBP)/-8 mmHg DBP)
- 2. Ace Inhibitors - 8mmHg (SBP)/-5 mmHg (DBP)
- 3. Calcium Channel Blocker - 9.45 mmHg (SBP)
- 4. Angiotensin Receptor Blockers - 8mmHg (SBP)/-5 mmHg (DBP)
- 5. Diuretics - 7.9 mmHg (SBP)/ -4.4 mmHg (DBP)
- Two tablespoons of **flaxseed** per day - 15 mmHg in SBP - 7 mmHg DBP
- American Heart Association Journal, Hypertension

7 SYSTEMS PLAN

DELIVERY SYSTEM

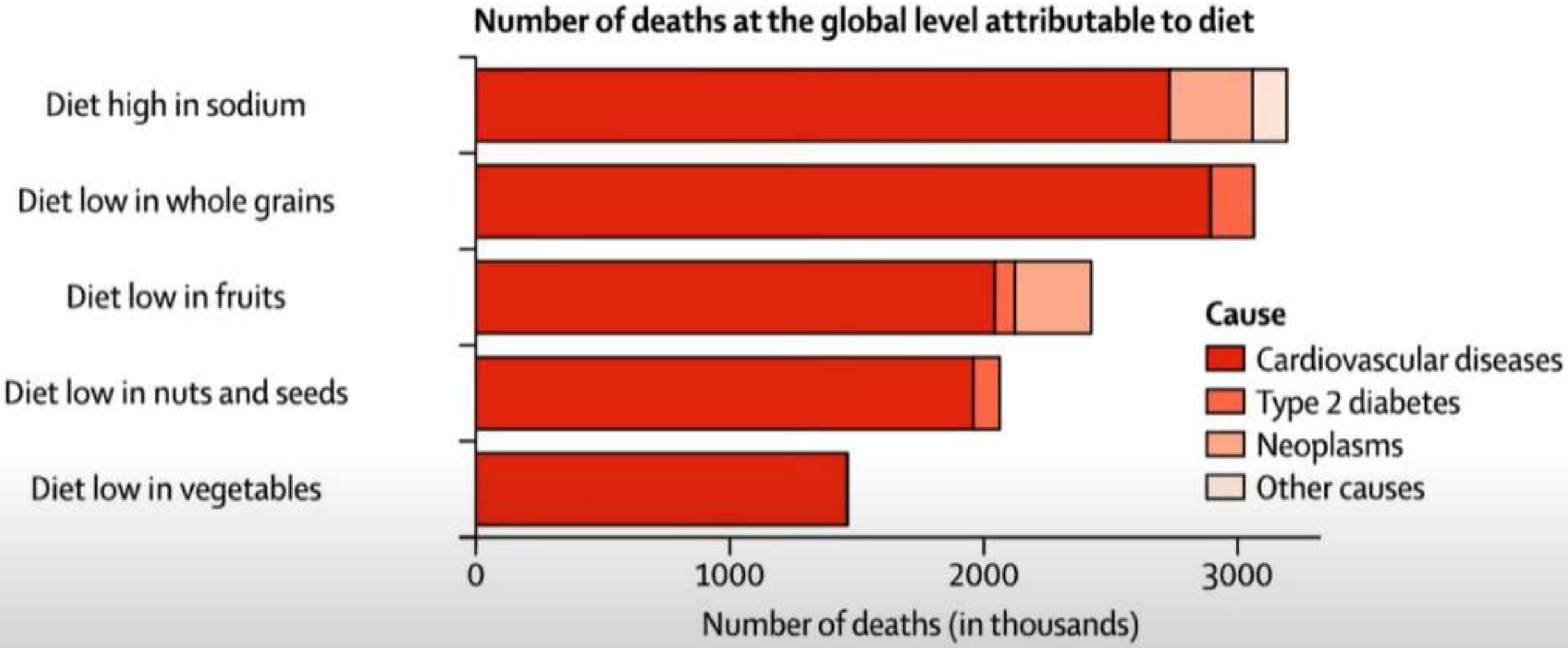


1. Heart
2. Blood vessels
3. Nutrient Transport-
   LDL, VLDL, Albumin…

Processed Foods Strongly Linked to 32 Poor Health Outcomes

- 50% elevated risk of **cardiovascular**-related mortality
- 48% increased risk of anxiety and other **mental illnesses**
- 12% higher likelihood of developing **type 2 diabetes**
- 40-60% augmented risk of obesity and **sleep** disturbances
- 21% higher risk of **all-cause mortality**.

Diet and Deaths



Fast-Food

A single fast-food entree has nearly half of an entire day's allowance of salt.

ESC
European Society of Cardiology

European Heart Journal (2022) **00**, 1–12
https://doi.org/10.1093/eurheartj/ehac208

CLINICAL RESEARCH
Epidemiology and prevention

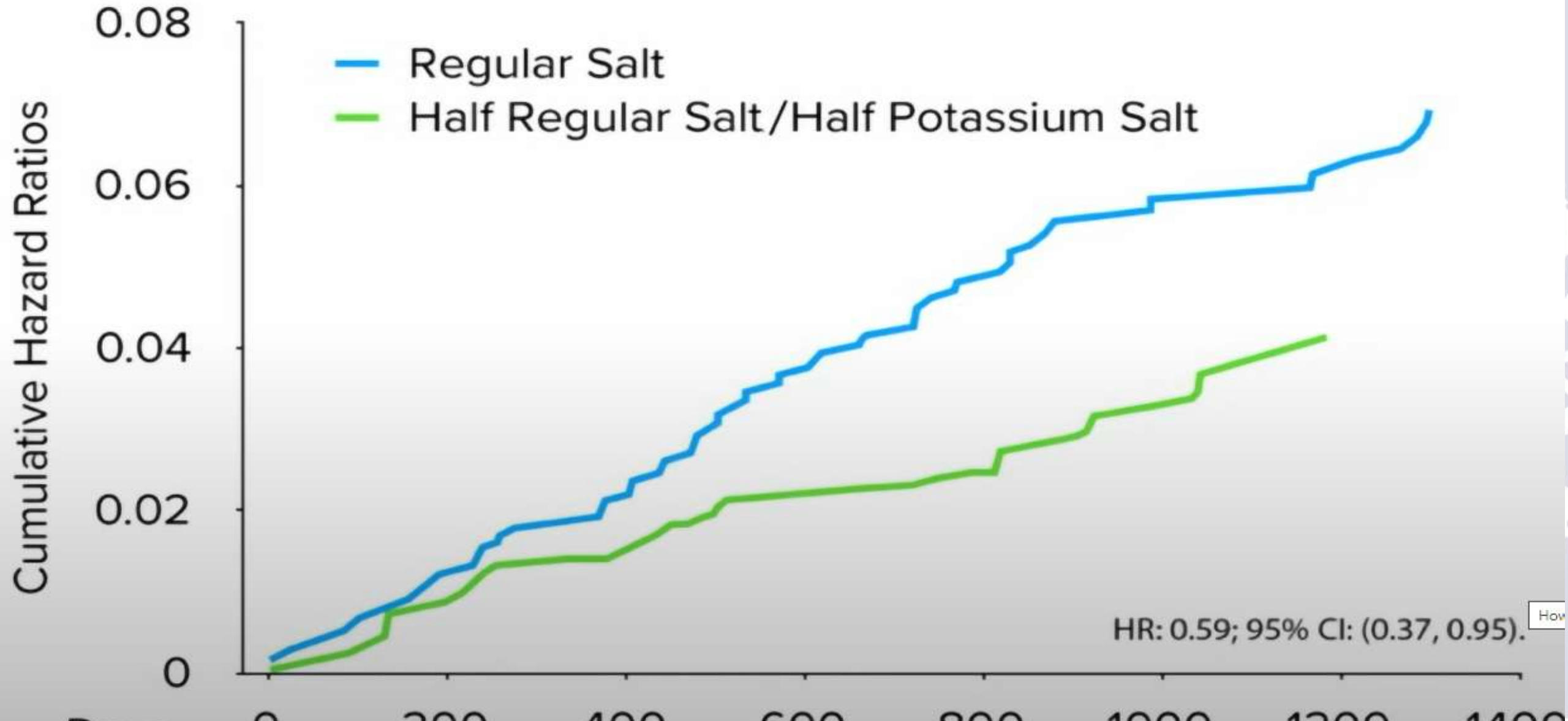
Adding salt to foods and hazard of premature mortality

Hao Ma[1], Qiaochu Xue[1], Xuan Wang[1], Xiang Li[1], Oscar H. Franco[2], Yanping Li [3], Yoriko Heianza[1], JoAnn E. Manson [3,4,5], and Lu Qi [1,6]*

premature mortality, which were more pronounced in participants with low intakes than those with high intakes of these foods (*P*-interaction = 0.02). In addition, compared with the never/rarely group, always adding salt to foods was related to 1.50 (95% CI, 0.72–2.30) and 2.28 (95% CI, 1.66–2.90) years lower life expectancy at the age of 50 years in women and men, respectively.

Received 14 September 2021; revised 11 March 2022; accepted 7 April 2022

Cumulative Hazard Ratios of Cardiovascular Diseas
Related Deaths for the Treatment and Control Grou



Recommended Food List

Foods listed in green are recommended. You want to **avoid** the foods listed in **red**.

FOODS TO EAT

Vegetables Low GI	Vegetables Medium GI	Fruit	Oils	Concentrated Proteins	Nuts & Seeds	**Legumes	Grains	Dairy	Beverages	Functional Foods
Cruciferous: broccoli, brussels sprouts, cabbages, cauliflower **Greens:** beet greens, bok choy, collard greens, escarole, kale, mustard greens, Swiss chard, watercress, spinach **Lettuce/Mixed greens** **Mushrooms** **Salsa** (sugar-free) **Sprouts:** alfalfa, broccoli or radish sprouts, bamboo shoots, etc. Squash: spaghetti, summer, yellow, zucchini **Other vegetables:** artichokes, asparagus, organic celery, chives, cucumbers, dill pickles, eggplants, garlic, green beans, hot peppers, kelp, leeks, mixed vegetable juices, okra, onions, organic sweet bell peppers, radishes, snow peas, organic tomatoes, water chestnuts	Beets Carrots Pumpkins Rutabagas Sweet potatoes or yams Turnips Winter squash Organic Yukon Gold Potatoes	**Berries:** blackberries, blueberries, raspberries, and organic strawberries Organic apples Apricots Cantaloupe Organic cherries Clementine Fresh Figs Organic grapes Honeydew melon Kiwifruits Mango Organic nectarines Oranges Organic peaches Organic pears Plums Tangerines Watermelon	**Best:** Avocados and Guacamole Olives **Good:** Extra virgin coconut oil Cold-pressed extra virgin olive oil Flaxseed oil Walnut oil Avocado oil Mayonnaise (made with avocado oil)	**Best:** Low-GI vegetables Tofu Tempeh Soy or veggie burger (read ingredients) Fish (wild caught) Beef (grass-fed) Lamb (grass-fed) Chicken (free-range) **Good:** Beef-lean Eggs (free -range) Cottage cheese Ricotta Mozzarella Parmesan	**Nuts:** Walnut Almonds Brazil nuts Macadamia Pecan Pistachios Hazelnuts **Seeds:** Sunflower Pumpkin Sesame seeds **Nut butter:** Almond butter **Not as good:** Peanuts Cashews Peanut butter (no sugar)	**Beans:** black, butter, cannellini, garbanzo, chickpeas, great northern, pinto, kidney, lima, navy, mung, fat free refried, green soy **Hummus** **Bean Soup** **Lentils:** beluga, French, and red variety **Peas:** split green or yellow peas	Amaranth, teff, or quinoa Rice Barley, buckwheat groats, millet Bulgar Popcorn Whole oats Whole wheat, spelt, or kamut berries **Pasta:** 100% whole wheat, spelt, kamut, or black bean **Crackers** **Breads:** mixed whole-grain or 100% whole-rye **Tortilla or Pita:** whole-wheat or low-carb	Butter or ghee Buttermilk Yogurt (plain) **Dairy Substitutes:** Almond milk (no sugar) Hemp milk (no sugar) Coconut milk (no sugar)	Water Coffee Herbal or Green teas Sparkling or Mineral water	Dynamic Daily Meal Dynamic GI Restore Dynamic Cardio-Metabolic Dynamic Inflam-Eze Dynamic GI Integrity Dynamic Detox

**FOODS TO BE CAREFUL WITH

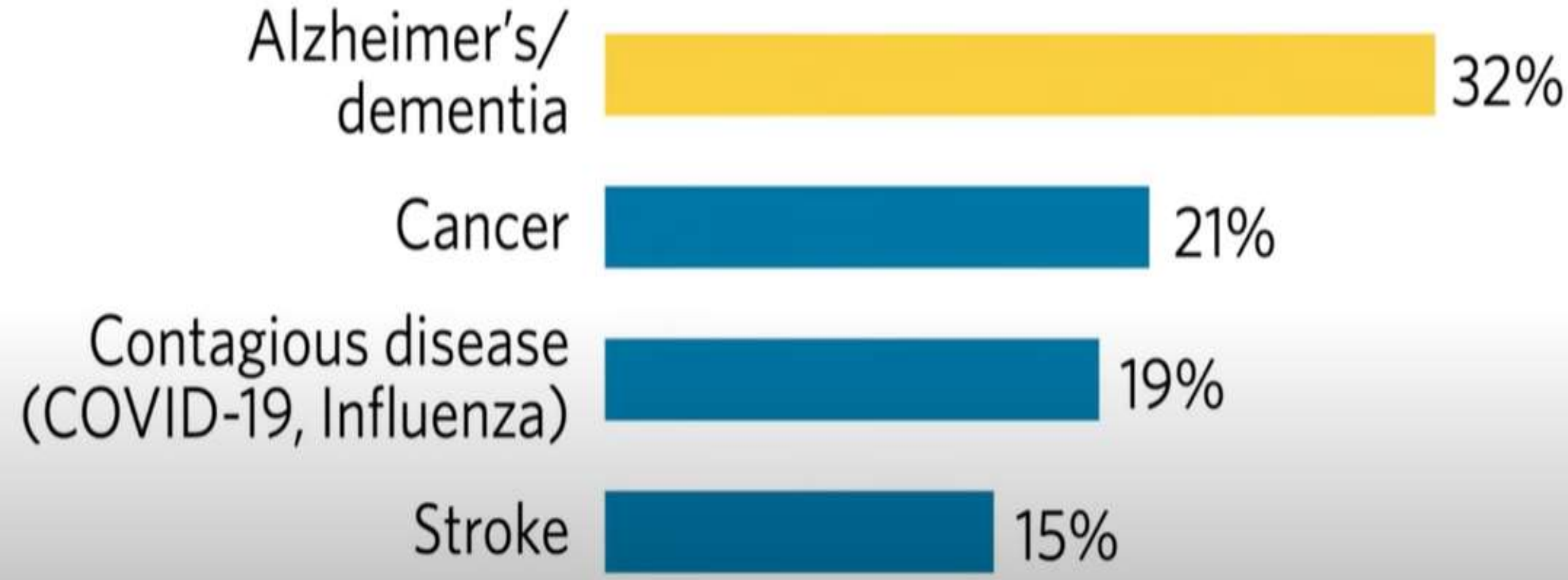
		Bananas Dried fruit Fruit juice Pineapples	Vegetable and Processed oils Canola oil Hydrogenated oil Margarine Peanut oil Sunflower oil Safflower oil Trans fats Vegetable shortening	Processed meat Deli Meat Hot Dogs Pork Sausage Salami Tuna	Nuts with sugar or chocolate Nut butter that contains toxic fats or sugar	Baked beans Peanuts Soybean oil	Flour tortilla Wheat bread White bread Pasta	All conventional dairy products including milk Processed cheese	Alcohol Soda Sugary beverages Fruit juices Enhanced or flavored water Diet/Artificially sweetened drinks	

**Avoid these foods if you have GI issues, inflammation, auto-immune disease, or diabetes.

Help Your Patients

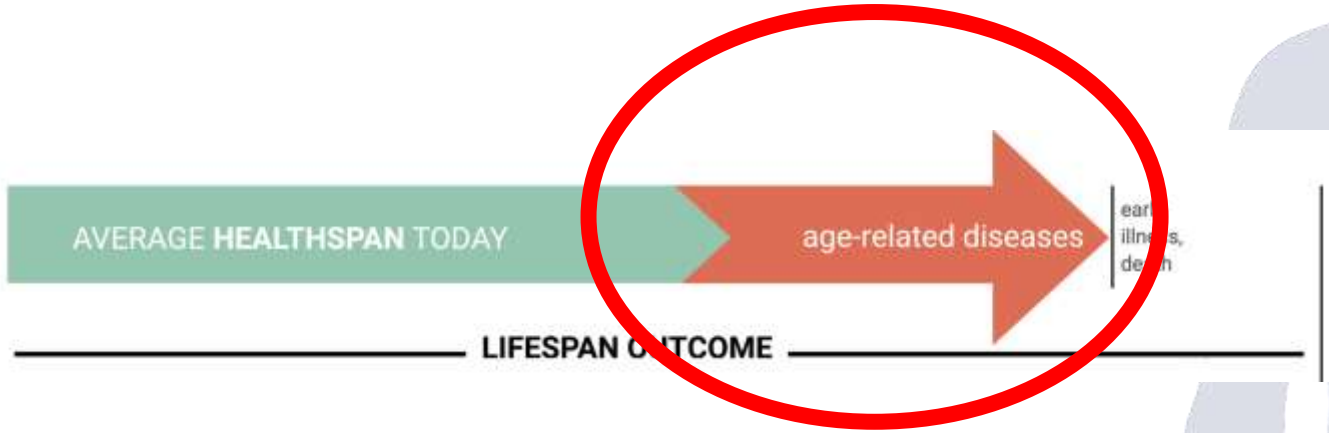
- Lose weight
- Maintain ideal BP
- Flax seeds (2T/day grind up)
- Decrease salt intake
- Maintain a healthy diet
- Test: BP

Retirees' most feared condition of later life



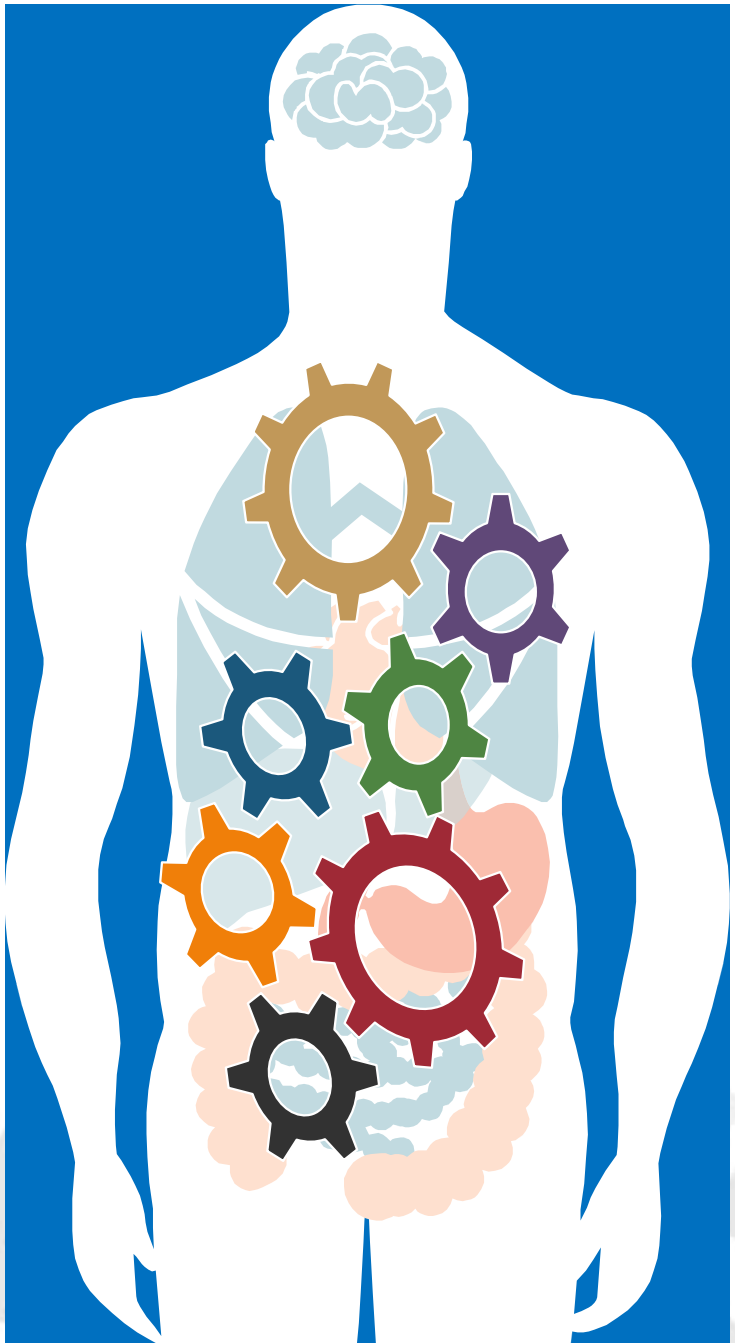
Leading Causes of Death

1. Heart disease
2. Cancer
3. Unintentional injuries
4. Chronic lower respiratory disease
5. Stroke and cerebrovascular diseases
6. Alzheimer's disease
7. Diabetes
8. Influenza and pneumonia
9. Kidney disease
10. Suicide



SYSTEMS PLAN

ALL SYSTEMS



1. Structure
2. Digestive
3. Delivery
4. Energy
5. Communication
6. Defense
7. Detox

7 SYSTEMS PLAN

IOS Press

Review

Alzheimer's Disease is Incurable but Preventable

Jack C
Center

The studies reviewed also revealed that another common misconception held by the general public is that individuals have no control over whether or not they develop dementia. The review showed that while the public's knowledge of genetic risk factors seems to be fair to

Accepted 30 December 2009

ELSEVIER

Alzheimer's & Dementia 7 (2011) 436–444

& Dementia

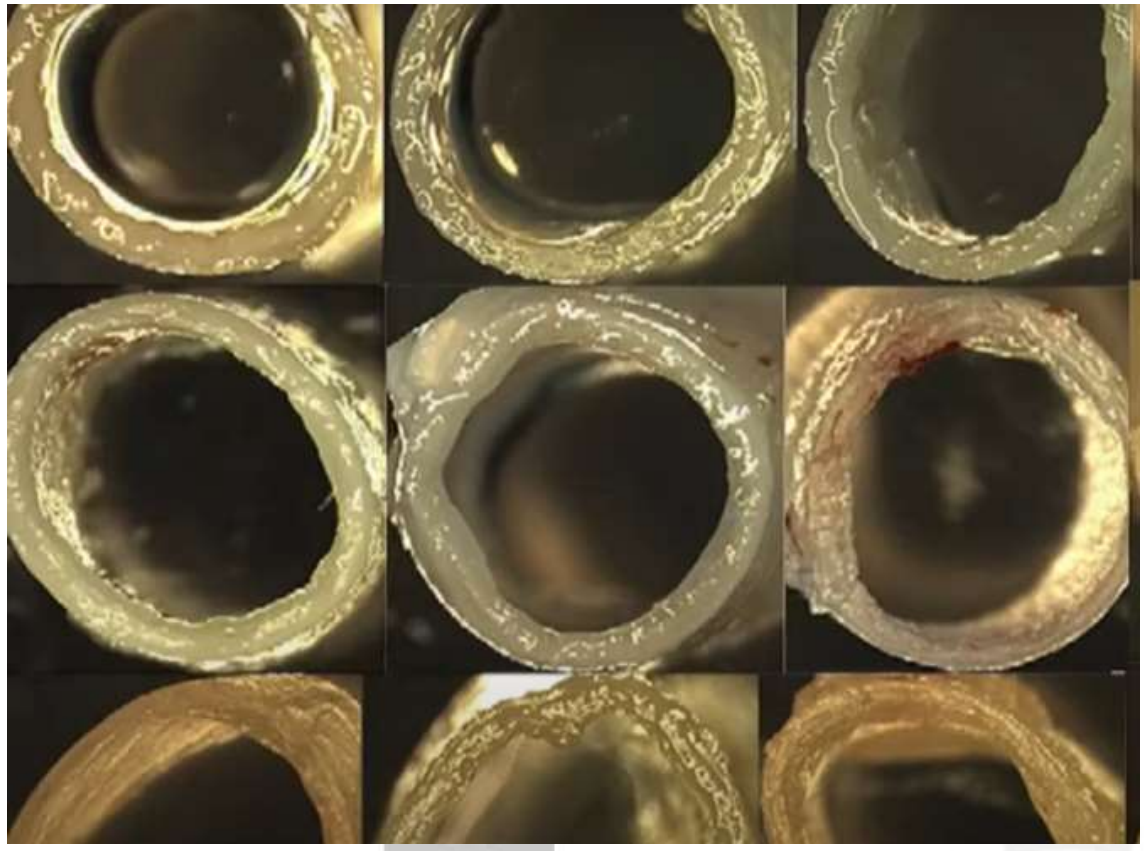
Intracranial atherosclerosis as a contributing factor to Alzheimer's disease dementia

Alex E [illegible] Kokjohn[a,d], [illegible]gh[g],

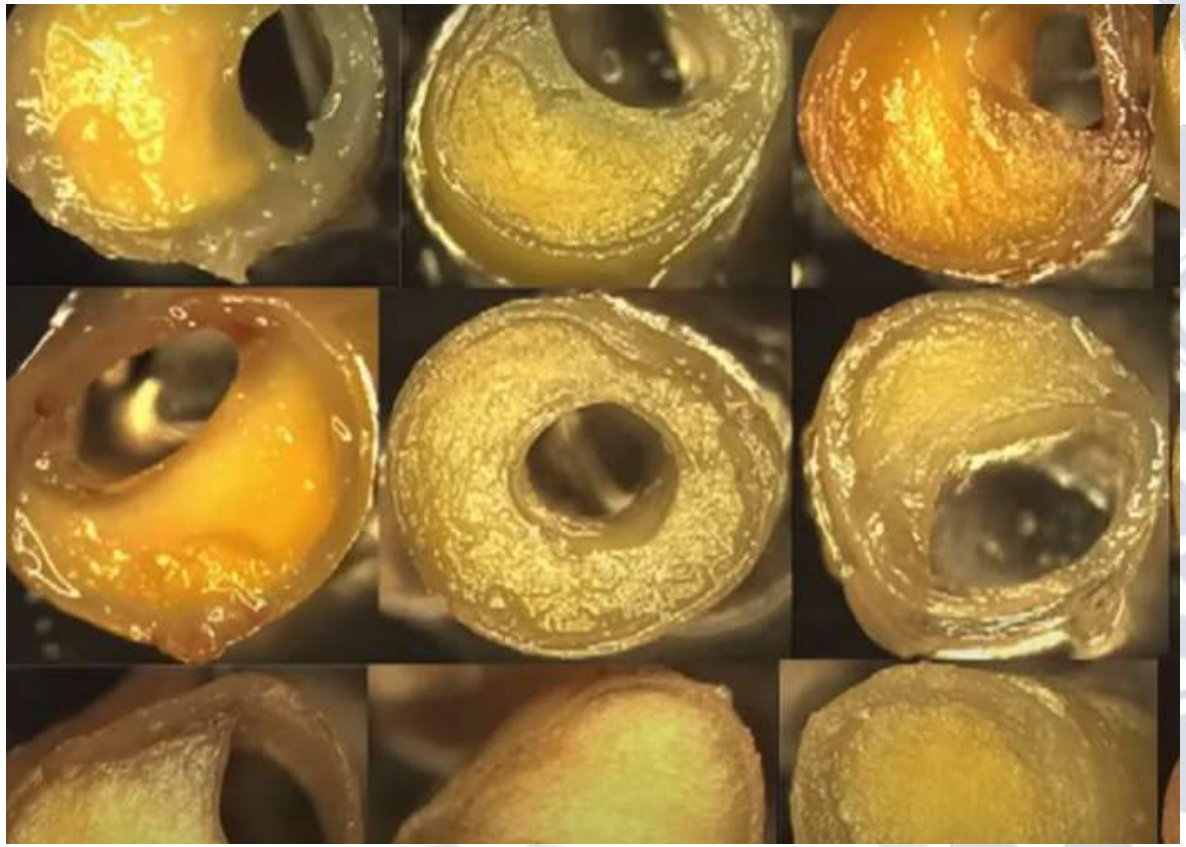
important than those measured at older ages.[35] There is emerging consensus that "what is good for our hearts is also good for our heads,"[36 37] making aggressive control of behavioural and

[a]The Longtine Center for Neurodegenerative Biochemistry, Banner Sun Health Research Institute, Sun City, AZ, USA
[b]Department of Health Studies and Gerontology, University of Waterloo, Waterloo, Ontario, Canada
[c]Department of Psychology, University of Waterloo, Waterloo, Ontario, Canada
[d]Department of Microbiology, Midwestern University, Glendale, AZ, USA
[e]Transcranial Doppler Center, Methodist DeBakey Heart and Vascular Center, The Methodist Hospital, Houston, TX, USA

Normal



Alzheimer's Disease



Cholesterol >225 = 25 x Higher Risk

Hypercholesterolemia is unanimously recognized to be a risk factor for sporadic AD, a form that accounts for the great majority of cases [3, 113]; of note, in hypercholester-

Table 4 Multivariate-adjusted ORs and 95% CIs for presence of NPs (CERAD score 1–3 vs 0) according to lipid profile levels[a]

Quantiles of lipid profiles	Range	OR (95% CI)	*p* Value
TC, mg/dL			
Q4 (vs Q1–3)	>224	24.8 (4.7–130.5)	0.0002

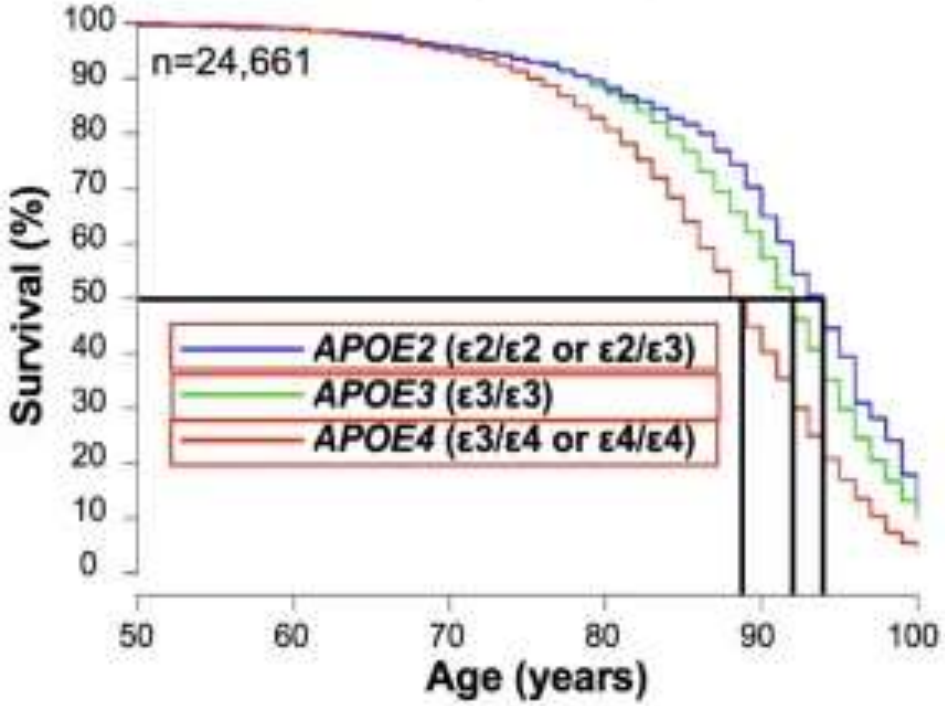
The Most Important Gene for Longevity?

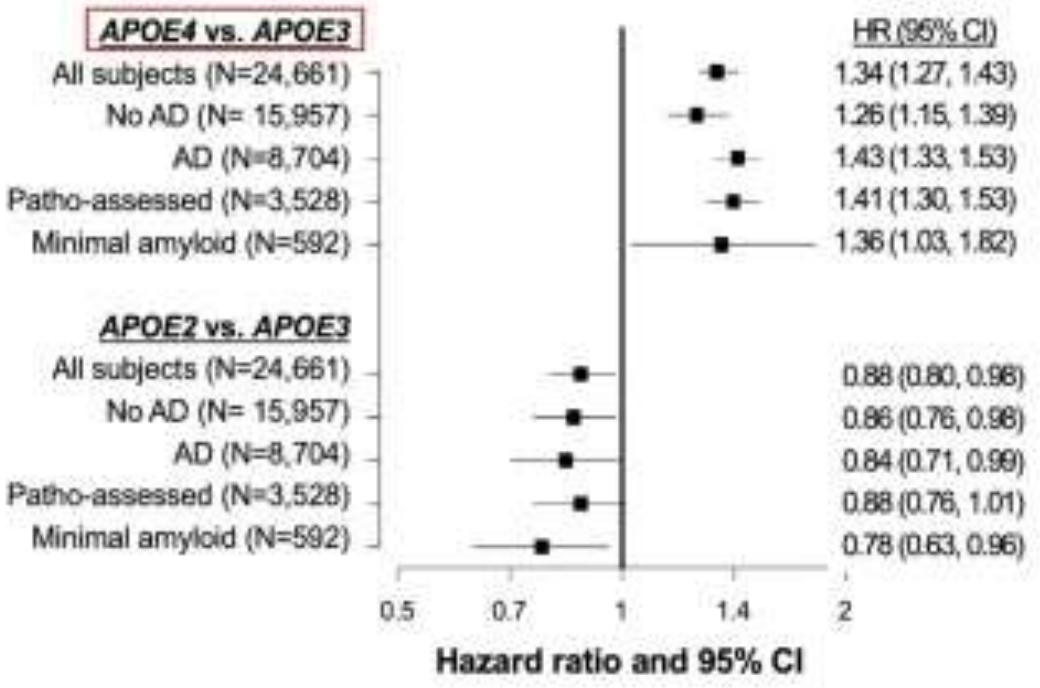
centenarians cohorts (Frisoni et al. 2001; Blanché et al. 2001; Rea et al. 2001; Jian-Gang et al. 1998). In parallel studies ApoE has also been identified as being the single most important gene associated with 'healthy longevity' in a host of individual studies as locally (Bennati et al. 2010; Rea et al. 2001), across Europe (Eggertsen et al. 1993; Deelan et al. 2011), in

APOE2 is associated with longevity independent of Alzheimer's disease

Mitsuru Shinohara[1,2*], Takahisa Kanekiyo[1,3], Masaya Tachibana[1,4], Aishe Kurti[1], Motoko Shinohara[1], Yuan Fu[1], Jing Zhao[1], Xianlin Han[5], Patrick M Sullivan[6], G William Rebeck[7], John D Fryer[1,3], Michael G Heckman[1,8], Guojun Bu[1,3*]

DOI: https://doi.org/10.7554/eLife.62199 **Published:** 19 October 2020





GENE SUMMARY

You will notice that some of the genes have a star ★ next to them. Based on your individual results, these genes have been identified as having a bigger impact on your pathways and individual health. It's important that you and your practitioner are aware of them, as they need to be considered along with your existing diet, lifestyle and medical history in creating your personalized 3X4 plan.

Gene	Variant	Result	Gene	Variant	Result
BENEFICIAL			**NO IMPACT**		
APOE	E2/E3/E4	E2/E3	GSTP1	Ile105Val A>G	AA
BHMT	Arg239Glu G>A	GA	GSTP1	Ala114Val C>T	CC
CYP1A2	–163 A>C	AA	HFE	C282Y/H63D	CY/HH
			HLA	DQ 2.2/2.5/8	DQ8/DQ2.2

that all relevant tests have been carried out and the data submitted.

Other opponents of the GEAC approval include two organizations backed by right-wing supporters of the ruling government led by prime minister Narendra Modi: the Swadeshi Jagaran Manch (the Forum for National Awakening), and the Bharatiya Kisan

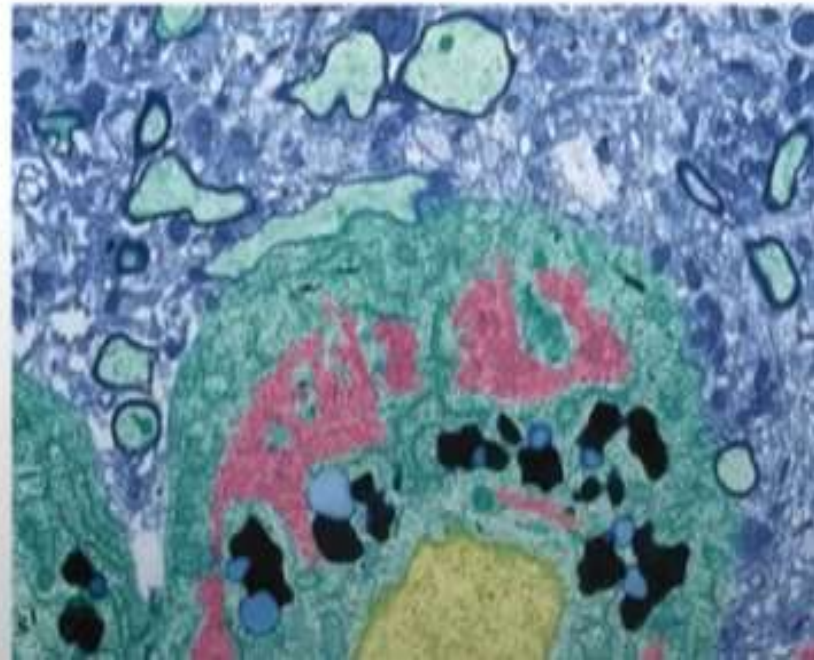
cations of existing data or minor additional data, the case could be resolved two or three months after the hearings begin. But should the court seek new data, such as on the effects of GM mustard oil in monkeys or chimpanzees, the process could take up to five years.

It's not the first time the GEAC has cleared transgenic mustard for evaluation in open fields: it gave its first approval in 2017. But the GEAC itself then went on to request further data on the impact on honeybees and other

THIS IS HOW AN ALZHEIMER'S GENE RAVAGES THE BRAIN

ct: Apolipoprotein E (*APOE*) is the major cholesterol carrier in the brain, aff

By Elie Dolgin



No gene variant is a bigger risk factor for Alzheimer's disease than one called *APOE4*. A study has now linked *APOE4* with faulty cholesterol processing in the brain, which leads to defects in the insulating sheaths that surround nerve fibres and facilitate the cells' electrical activity.

Preliminary results hint that these changes

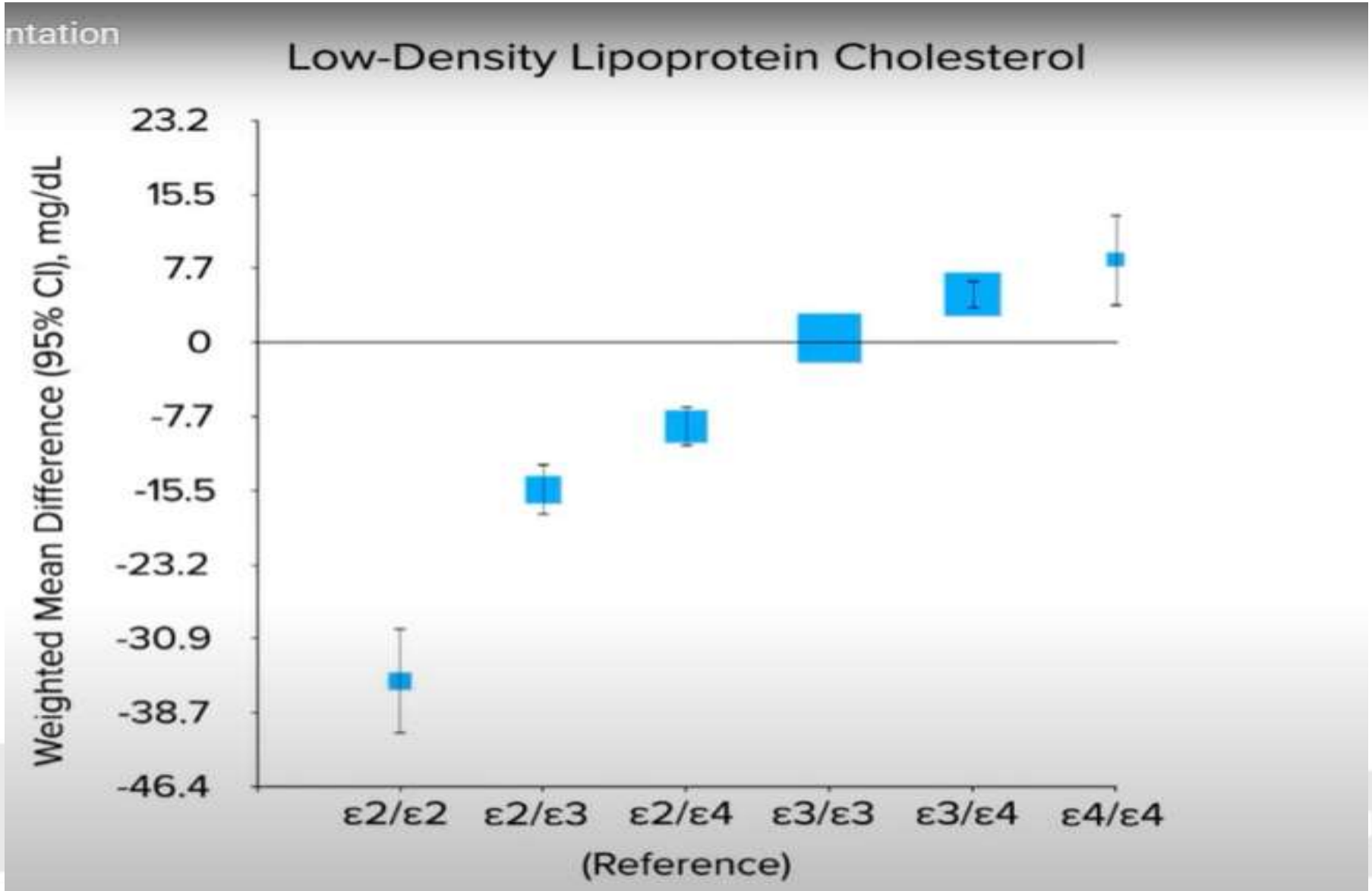
TABLE 1

Risk for MCI or dementia due to AD based on *APOE* genotype[4]

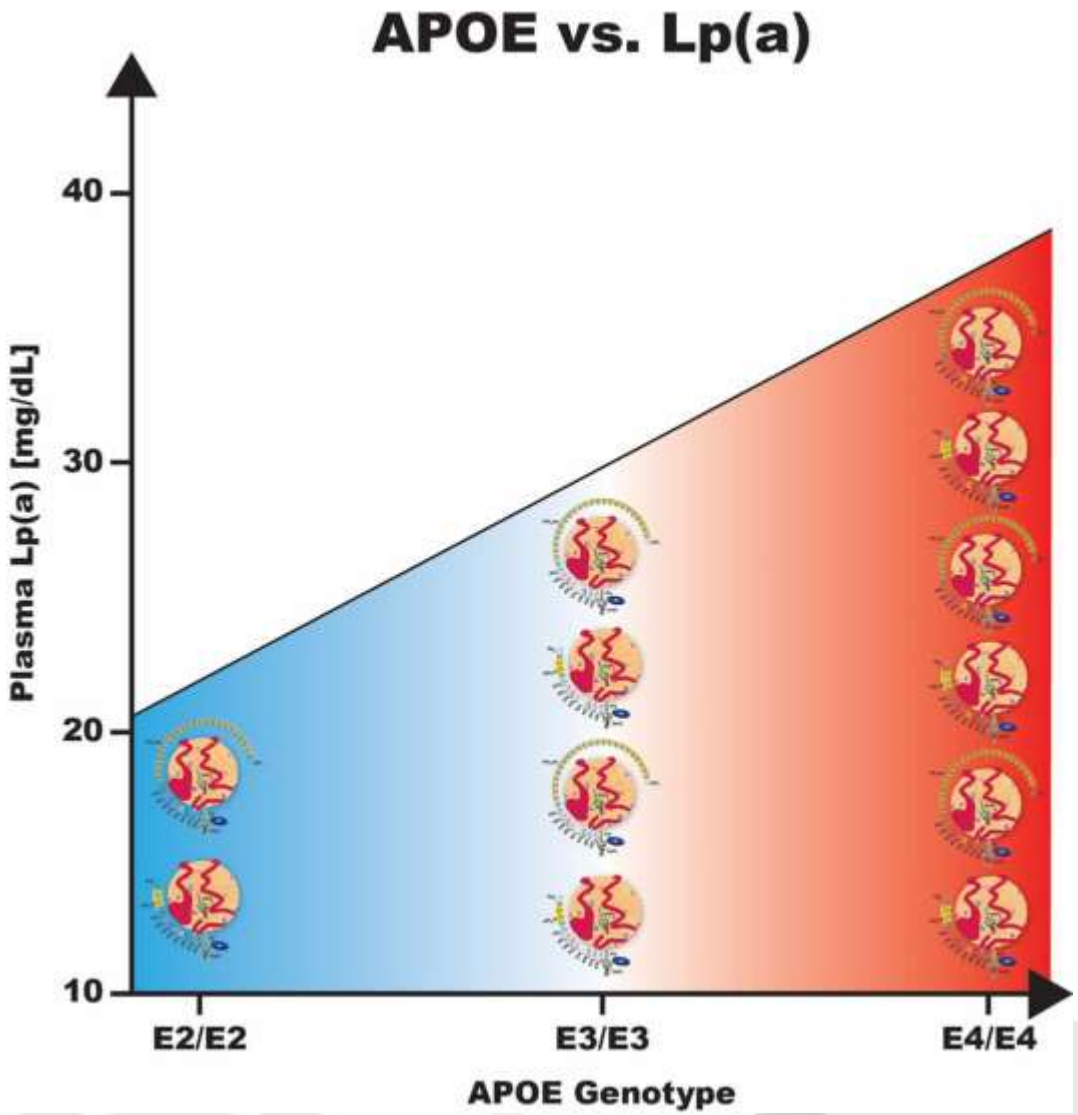
APOE genotype[a]	Lifetime risk estimate[b]
ε4/ε4	30%-55%
ε3/ε4	20%-25%
ε3/ε3	10%-15%

AD, Alzheimer disease; *APOE*, apolipoprotein; MCI, mild cognitive impairment.

APOE and LDL


ntation
Low-Density Lipoprotein Cholesterol
Weighted Mean Difference (95% CI), mg/dL
23.2
15.5
7.7
0
-7.7
-15.5
-23.2
-30.9
-38.7
-46.4
ε2/ε2
ε2/ε3
ε2/ε4
ε3/ε3
ε3/ε4
ε4/ε4
(Reference)

Lp(a)


APOE vs. Lp(a)
Plasma Lp(a) [mg/dL]
40
30
20
10
E2/E2
E3/E3
E4/E4
APOE Genotype

Total Cholesterol
Above Range · 204 Mg/dL

Lipoprotein (a)
In Range · 17 Nmol/L

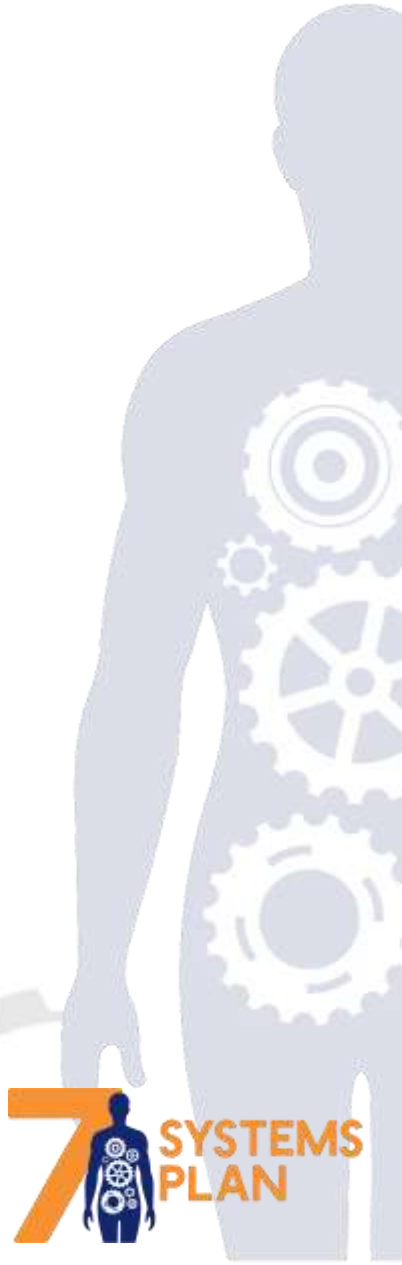
Apolipoprotein B (ApoB)
In Range · 87 Mg/dL

High-Sensitivity C-Reactive Protein (hs-CRP)
In Range · 0.4 Mg/L

HDL Large
In Range · 8313 Nmol/L

LDL Pattern
In Range A

HDL-Cholesterol
In Range · 77 Mg/dL



7 SYSTEMS PLAN

Diet Trumps Genes

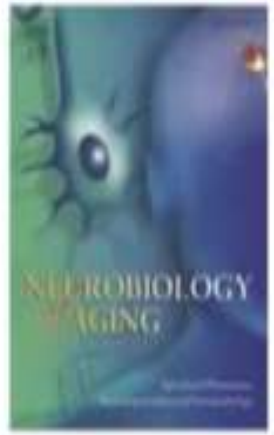
- **Nigerian blacks** have the highest observed frequency of the APOE ε4 allele in the world.
- Their cholesterol is among the lowest in studies of populations with APOE ε4.
- In contrast with other populations, the APOE ε4 allele was not significantly associated with Alzheimer's disease or dementia.

Neurobiology of Aging 35 (2014) S74–S78

Contents lists available at ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging



Review

Dietary and lifestyle guidelines for the prevention of Alzheimer's disease

Neal D. Barn
Celeste A. d
Brendan Luc

Vegetables, legumes (beans, peas, and lentils), fruits, and whole grains should replace meats and dairy products as primary staples of the diet.

[a] Department of Medicine, George Washington University School of Medicine, Washington, DC, USA
[b] Physicians Committee for Responsible Medicine, Washington, DC, USA

Medicina 2022, 58, 1025.

Review

Plants, Plants, a … d Nutrients and Their Protective … Alzheimer's Disease, and O…

Helen Ding, Allison B. Reis…

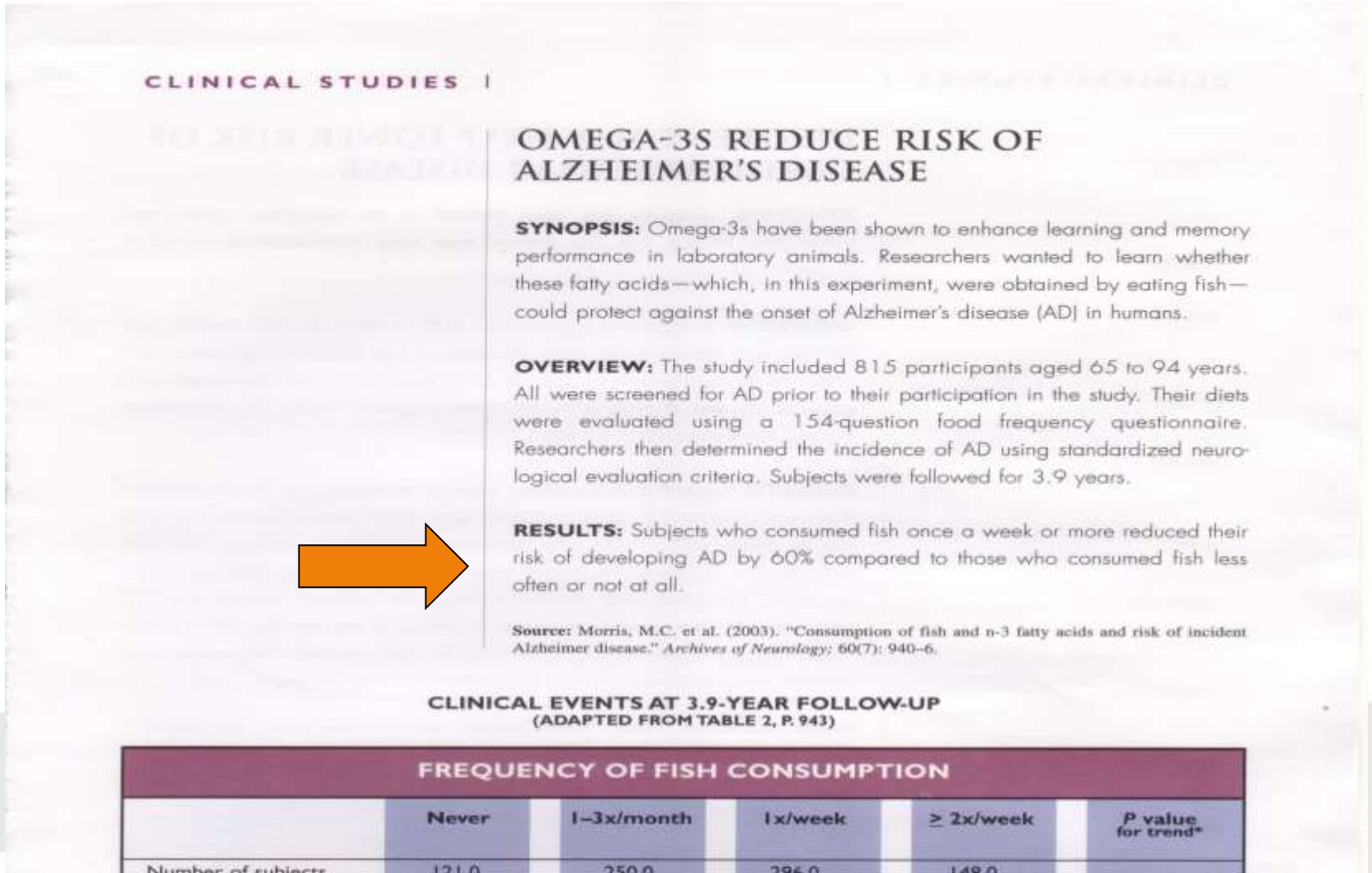
…en.ding@nyulangone.org (H.D.);
…e.org (A.P.)

* Correspondence: lora.kasselman@nyulangone.org

and potentially avoiding AD. At the core, the key takeaways are the following:

1. Reduce processed sugars
2. Reduce fats, especially saturated fat
3. Reduce animal products (meat, dairy, cheese)
4. Reduce processed foods
5. Consume more plants of all varieties, especially greens and beans
6. Increase fruit consumption, especially berries
7. Reduce salt consumption

60% Less Alzheimer's Disease



CLINICAL STUDIES |

OMEGA-3S REDUCE RISK OF ALZHEIMER'S DISEASE

SYNOPSIS: Omega-3s have been shown to enhance learning and memory performance in laboratory animals. Researchers wanted to learn whether these fatty acids—which, in this experiment, were obtained by eating fish—could protect against the onset of Alzheimer's disease (AD) in humans.

OVERVIEW: The study included 815 participants aged 65 to 94 years. All were screened for AD prior to their participation in the study. Their diets were evaluated using a 154-question food frequency questionnaire. Researchers then determined the incidence of AD using standardized neurological evaluation criteria. Subjects were followed for 3.9 years.

RESULTS: Subjects who consumed fish once a week or more reduced their risk of developing AD by 60% compared to those who consumed fish less often or not at all.

Source: Morris, M.C. et al. (2003). "Consumption of fish and n-3 fatty acids and risk of incident Alzheimer disease." *Archives of Neurology;* 60(7): 940–6.

CLINICAL EVENTS AT 3.9-YEAR FOLLOW-UP
(ADAPTED FROM TABLE 2, P. 943)

FREQUENCY OF FISH CONSUMPTION					
	Never	1–3x/month	1x/week	≥ 2x/week	*P* value for trend*
Number of subjects	121.0	250.0	296.0	148.0	

SYSTEMS PLAN

Help Your Patients

- Eat right
- Maintain ideal cholesterol
- Maintain ideal blood sugar
- Test: APOE, comprehensive tree pee test

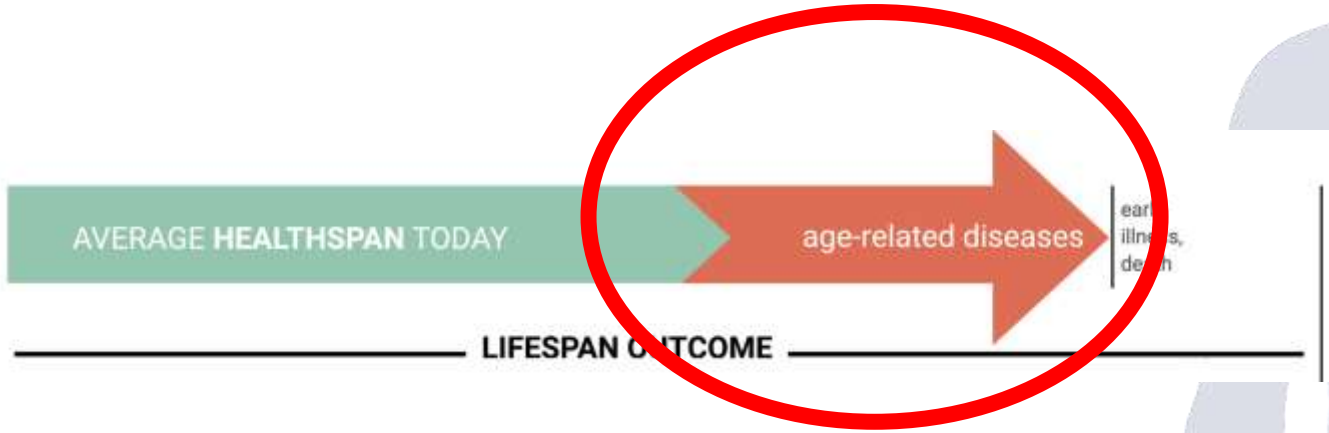
The Comprehensive Tree Pee Test for Men

Go to a tree and pee

- If it attracts a lot of ants- high glucose- diabetes
- If it dry too fast- high sodium-hypertension
- If you forgot to open your pants to pee- Alzheimer's
- If you have trouble hitting the tree- Parkinson's
- If you pee on your feet- prostate
- If you can't smell the pee- ?????

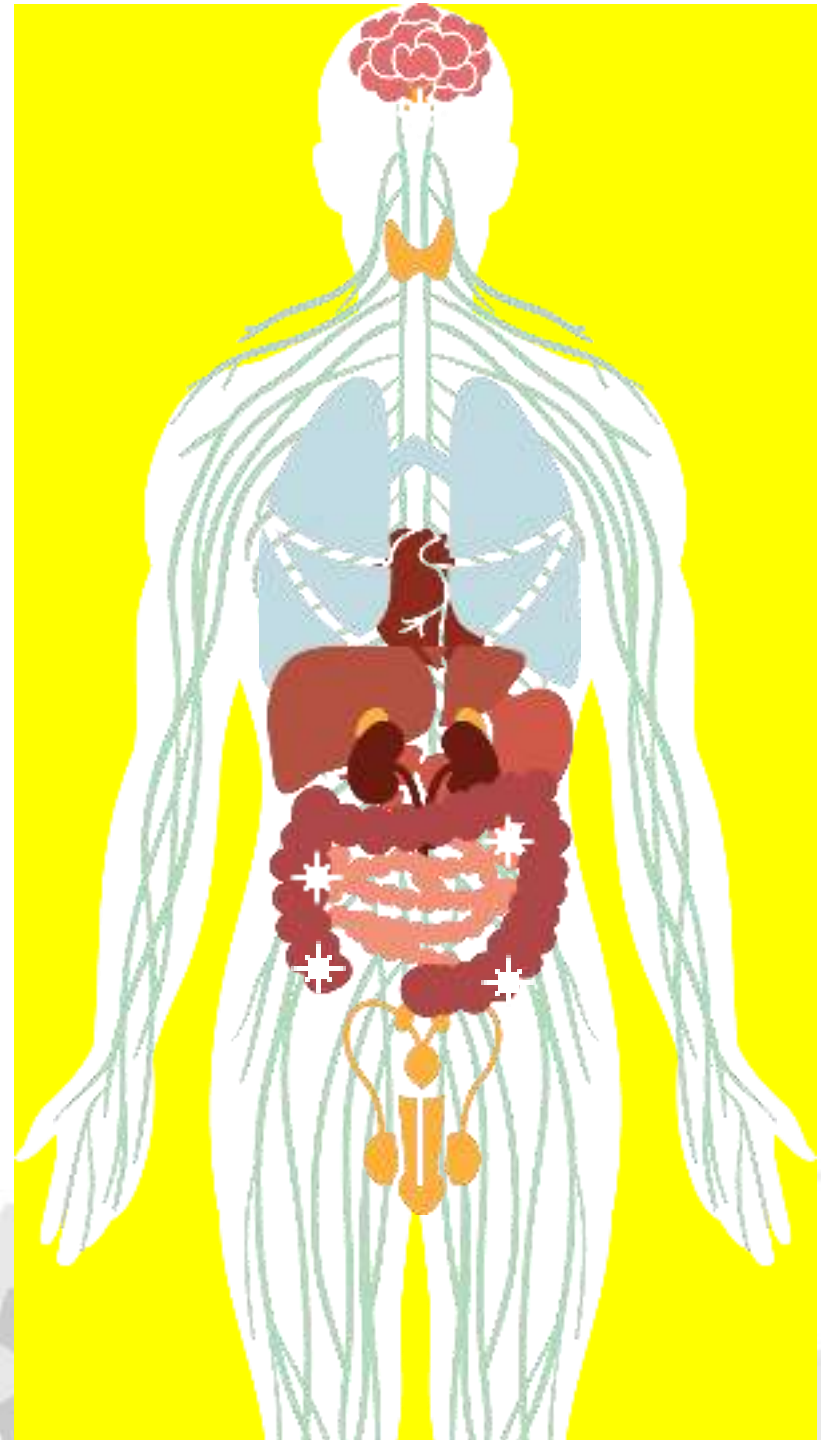
Leading Causes of Death

1. Heart disease
2. Cancer
3. Unintentional injuries
4. Chronic lower respiratory disease
5. Stroke and cerebrovascular diseases
6. Alzheimer's disease
7. Diabetes
8. Influenza and pneumonia
9. Kidney disease
10. Suicide



SYSTEMS PLAN

Communication System



1. **Hormones**- 50
2. Nerves- 100 B neurons
3. Neurotransmitters- 100

SYSTEMS PLAN

Insulin- the Energy and Fat Storage Hormone

High levels of insulin were predictive of:

- **-obesity**
- -heart disease
- -hypertension
- -stroke
- -cancer
- **-type 2 diabetes**

Lower levels of insulin had no disease!

No weight problems!

208 healthy people (not fat) followed for 11 years

7 SYSTEMS PLAN

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Long-Term Effects of Intensive Glucose Lowering on Cardiovascular Outcomes

68%

"an intensive therapeutic approach targeting normal glycated hemoglobin levels with the use of multiple medications is associated with higher mortality than is a standard approach"

N Engl J Med. 2011 Mar 3;364(9):818-28. PMID: 21366473 below

he writing group
I.D., McMaster Uni-
Health Sciences,

The New England
Journal of Medicine

VOL

RED

"3234 nondiabetic persons with elevated fasting and post-load plasma glucose concentrations . . ."

- Placebo
- Metformin (850 mg twice daily)
- Lifestyle modification (7% weight loss and 150 minutes of physical activity)

ABSTRACT

Backgrou
ly 8 percen
factors — e
the fasting
weight, an
reversible.
factors with a lifestyle-intervention program or the administration of metformin would prevent or delay the development of diabetes.

Methods We randomly assigned 3234 nor
persons with elevated fasting and post-load

ed
, is
xi-
ed
ng
o-
es.
The diagnosis is often delayed until complications are present.[4] Since current methods of treating diabetes

N Engl J Med 345(11):790-797 (2001)

The New England
Journal of Medicine

VOLUME 346 FEBRUARY 7, 2002 NUMBER 6

"Lifestyle changes and treatment with metformin both reduced the incidence of diabetes in persons at high risk. The lifestyle intervention was more effective than metformin."

RED

ABSTRAC

Backgro ly 8 percent of adults in the United States. Some risk factors — elevated plasma glucose concentrations in the fasting state and after an oral glucose load, overweight, and a sedentary lifestyle — are potentially reversible. We hypothesized that modifying these factors with a lifestyle-intervention program or the administration of metformin would prevent or delay the development of diabetes.

Methods We randomly assigned 3234 nor persons with elevated fasting and post-load

alled
s, is
a serious, costly disease affecting approximately 8 percent of adults in the United States.[1] Treatment prevents some of its devastating complications[2,3] but does not usually restore normoglycemia or eliminate all the adverse consequences. The diagnosis is often delayed until complications are present.[4] Since current methods of treating diabetes

N Engl J Med 345(11):790-797 (2001)

Sheila

Diabetes
High cholesterol
Weight Problems
Hypertension
Kidney problems
Pancreatitis
Many medications

Sheila

Multiple System Failure

Heather: 90 Days on the 7 Systems Plan

Off all 4 of her diabetic medications (and 11 more)

Blood sugar 90

Down 40 pounds

Mike

Dan

Help Your Patients

- Reverse diabetes
- Maintain ideal blood sugar
- Optimize hormones (7 key)
- Test: insulin

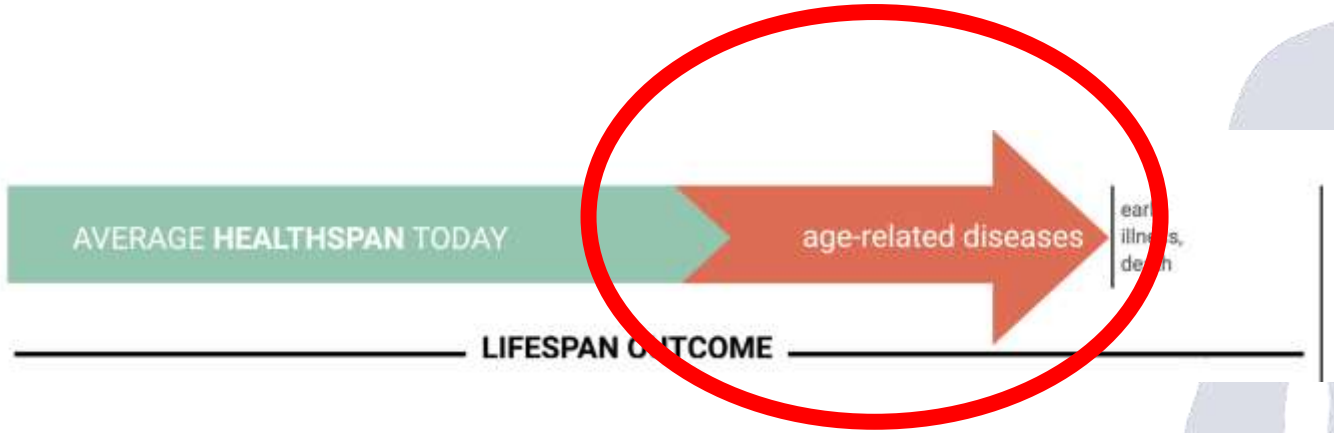
7 SYSTEMS PLAN

How To Check Insulin

1. Fasting insulin- should be < 5
2. Pinch test

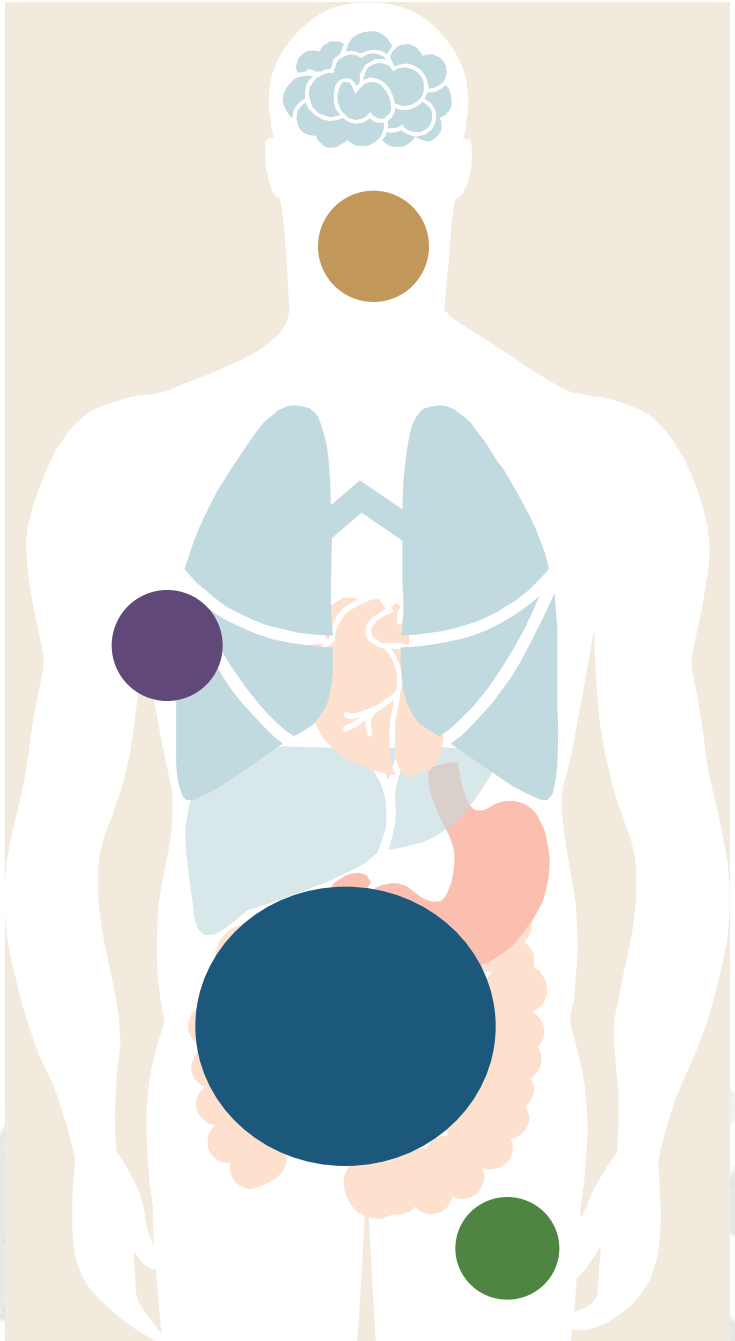
Leading Causes of Death

1. Heart disease
2. Cancer
3. Unintentional injuries
4. Chronic lower respiratory disease
5. Stroke and cerebrovascular diseases
6. Alzheimer's disease
7. Diabetes
8. Influenza and pneumonia
9. Kidney disease
10. Suicide



SYSTEMS PLAN

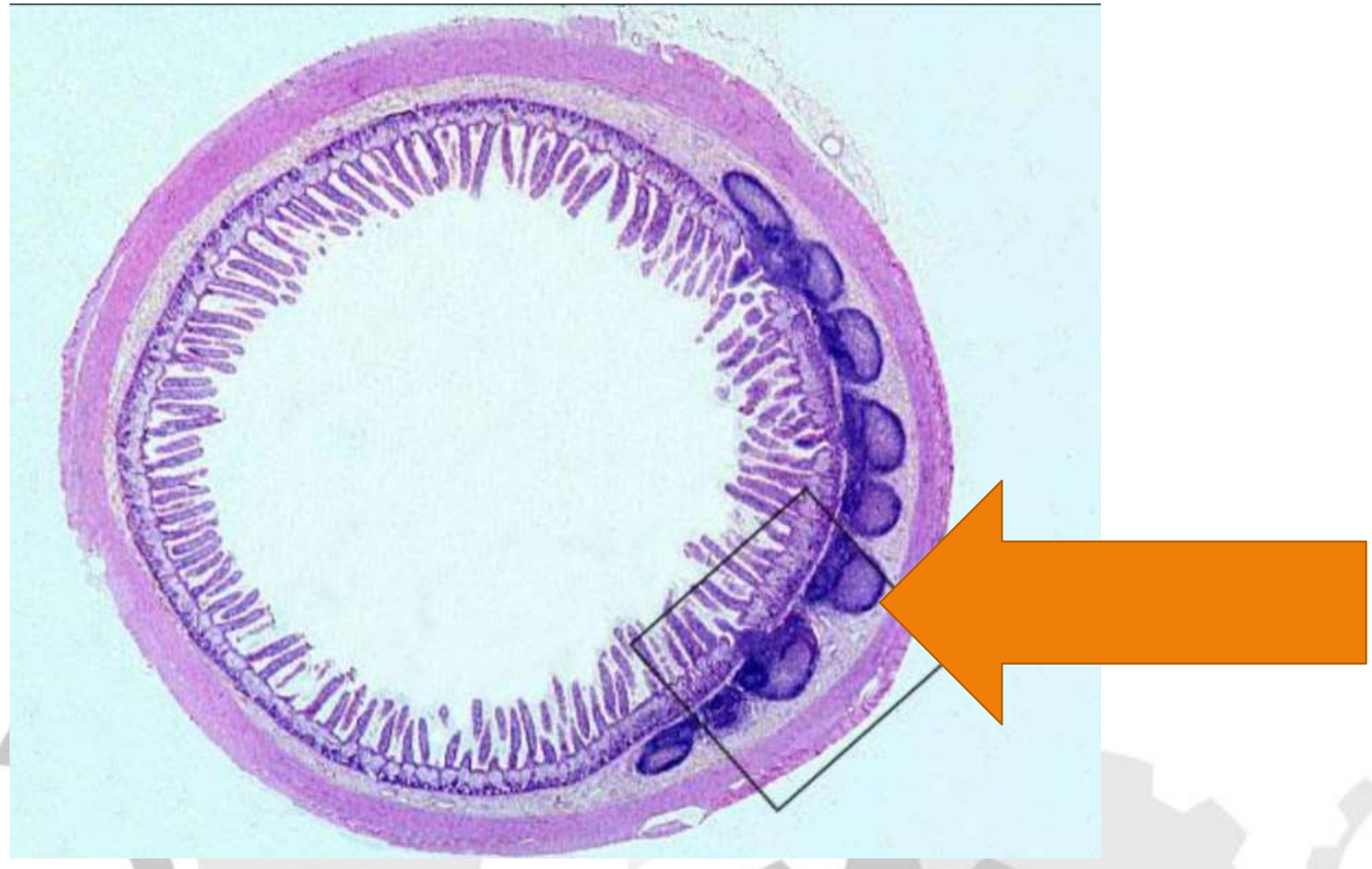
DEFENSE SYSTEM



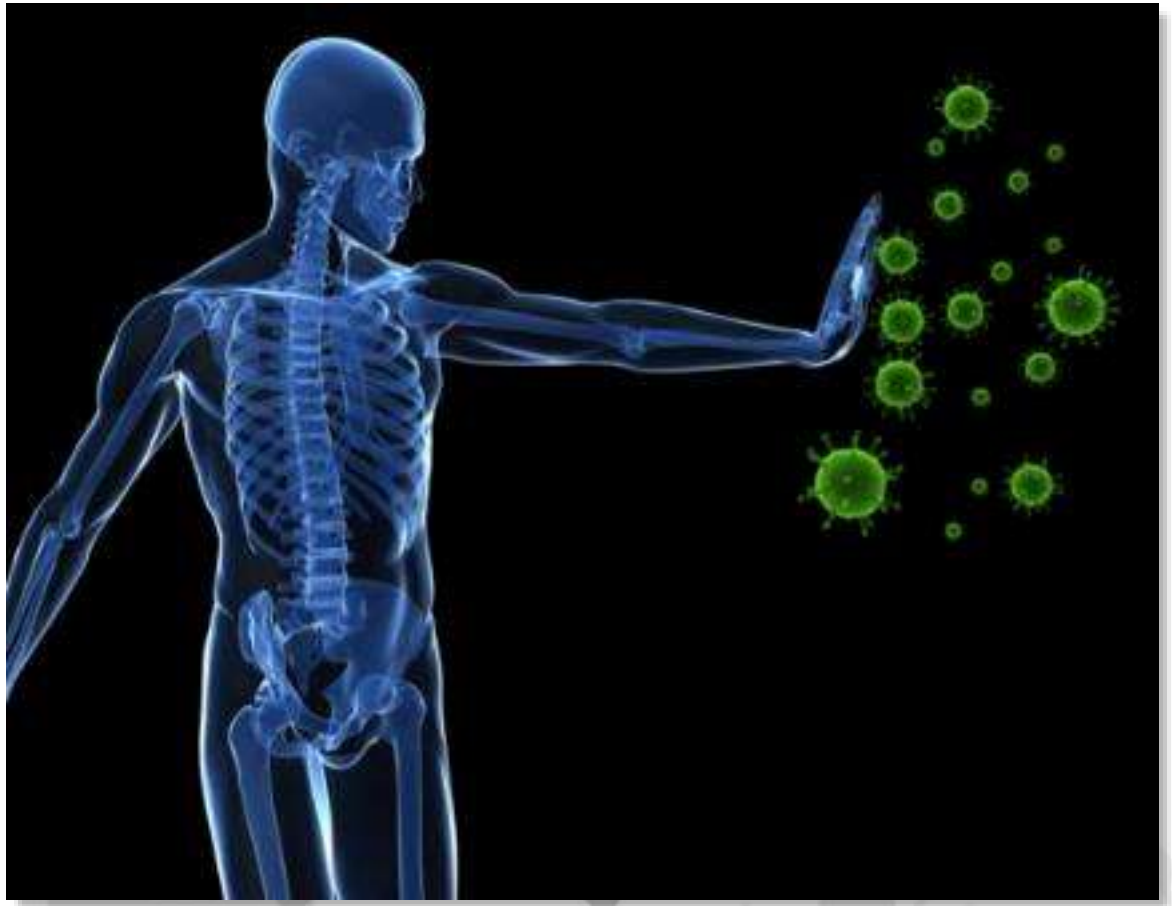
1. Tonsils
2. Lymph
3. Bone Marrow
4. **Gut Lymph Tissue**

SYSTEMS PLAN

Gut Lymphatic Tissue



Defense System Balance



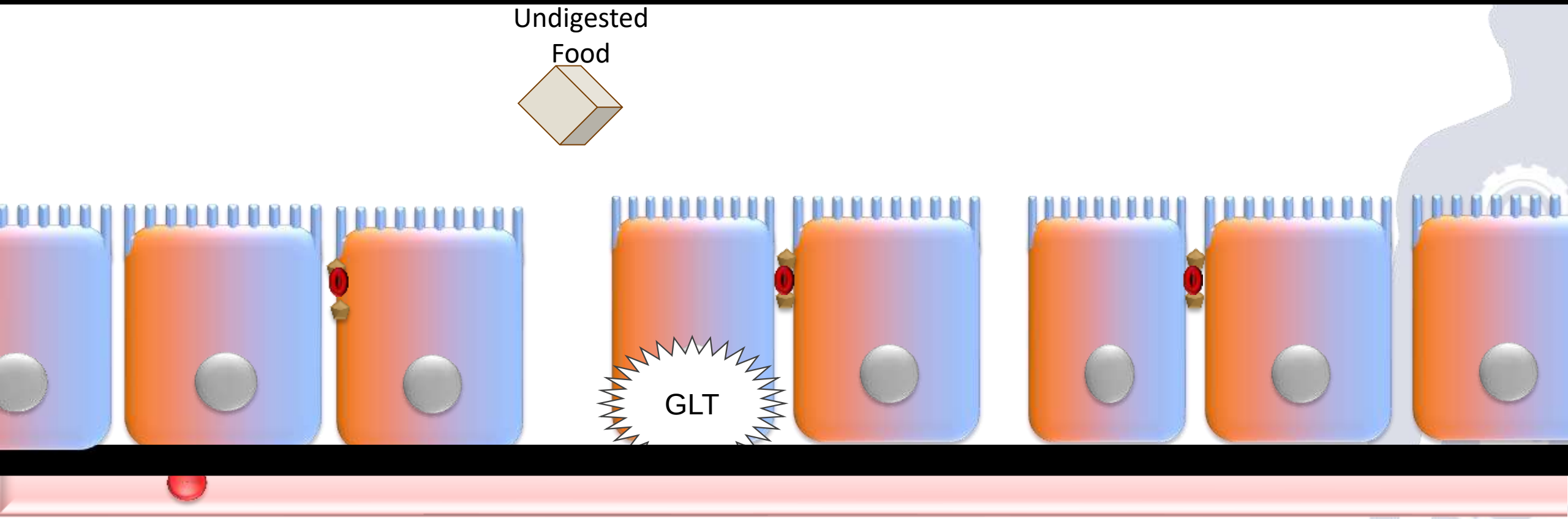
Under Function

- Colds • Infection
- Bronchitis • Flu

Over Function

- Weight gain
- Asthma and allergies
- Inflammation
- Autoimmune disease

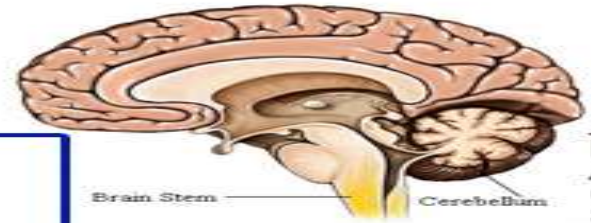
Unhealthy Gut (Leaky Gut)



Tissues of The Body Affected By Autoimmune Attack

Thyroid
Hashimoto's Thyroiditis
Graves Disease

Triggers
1. Stress
2. Hormones
3. Metals
4. Food Antigens
5. Pesticides & Poisons



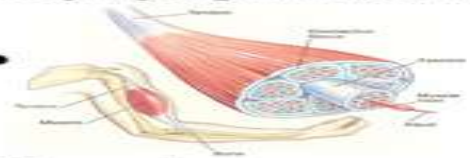
Brain
Multiple Sclerosis
Autism
Guillain-Barre Syndrome
Psychological

Blood
Leukemia
Lupus
Hemolytic
Dysglycemia

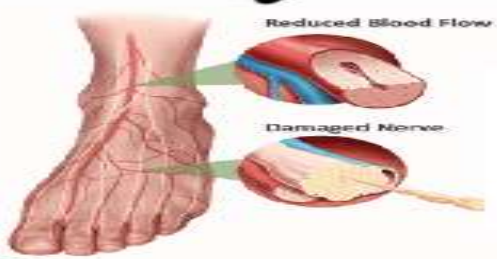
Autoimmune Disorder

Bones
Rheumatoid Arthristis
Ankylosing Spondylitis
Polymyalgia Rheumatica

GI Tract
Celiac
Chron's Disease
Ulceratic Colitis

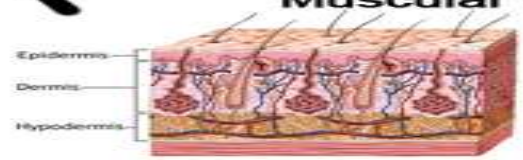


Muscles
Fibromyalgia
Muscular Dystrophy



Nerves
Peripheral Neuropathy
Diabetic Neuropathy

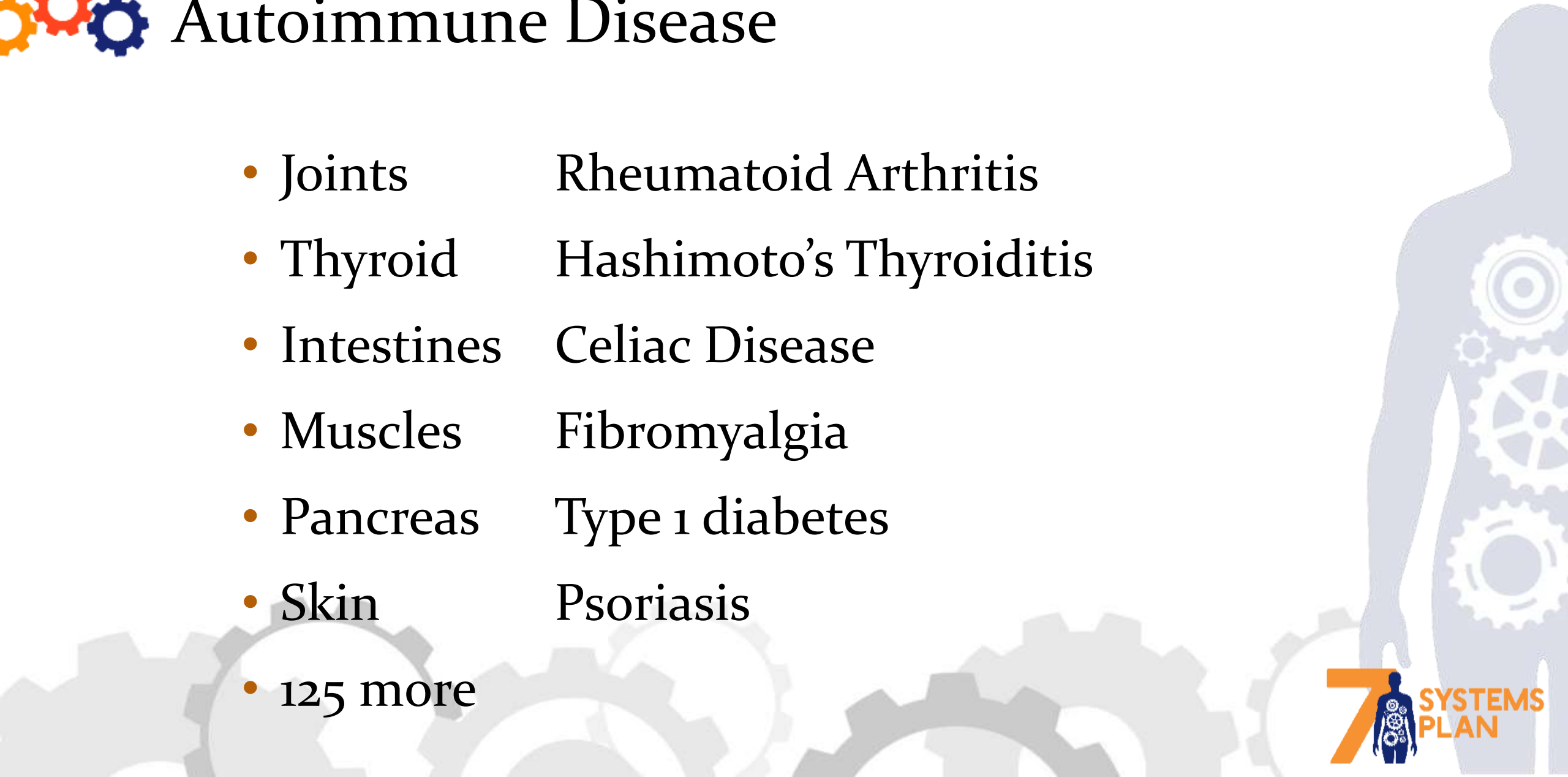
Lungs
Asthma
Wegener's Granulomatosis



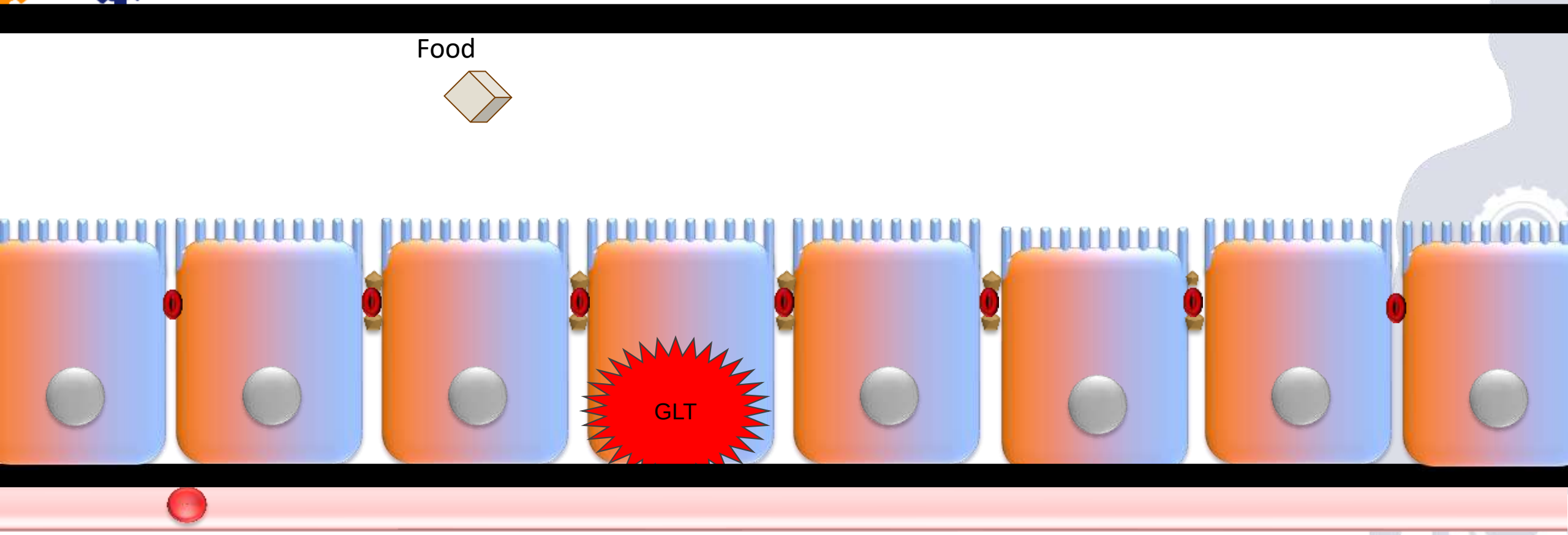
Skin
Eczema
Psoriasis
Scleroderma
Vitiligo

Autoimmune Disease

- Joints — Rheumatoid Arthritis
- Thyroid — Hashimoto's Thyroiditis
- Intestines — Celiac Disease
- Muscles — Fibromyalgia
- Pancreas — Type 1 diabetes
- Skin — Psoriasis
- 125 more



Heal The Gut



Blood Vessel

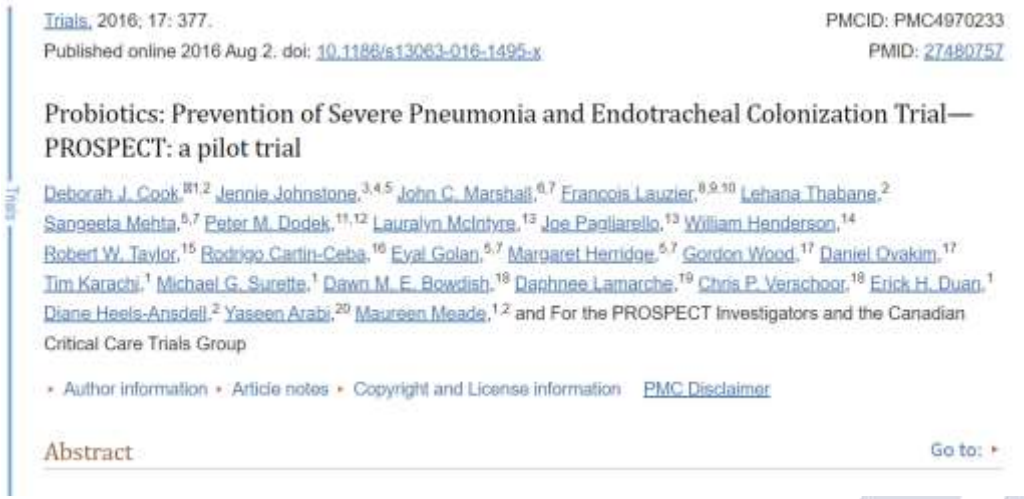
COX-2

5-LOX

SYSTEMS PLAN

Probiotics and Fermented Foods

- Oral administration of probiotics **reduces pneumonia**, while **increases pulmonary functions** without severe adverse effects.



Trials. 2016; 17: 377.
Published online 2016 Aug 2. doi: 10.1186/s13063-016-1495-x
PMCID: PMC4970233
PMID: 27480757

Probiotics: Prevention of Severe Pneumonia and Endotracheal Colonization Trial—PROSPECT: a pilot trial

Deborah J. Cook,[1,2] Jennie Johnstone,[3,4,5] John C. Marshall,[6,7] Francois Lauzier,[8,9,10] Lehana Thabane,[2] Sangeeta Mehta,[5,7] Peter M. Dodek,[11,12] Lauralyn McIntyre,[13] Joe Pagliarello,[13] William Henderson,[14] Robert W. Taylor,[15] Rodrigo Cartin-Ceba,[16] Eyal Golan,[5,7] Margaret Herridge,[5,7] Gordon Wood,[17] Daniel Ovakim,[17] Tim Karachi,[1] Michael G. Surette,[1] Dawn M. E. Bowdish,[18] Daphnee Lamarche,[19] Chris P. Verschoor,[18] Erick H. Duan,[1] Diane Heels-Ansdell,[2] Yaseen Arabi,[20] Maureen Meade,[1,2] and For the PROSPECT Investigators and the Canadian Critical Care Trials Group

Abstract Go to: •

The most effective clinical outcomes across all disease spectrums can result from normalization of gut function

LONGEVITY

7 SYSTEMS PLAN

Help Your Patients

- Fix their Digestive System (5R)
- Use probiotics
- Optimize the Defense System

7 SYSTEMS PLAN

Leading Causes of Death

1. Heart disease
2. Cancer
3. Unintentional injuries
4. Chronic lower respiratory disease
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6. Alzheimer's disease
7. Diabetes
8. Influenza and pneumonia
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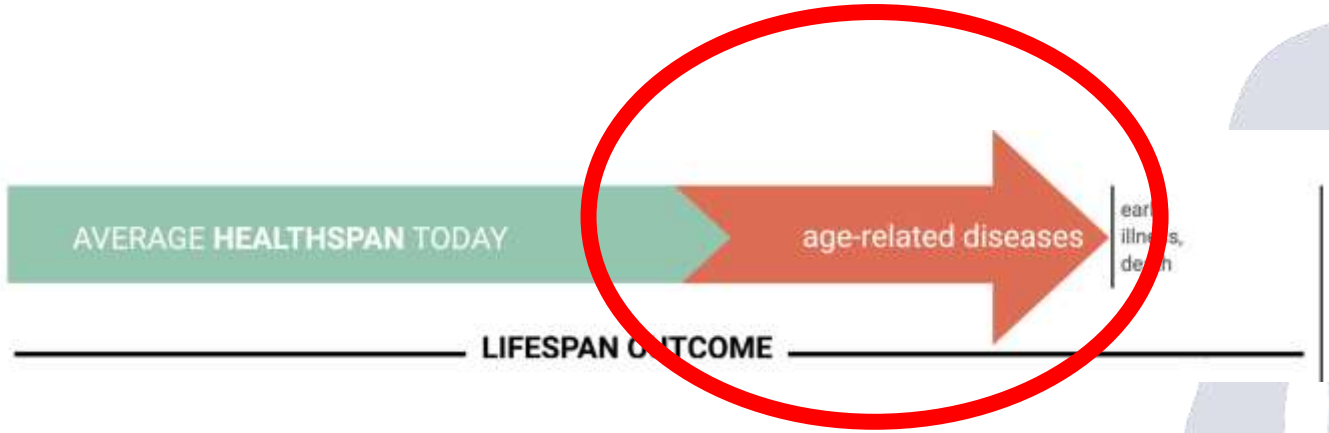
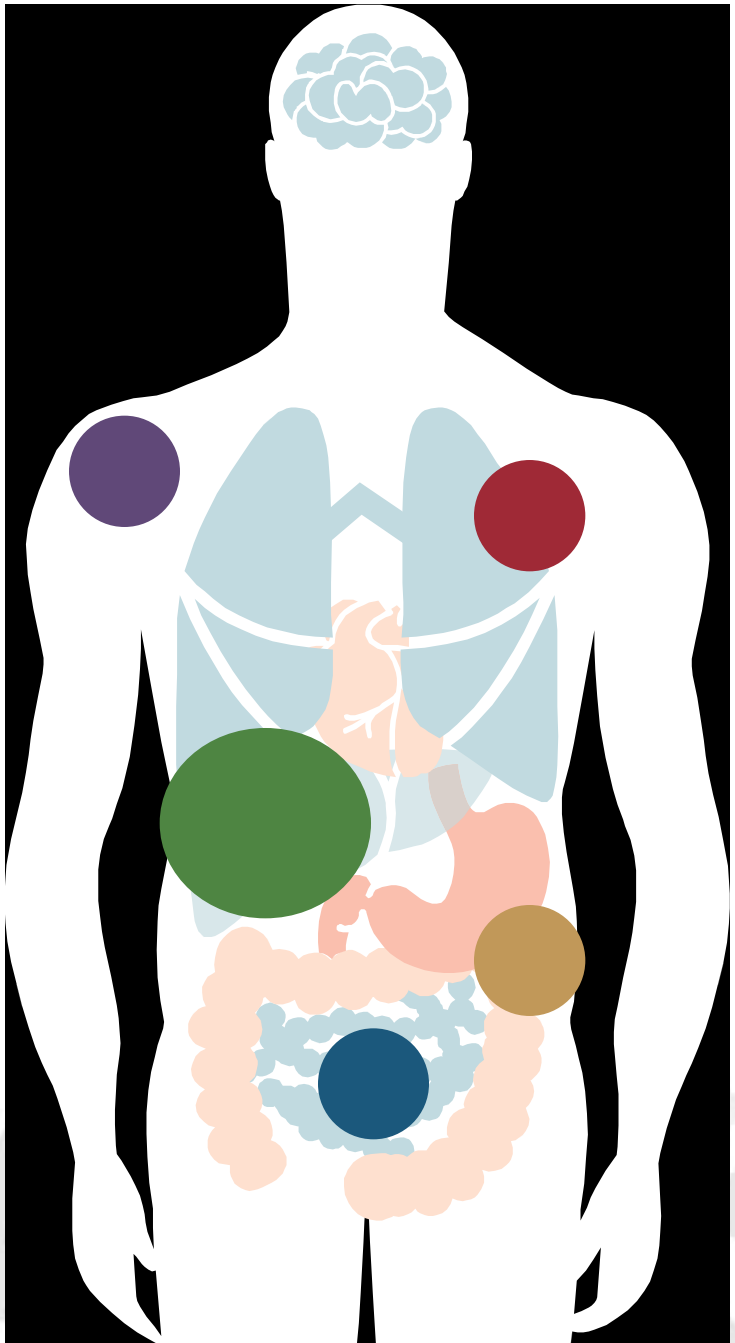


SYSTEMS PLAN

DETOX SYSTEMS

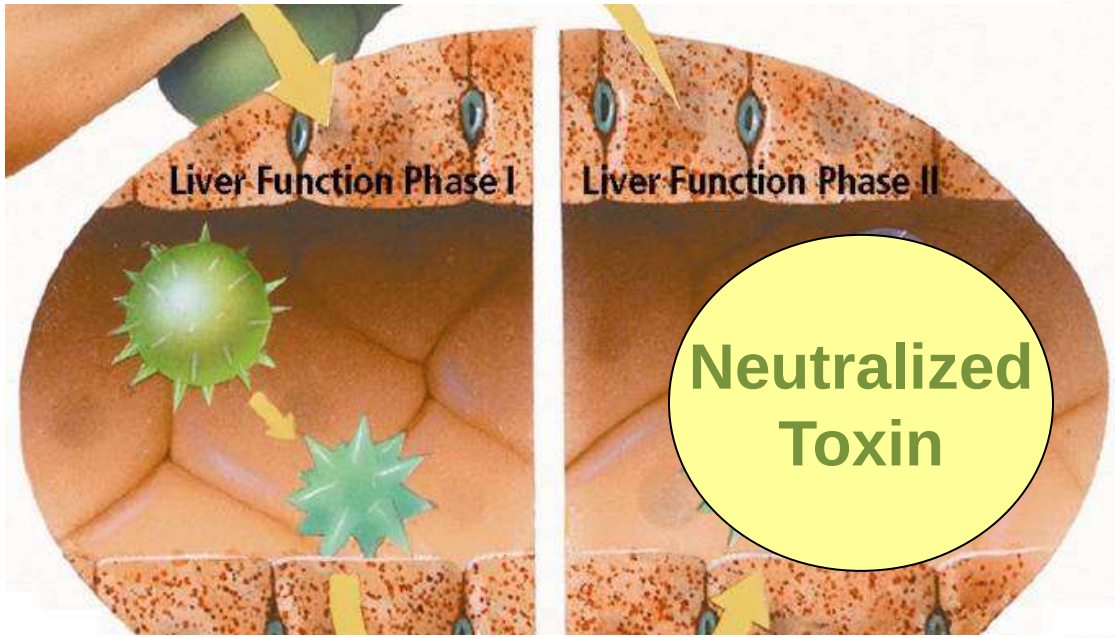


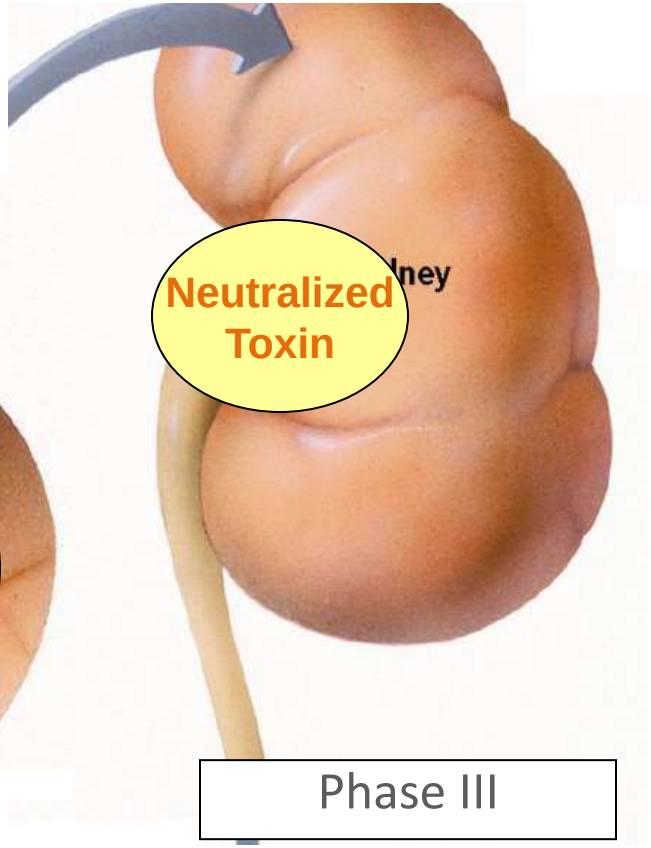
1. Kidneys
2. Skin
3. Liver
4. Colon
5. Lungs

7 SYSTEMS PLAN

Phase III: Increased urinary alkalinity supports excretion of many biotransformed toxins

Phase I



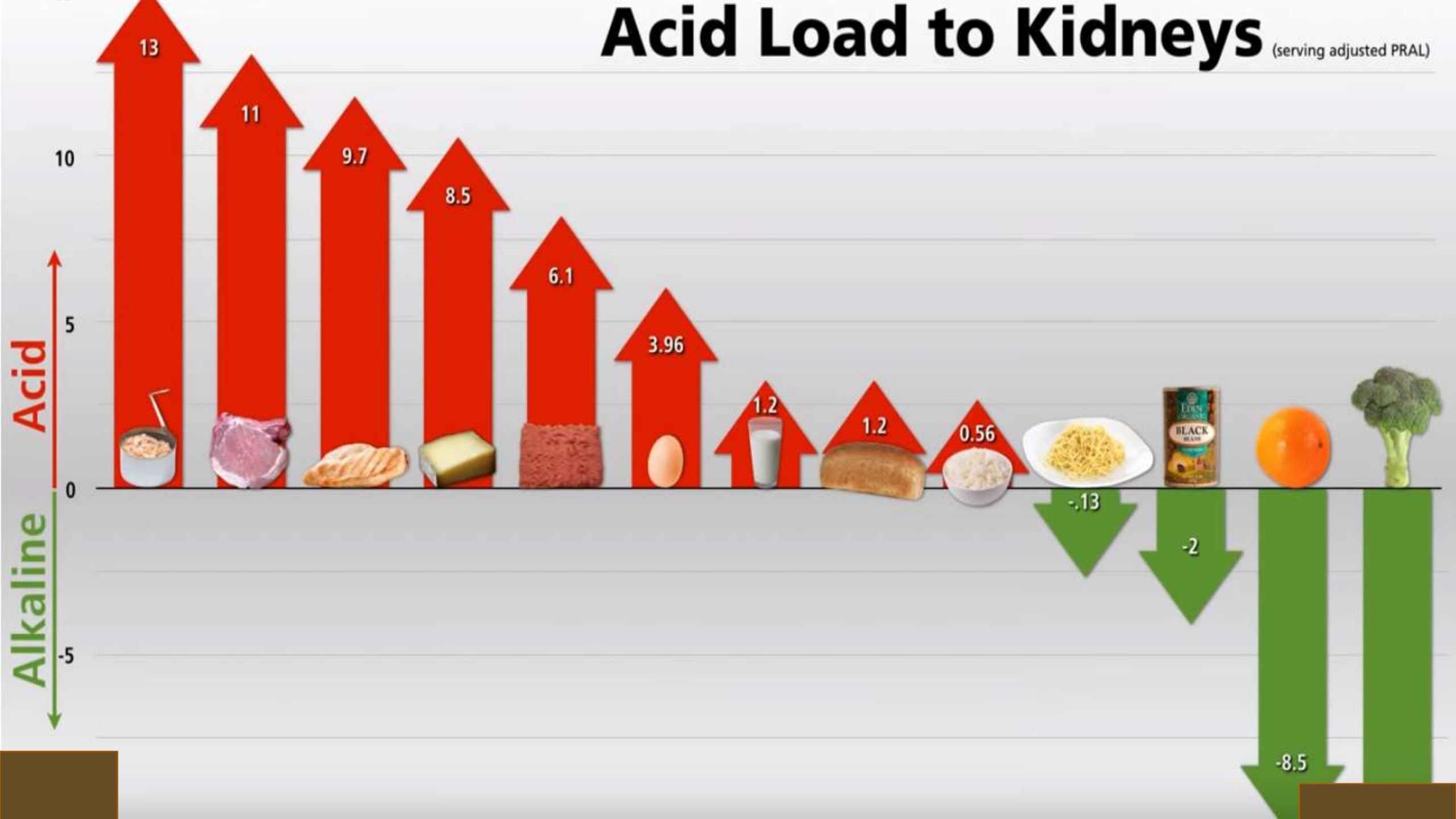


Functionalization

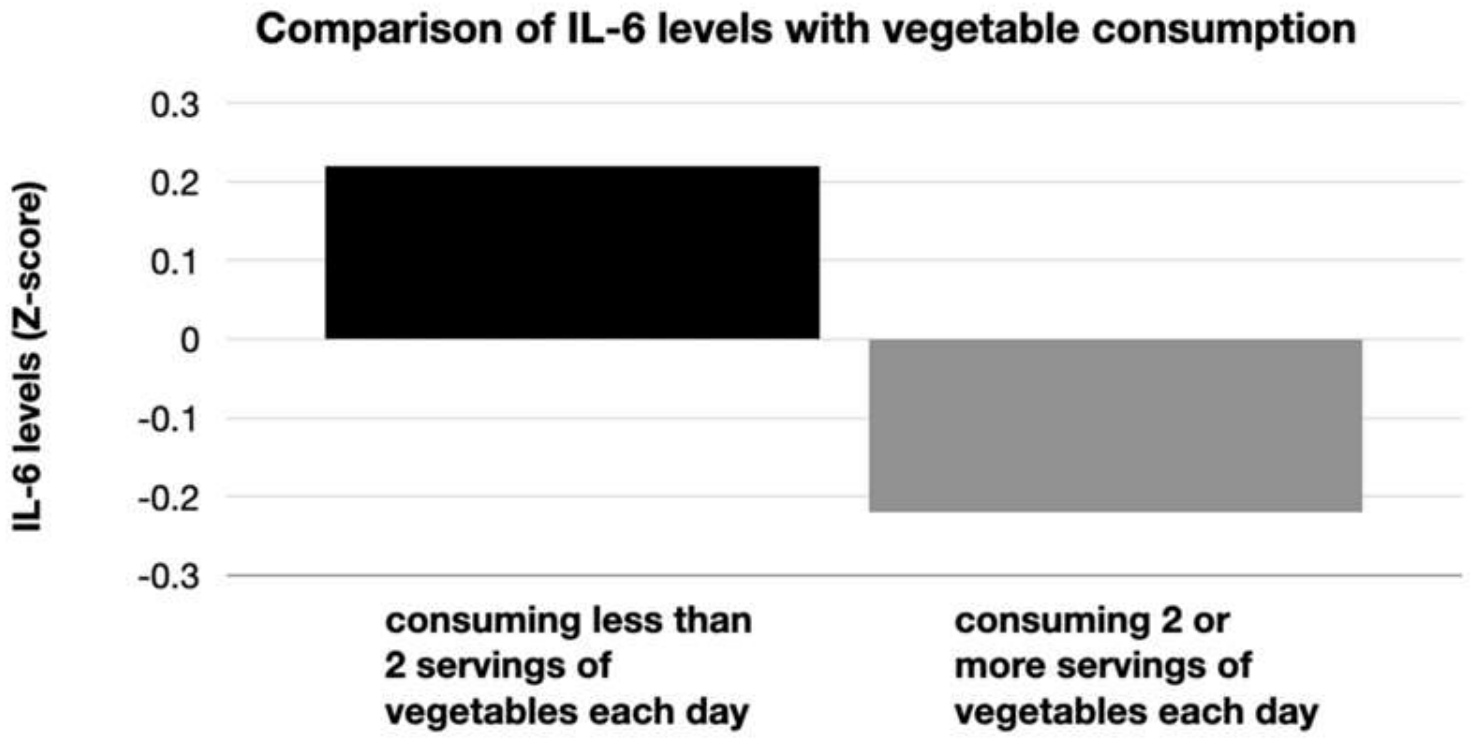
Phase II

Alkaline urine supports excretion

Acid Load to Kidneys (serving adjusted PRAL)

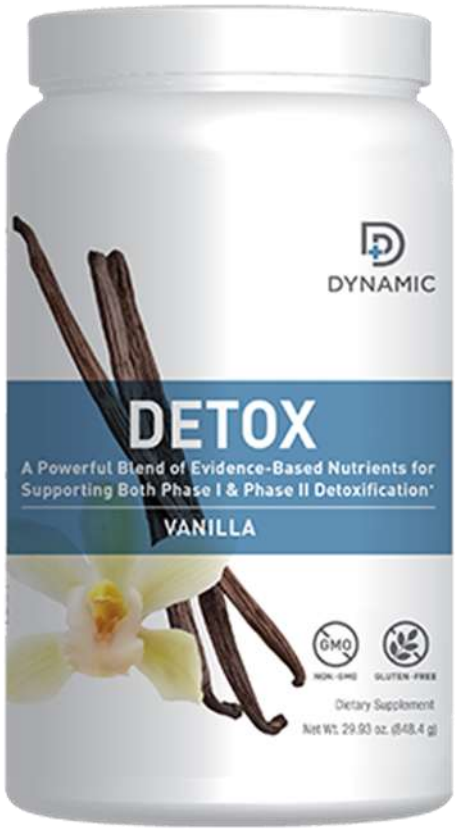


Vegetables Decrease Inflammation and Increase pH



Help Your Patients

- Eat more vegetables
- Detox and avoid toxins
- Have the correct pH
- Support their Detox System
- Test: pH



7 SYSTEMS PLAN

Leading Causes of Death

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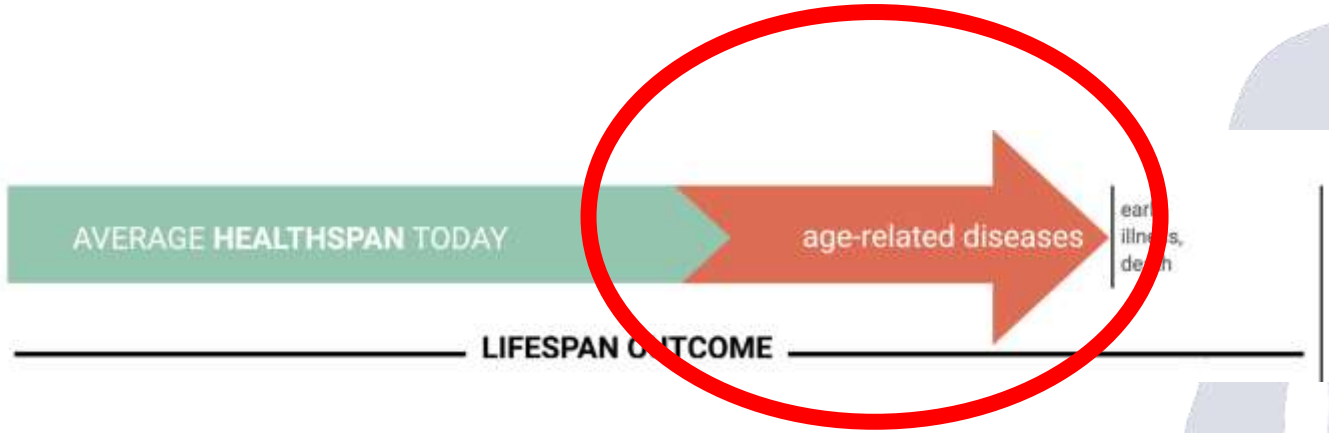
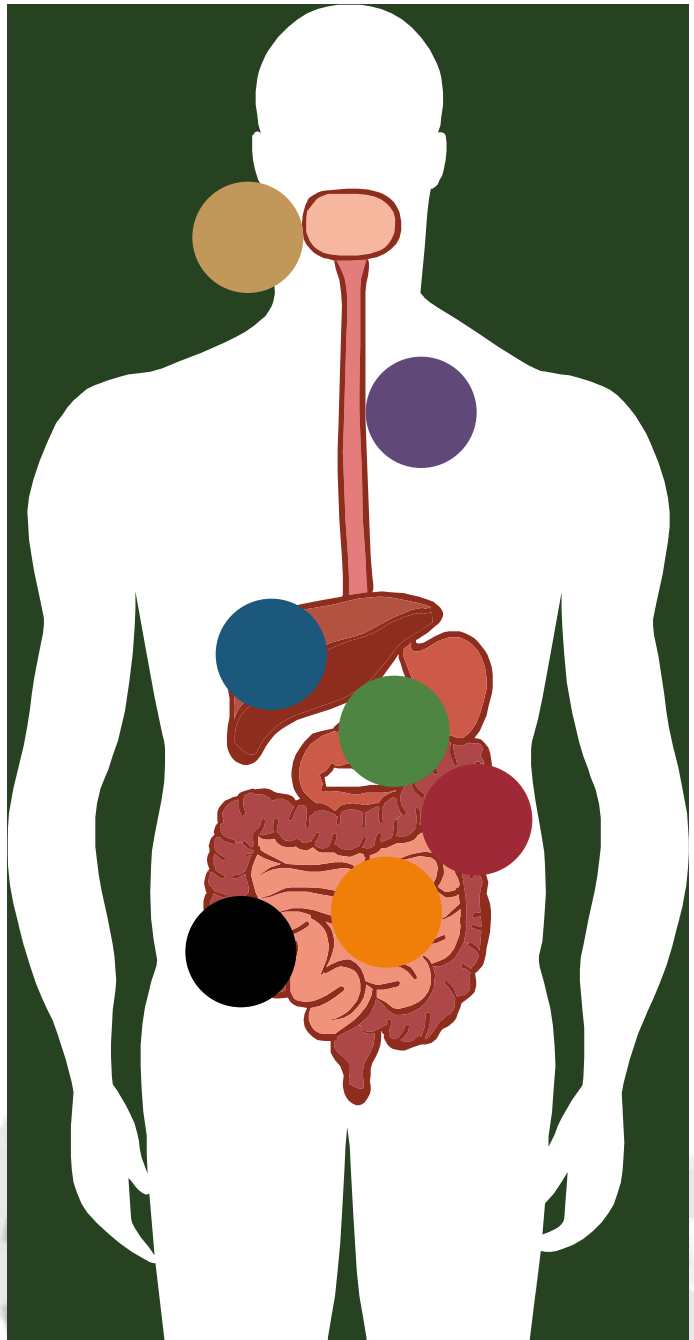


DIGESTIVE SYSTEM



1. Mouth
2. Esophagus
3. Stomach
4. Liver
5. Pancreas
6. Small Intestine
7. Colon

SYSTEMS PLAN

Neurotransmitters: Happiness

SYSTEMS PLAN

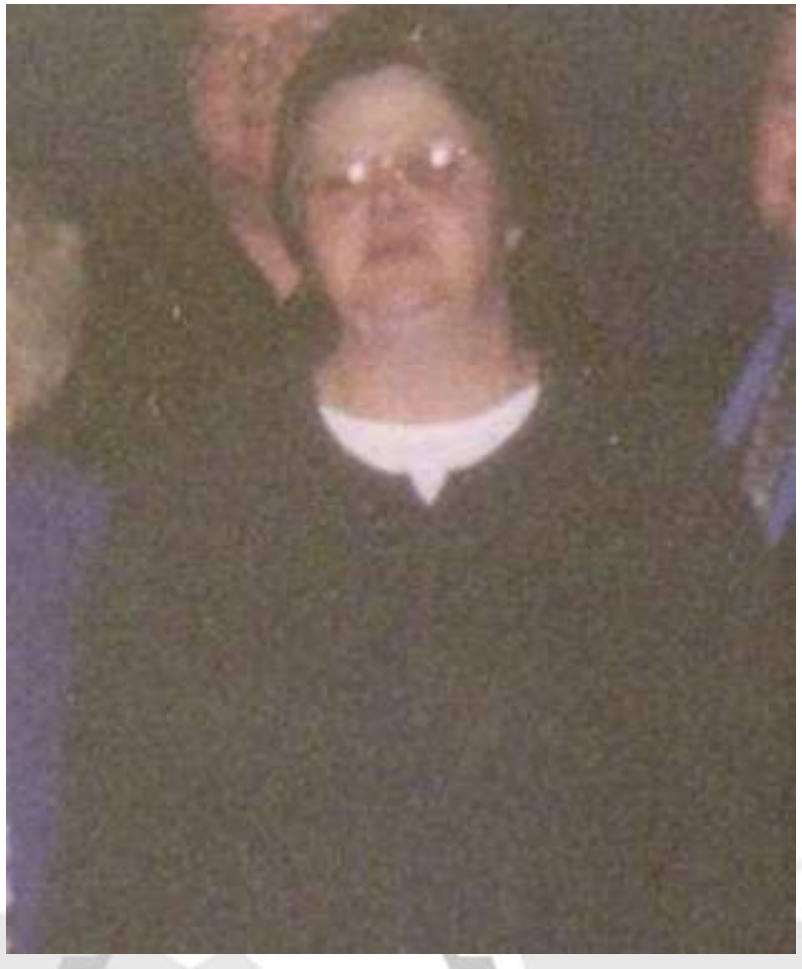
What Makes Neurotransmitters?

Microbes in the gut make neurotransmitters

Dopamine	Serotonin	GABA
	95%	

SYSTEMS PLAN

Sharon



Diane

A Second Key: Omega-3 And Brian Health

Suicide Risk Associated with Low Omega-3 Fatty Acids

By Kenneth J. Bender, PharmD, MA

October 8, 2011

Major Depressive Disorder, Military Mental Health, Suicide

"I'm all over it, because I'm looking for something to help," declared Army Vice-Chief of Staff General Peter W. Chiarelli, quoted in USA Today News September 20, in his response to a study finding an increased risk of suicide in US military personnel with low Omega-3 fatty acid serum levels.

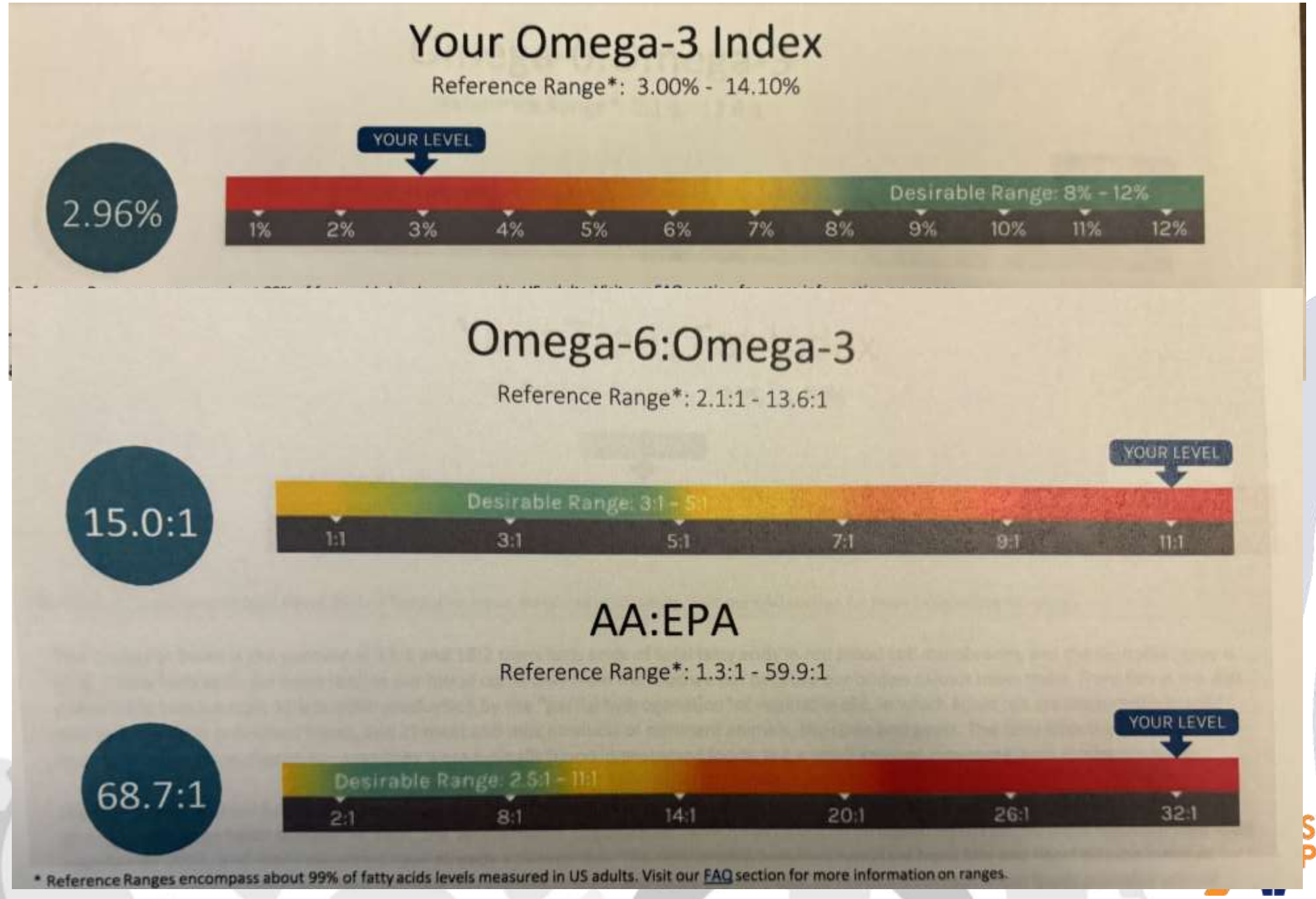
Omega 6 to Omega 3 Ratio 2:1 Ideal (18:1)

- Omega 6: processed foods and seed oils
- Omega 3: fish, nuts, supplements

SYSTEMS PLAN

Suicide

- Mother contacts me concerned for her 18-year-old daughter
- Tests?
- AA:EPA 68:1, anemic, terrible diet


Your Omega-3 Index
Reference Range*: 3.00% - 14.10%
YOUR LEVEL
2.96%
Desirable Range: 8% - 12%
1% 2% 3% 4% 5% 6% 7% 8% 9% 10% 11% 12%
Omega-6:Omega-3
Reference Range*: 2.1:1 - 13.6:1
15.0:1
YOUR LEVEL
Desirable Range: 3:1 - 5:1
1:1 3:1 5:1 7:1 9:1 11:1
AA:EPA
Reference Range*: 1.3:1 - 59.9:1
68.7:1
YOUR LEVEL
Desirable Range: 2.5:1 - 11:1
2:1 8:1 14:1 20:1 26:1 32:1
* Reference Ranges encompass about 99% of fatty acids levels measured in US adults. Visit our FAQ section for more information on ranges.

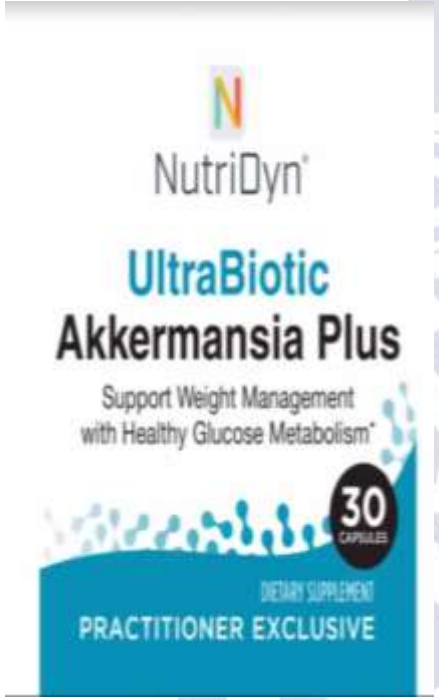
Antidepressants?

- Antidepressants increase the risk of suicide, violence and homicide at all ages
- The FDA admitted in 2007 that SSRIs can cause madness at all ages and that the drugs are very dangerous

7 SYSTEMS PLAN

Help Your Patients

- Maintain heathy NT levels (Digestive System)
- Decrease omega-6 (vegetable and seed oils)
- Increase omega-3 (take supplements)
- Test omega-6:omega-3 levels
- Use Probiotics
- Test: Omega-3 Index Plus test



7 SYSTEMS PLAN

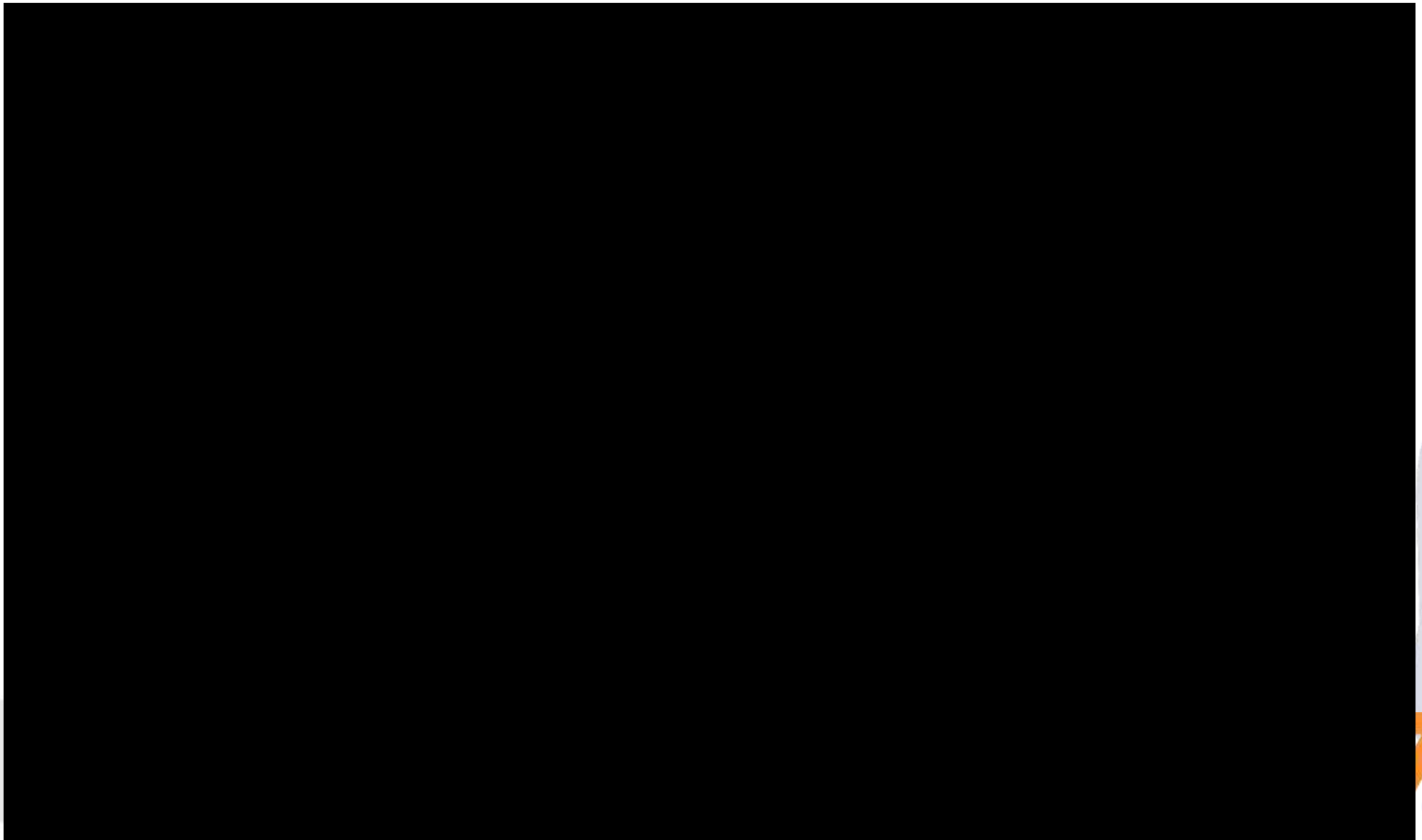
7 Systems Plan

Average American

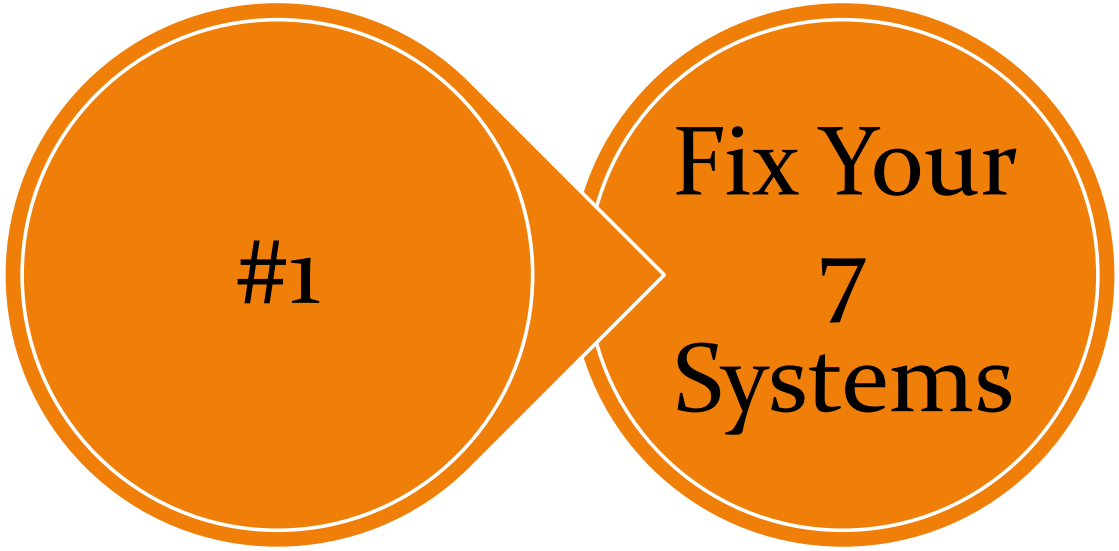
7 SYSTEMS PLAN

7 Systems Plan

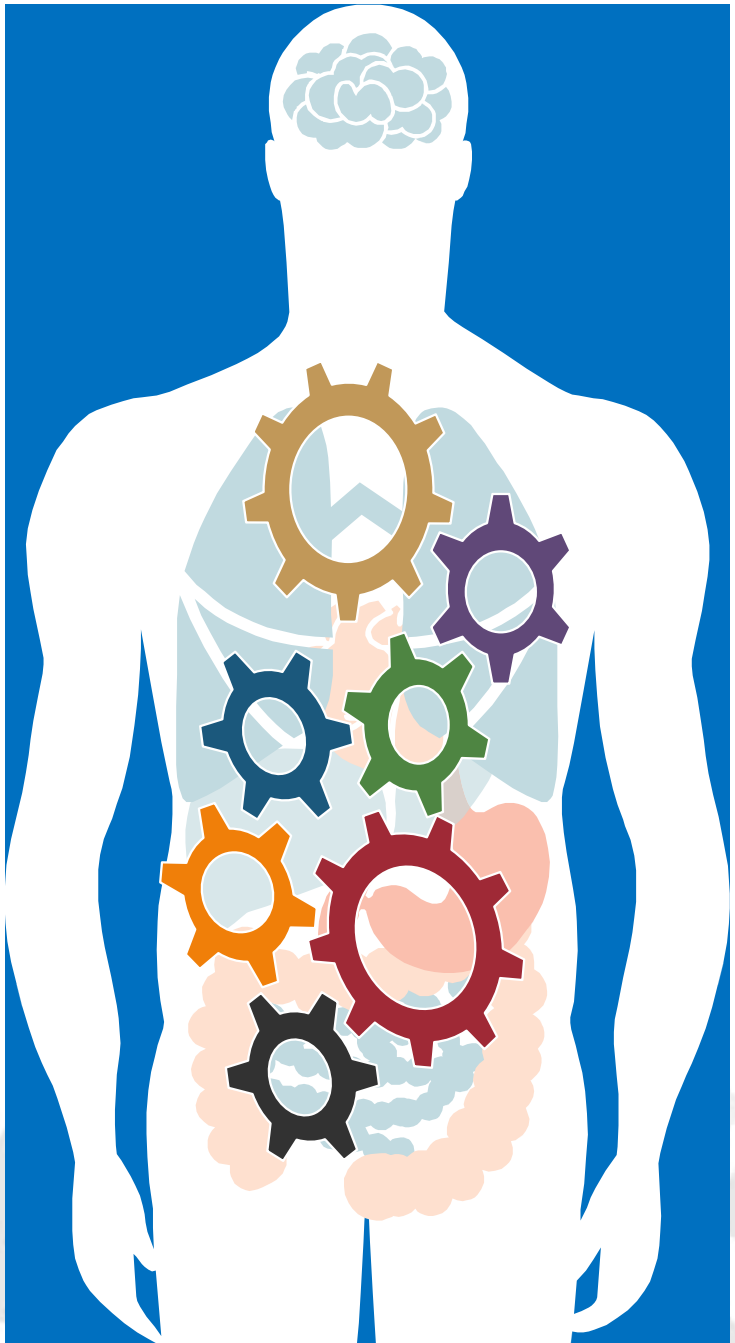
Average American



#1 Thing to do to Live Longer?



HEALTHSPAN WITH STRATEGIC PROTOCOLS TO IMPROVE WELLNESS



For Health, Weight Loss and Longevity

1. Structure
2. Digestive
3. Delivery
4. Energy
5. Communication
6. Defense
7. Detox

7 SYSTEMS PLAN

The Secrets to a Long and Healthy Life

7 SYSTEMS PLAN

Blue Zone- It Started with a Study

- The term “Blue Zone” refers to locations throughout the world that appear to be longevity hotbeds. In other words, it is believed that there are certain locations where residents live longer.

The Blue Zones: areas of exceptional longevity around the world

S.F. Vatner et al.

Rica; Sardinia, Italy; Ikaria, Greece; Okinawa, Japan (Buettner and Skemp, 2016; Huang and Mark Jacquez, 2017). In these areas the number of centenarians, i.e., those reaching the age of 100 is 10 times greater than the average in the United States. These regions are characterized by cultural preferences which discourage over-eating and

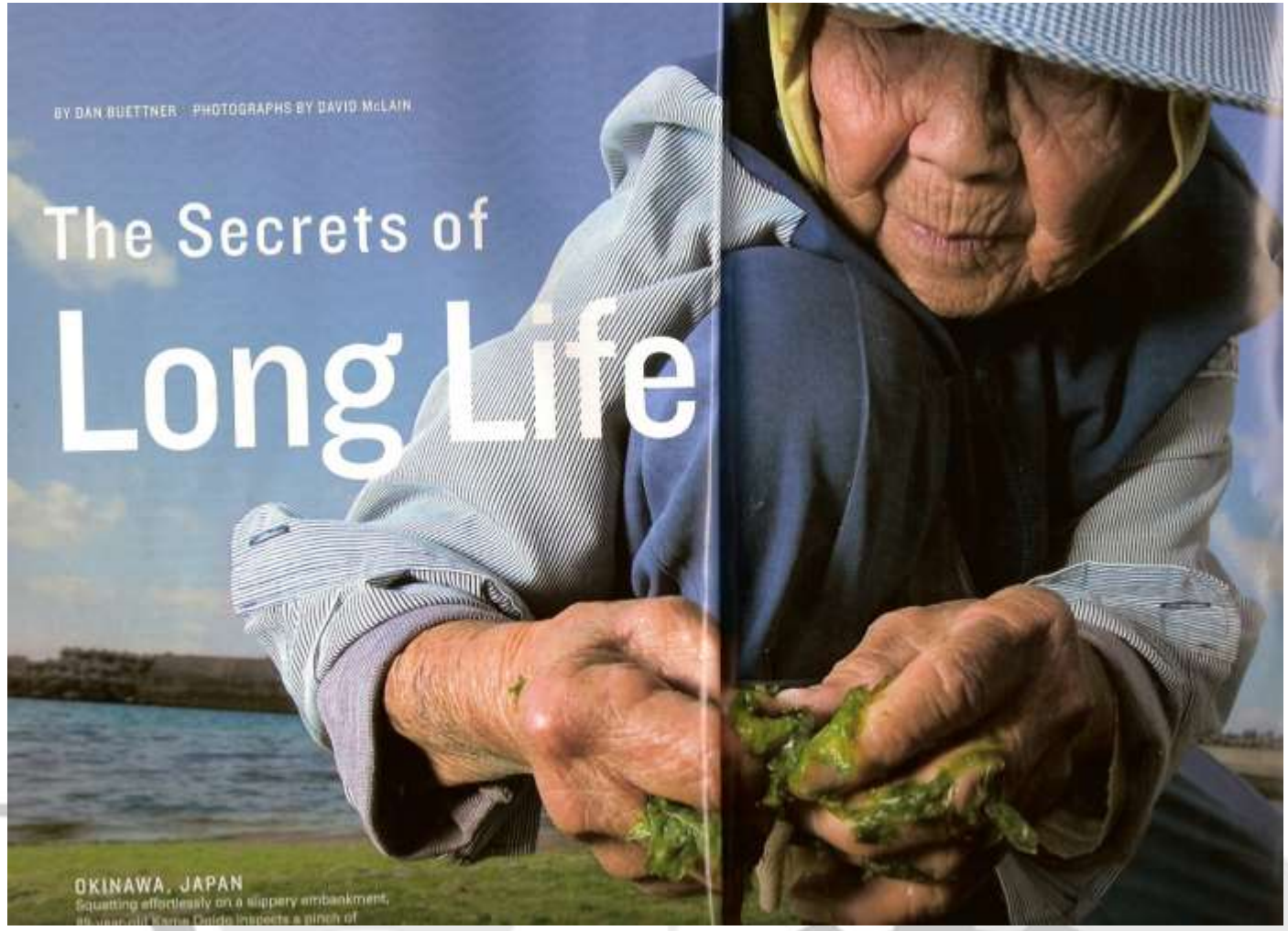
places where people tend to live unusually long lives. They are called "blue zones" because of the color used by one demographer to map these longevity "hotspots." With guidance of what he calls

reduce oxidative stress and protect against the deleterious effects of

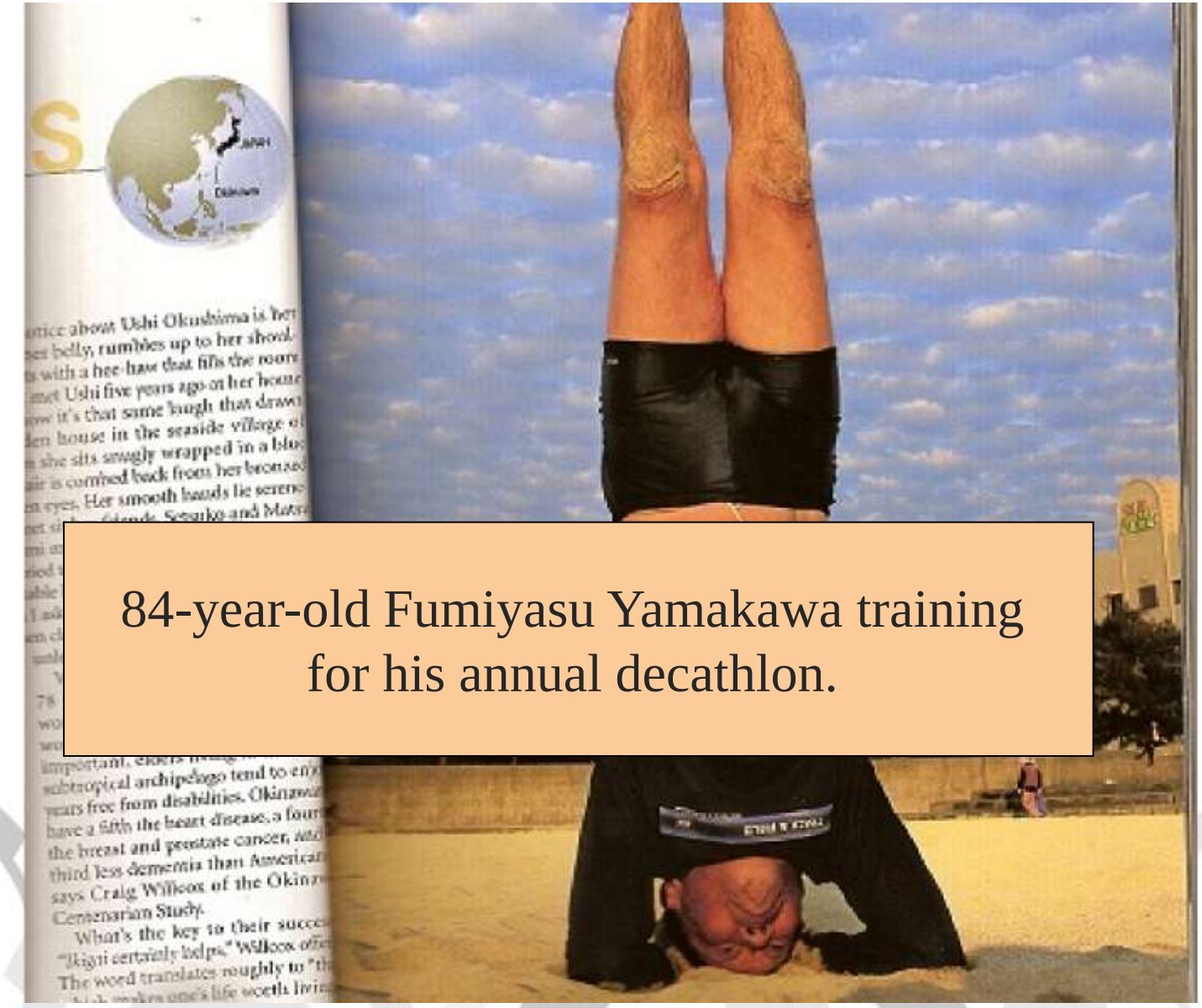
HEALTHSPAN WITH STRATEGIC PROTOCOLS TO IMPROVE WELLNESS

7 SYSTEMS PLAN

Okinawa


BY DAN BUETTNER · PHOTOGRAPHS BY DAVID McLAIN
The Secrets of
Long Life
OKINAWA, JAPAN
Squatting effortlessly on a slippery embankment,

Japan



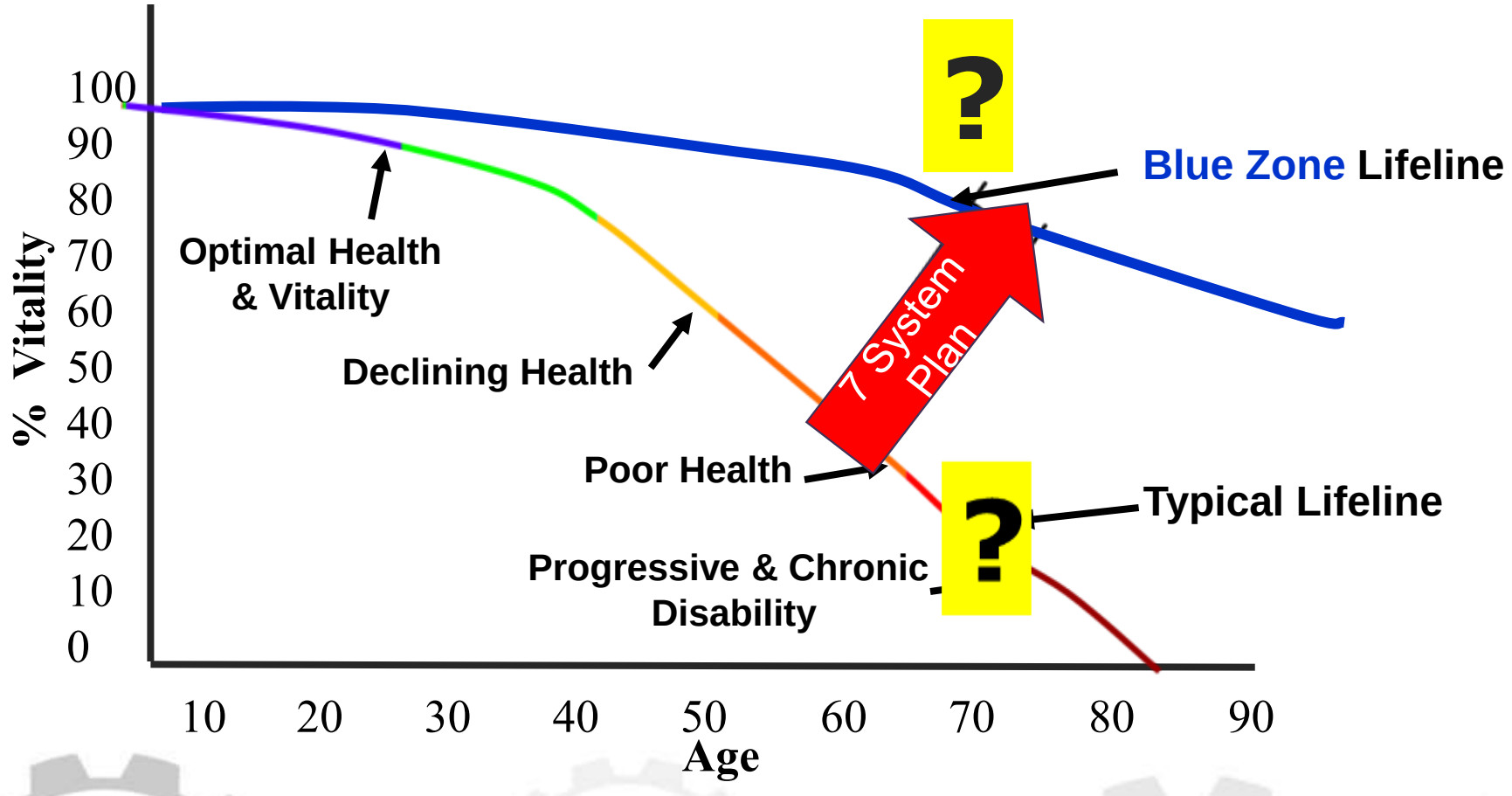
84-year-old Fumiyasu Yamakawa training for his annual decathlon.

Sardinia, Italy

- Nursing homes and senior living are a foreign language to 103-year-old Giovanni Sannai

Loma Linda, California

Blue Zone



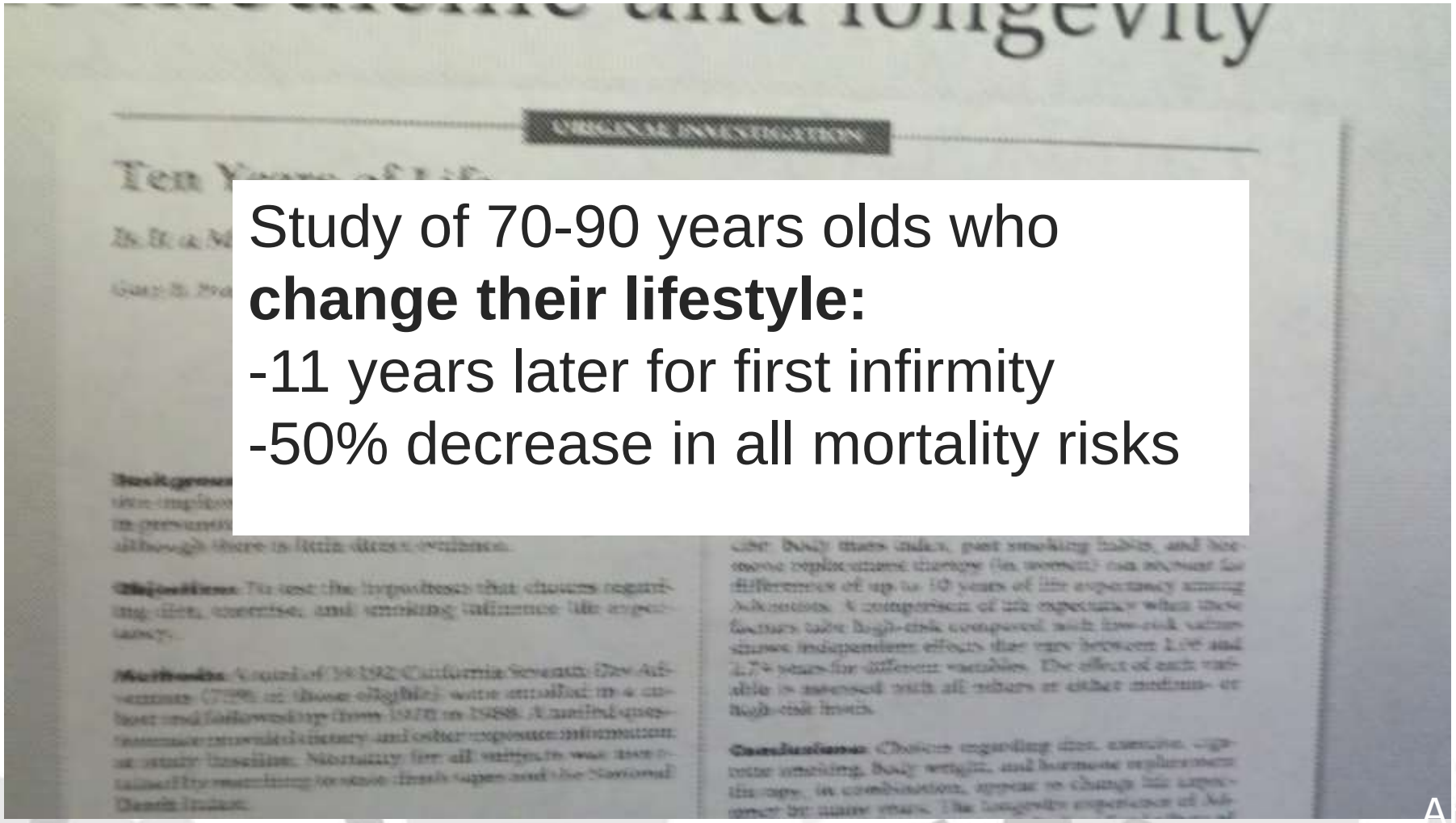
Fries, J. *NEJM*. 1980; 303:130-135.

Vita, AJ *et al*. *NEJM*. 1998;338:1035-1041.

7 SYSTEMS PLAN

If You Start at Age 70, Can You Still Make a Difference?

Get an Extra 10 Years of Life



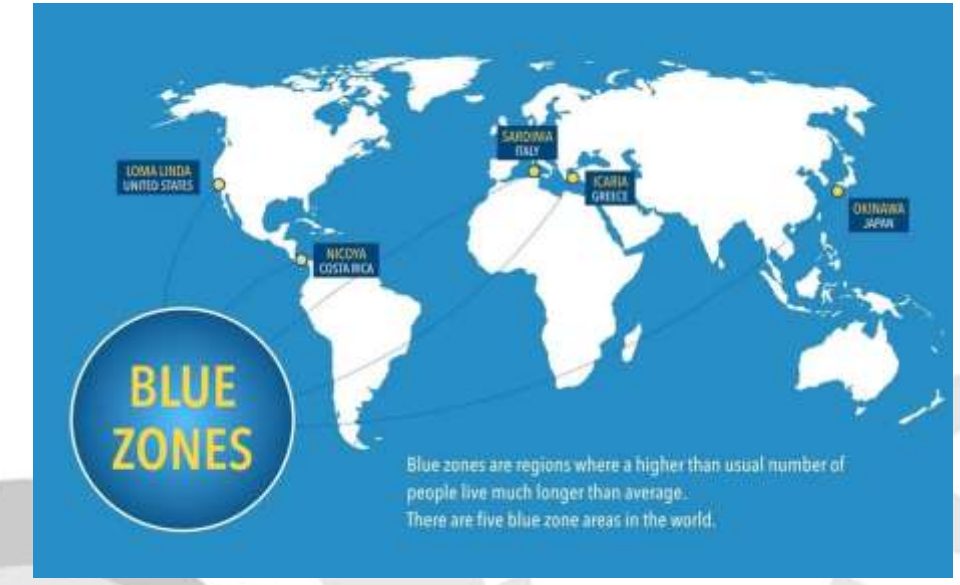
Study of 70-90 years olds who **change their lifestyle:**

-11 years later for first infirmity

-50% decrease in all mortality risks

Bob and Marian

9 Lessons From 100-Year-Olds in "The Blue Zones"



1. Move Naturally

- Emphasize incidental activities such as:
  - walking to work or school
  - cycling
  - walking when talking on the phone
  - work in your garden or yard with hand tools rather than mechanical conveniences.

2. Know Your Purpose

- Have a reason for waking up in the morning. According to the author, knowing your sense of purpose adds up to **seven years** to your life expectancy.

3. Take it Easy / Banish Stress

- Even people in the Blue Zones experience stress, but they've created **routines to shed stress**, whether it's meditating, napping, or going to happy hour like the Sardinians.

Perspective- Who is the Winner?

Perspective- Who Is The Winner?

Successful Stress Management

Benefits:

- Reduces risk for all chronic conditions
- Improves quality of life
- Conserves energy
- Restores sense of control
- Supports good choices
- Preserve organ health
- Helps control weight!!!

- Remember:

“Life isn’t about waiting for the storm to pass.
It’s about learning to dance in the rain.”

4. Don’t Overeat

- The Okinawans call it Hara Hachi Bu, and it’s a mantra that reminds them to stop eating when they’re **80% full**.

7 SYSTEMS PLAN

5. Eat plants

- **Beans** are a cornerstone of most centenarians' diets, with small portions of **meat** consumed five times per month on average.

6. Drink in Moderation, if you Choose

- Moderate and regular consumption of alcohol—1 to 2 drinks per day— is also a common theme among Blue Zone inhabitants.
- But only if this fits with your ethos—a group of Seventh-day Adventists in California abstain from alcohol and are still in a Blue Zone.

How Much?

Men- What Is The First Thing You See?

7. Belong to a Spiritual Community

- Belonging to a **spiritual community that shares beliefs** was a common theme among Blue Zone inhabitants.

Does Going to Church Cut Death Rates?

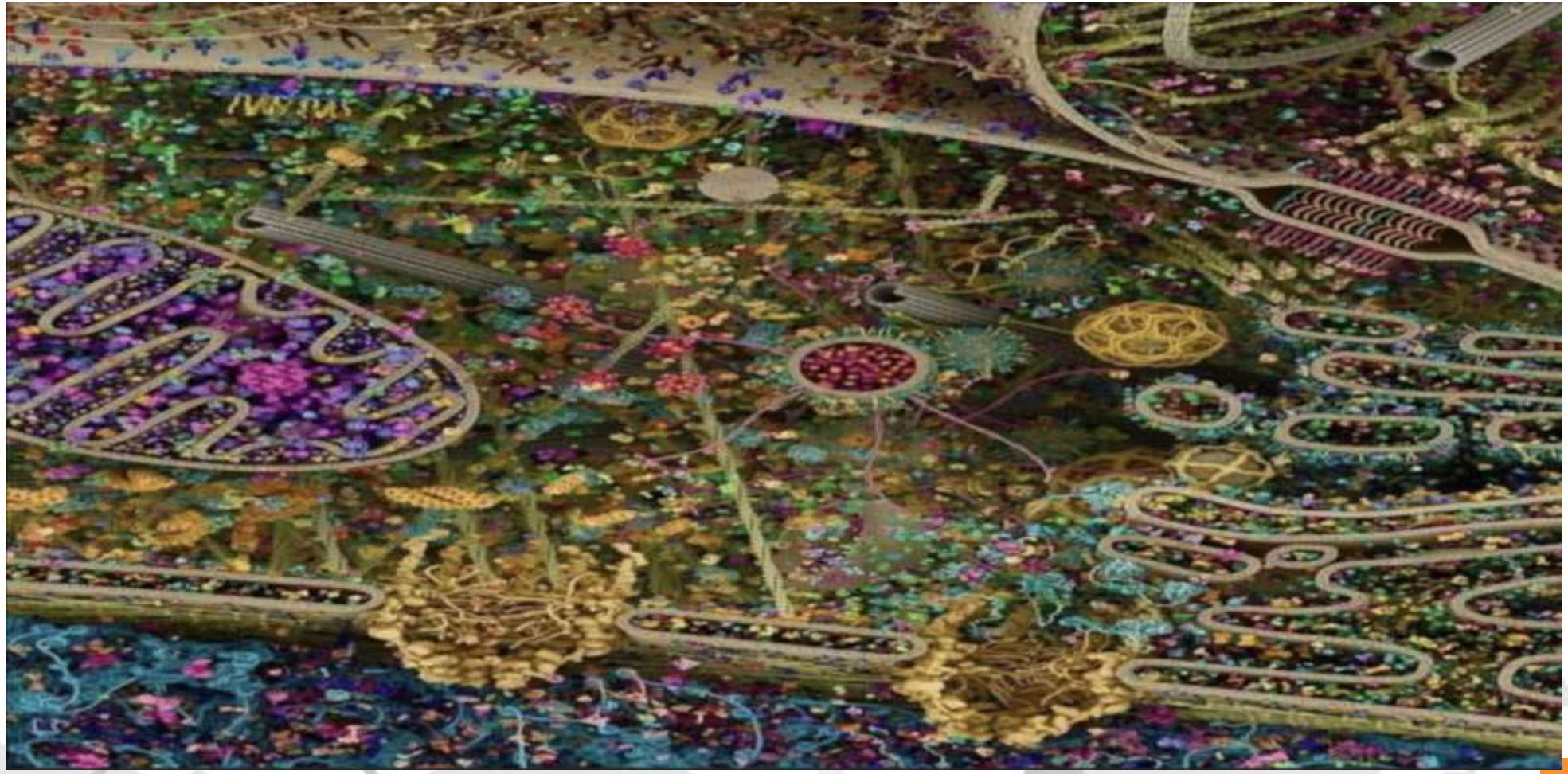
Results showed that people who attended a religious service at least once a week had a **20% lower risk of death from all causes**, compared with people who did not attend any religious services.

"Interestingly, the protection against mortality provided by religion **cannot be entirely explained by expected factors** that include enhanced social support of friends or family, lifestyle choices and reduced smoking and alcohol consumption,"

Journal of Psychology and Health. First published on November 17th 2008. DOI: 10.1080/08870440802311322

SYSTEMS PLAN

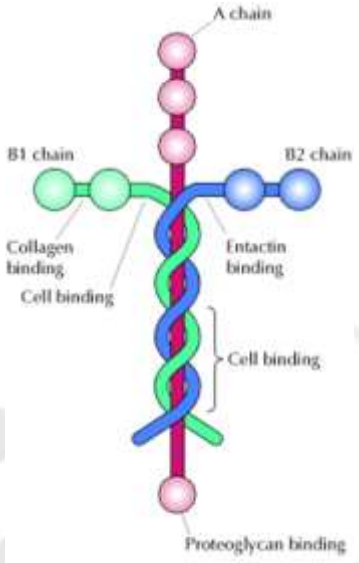
Image of Human Cell

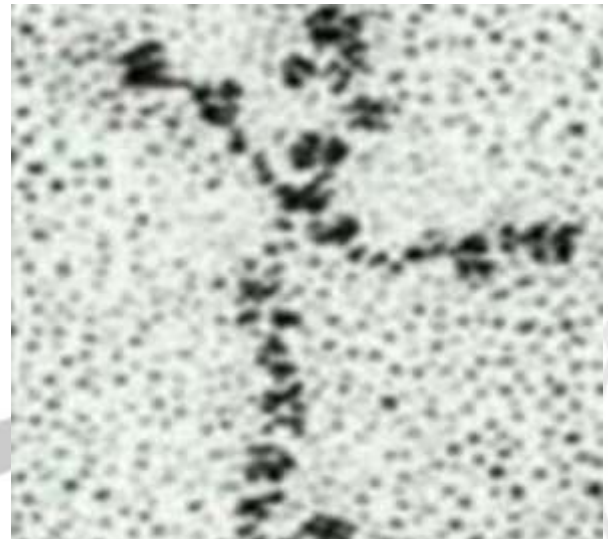


SYSTEMS PLAN

Laminin is a Cell Adhesion Molecule

- It's the stuff that holds the membranes of our bodies together.
- The shape of the "glue" that holds us together???
- Psalm 139:14 says, we are fearfully and wonderfully made.





Colossians 1:16-17

“For in him all things were created: things in heaven and on earth, visible and invisible, whether thrones or powers or rulers or authorities; all things have been created through him and for him.

He is before all things, and in him **all things hold together**.”

8. Put Loved Ones First

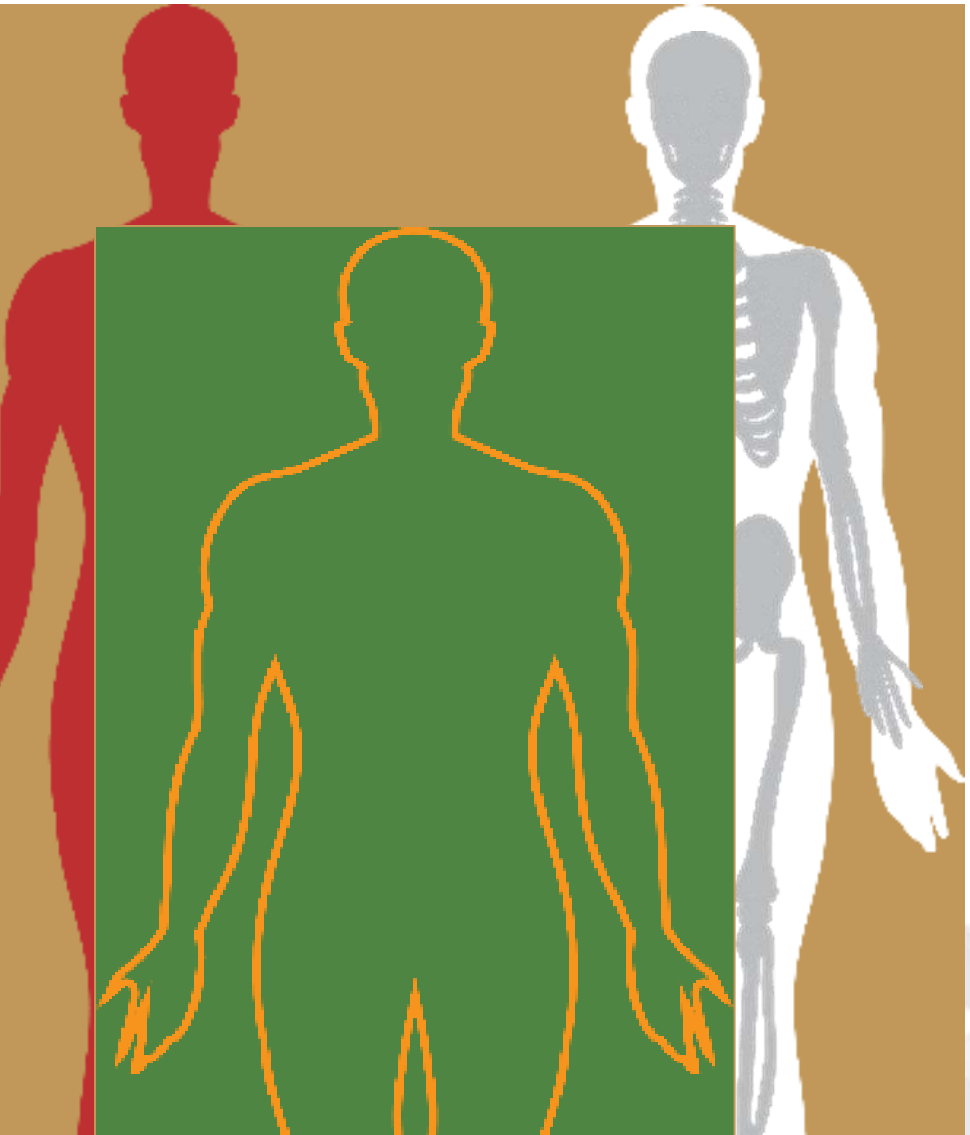
- Put families first, including investing in your children, committing to a partner, and keeping aging parents and grandparents nearby.

9. Stay Social

- Build a **social circle that supports healthy behaviors**. Happiness is contagious.

You Are Never Too Old-Don and Millie 91

STRUCTURAL SYSTEM



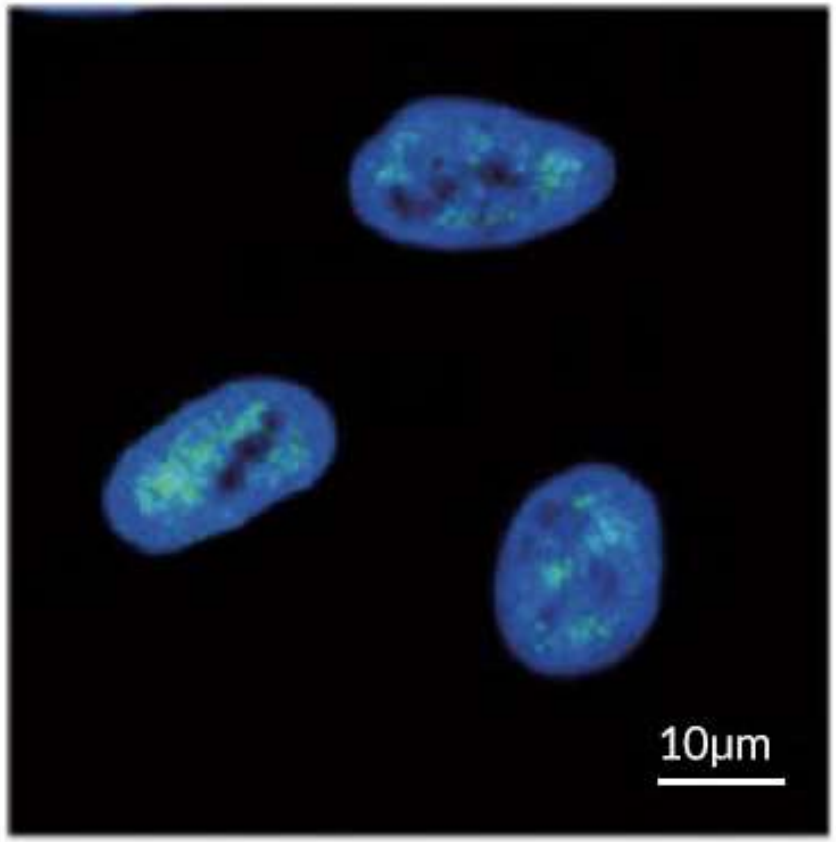
1. Bone
2. Muscle
3. Fat

A Powerful Tool for Longevity: Autophagy

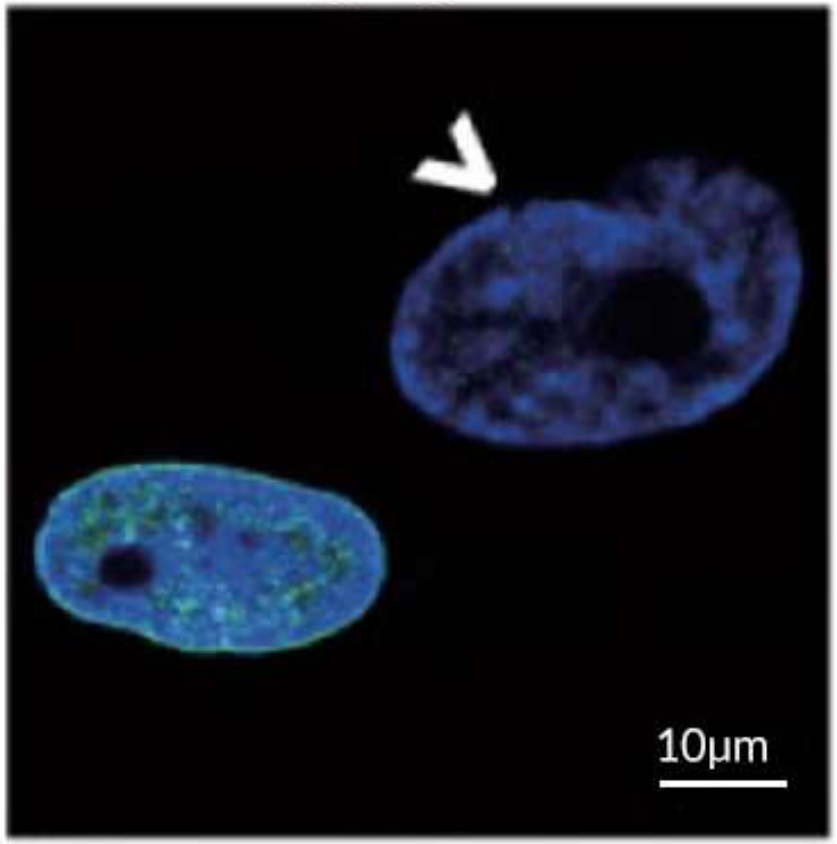
Autophagy

- Autophagy (Latin for **self-eating**) is a process that occurs when the body cleanses damaged cells by "eating them."
- Cells use autophagy to degrade their old and damaged parts to:
  - repair cells
  - generate new cells
  - generate energy

Normal Cell



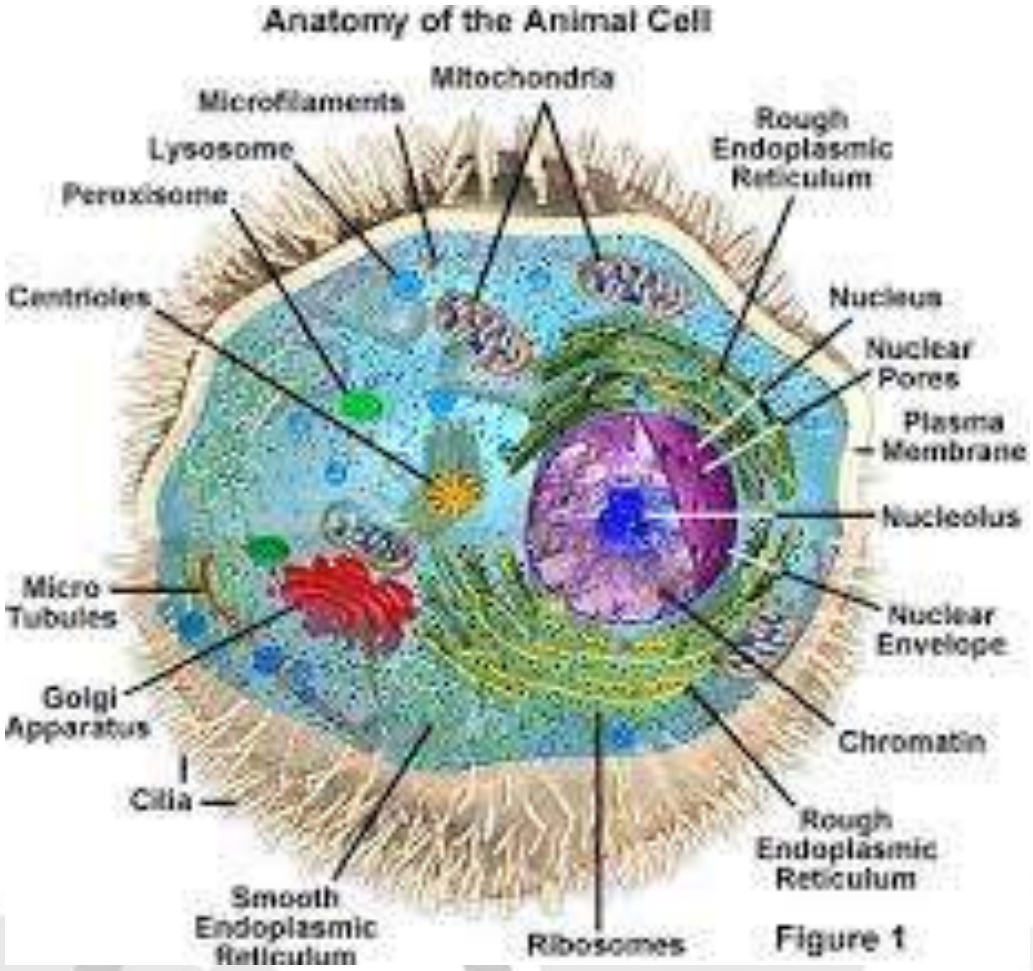
Aging Cell

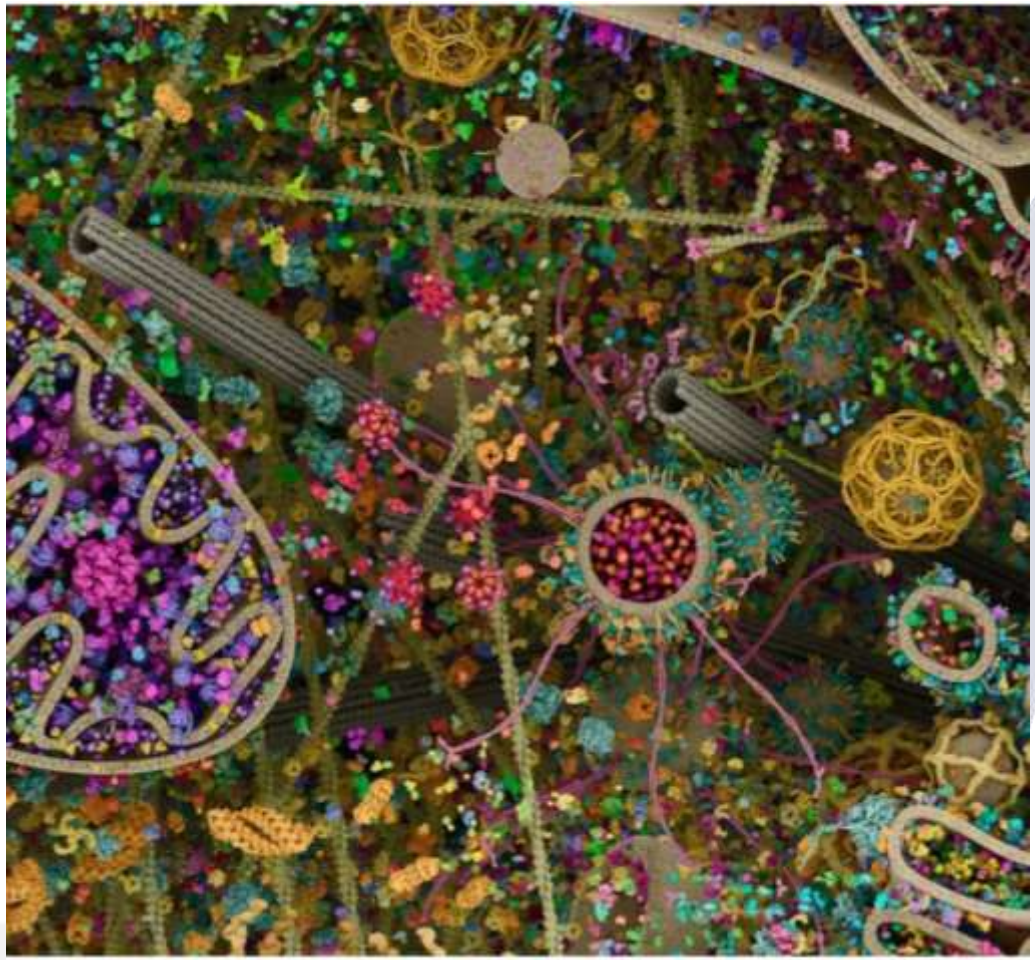


SYSTEMS PLAN

SYSTEMS PLAN

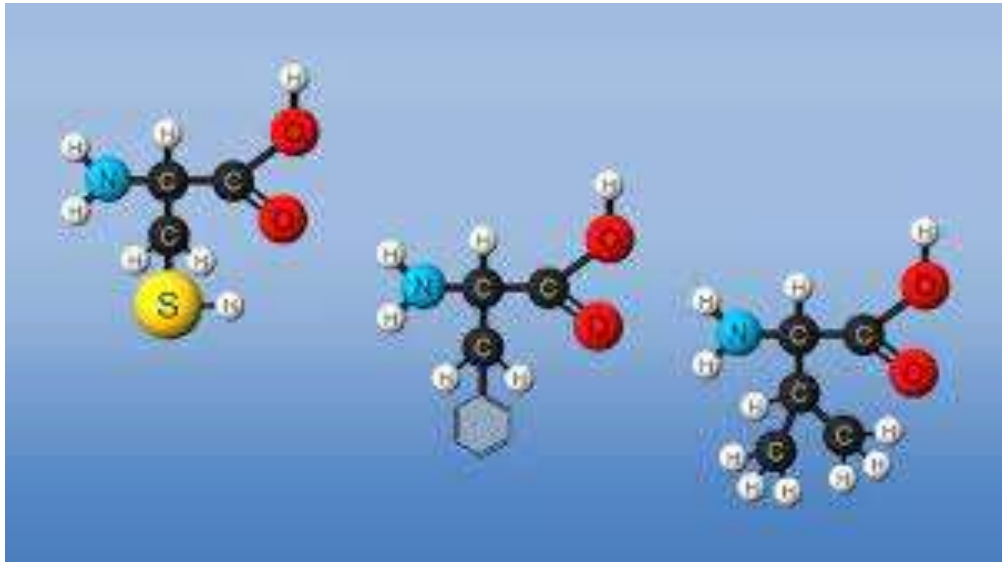
Cell





SYSTEMS PLAN

Old Proteins

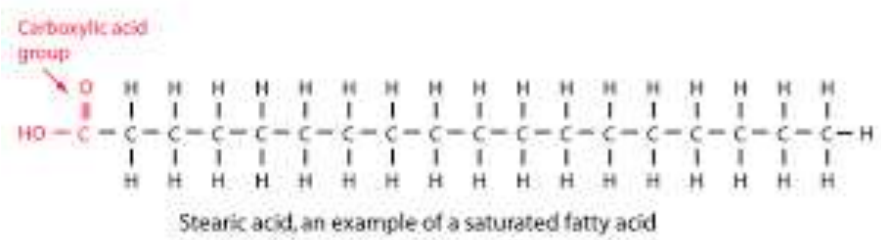


- Burned for energy
- Broken into component amino acids
- Used to make new cells

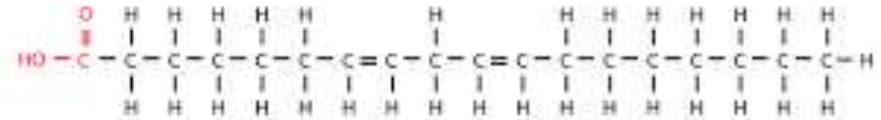
Before Autophagy

After Autophagy

Old Fats



Stearic acid, an example of a saturated fatty acid



Linoleic acid, an example of an unsaturated fatty acid

- Burned for energy
- Broken into component fatty acids
- Used to make new cells

SYSTEMS PLAN

Before Autophagy

After Autophagy

SYSTEMS PLAN

How to Stimulate Autophagy

Deplete stored glucose (glycogen)

- Fasting
- TRE
- Calorie restriction

Stimulate Autophagy

- Exercise
- Foods- coffee, tea, mushrooms,
- Spermidine

How to Stimulate Autophagy

Deplete stored glucose

- **Fasting**
- TRE
- Calorie restriction

How Much Glycogen do We Store?

- A healthy adult body can store about 500 grams of carbohydrate
  - **Skeletal muscles** store about **400** grams or glycogen
  - The **liver** stores **100** grams of glycogen
  - Your **blood** circulates roughly **25** grams as glucose

This means your body is capable of storing about 2,000 calories of carbohydrates.

-

FASTING

- The greatest acceleration of autophagy takes place after 24-48 hours of fasting.

cient to interfere with autophagy. There is already a substantial amount of leucine present in blood and cells in your body, and the small amount of leucine in the stevia will not have much of an effect. Another comment is that 5 days of fasting is too long for activating autophagy. The greatest acceleration of autophagy takes place after 24–48 h of fasting.

Fasting For The Treatment Of Psoriasis

10-day water fast

Whole food diet

Psoriasis

Figure 1. Right hand before fasting

Figure 3. Left and right feet before fasting

- Autoimmune disease
- Most develop psoriasis first
- Then Psoriatic Arthritis

SYSTEMS PLAN

After 10 Day Water Fast

Figure 1. Right hand before fasting

Figure 3. Left and right feet before fasting

4 Month Follow-up on Whole Food Diet




SYSTEMS PLAN

How to Stimulate Autophagy

Deplete stored glucose

- Fasting
- **TRE**
- Calorie restriction

TRE and Autophagy

Eat dinner

Sleep

No breakfast (17)- some autophagy?

No lunch (24)- Accelerated autophagy

SYSTEMS PLAN

Time Restricted Eating and Autophagy

17 hour fast?

24 hour fast

Prolonged fasting (2 days or more)

Exercise

- Autophagy is activated in skeletal muscle in response to exercise.
- 30 minutes of exercise was sufficient to induce GFP-LC3 puncta (autophagosome) formation.

Autophagy-Dependent Beneficial Effects of Exercise – PMC www.ncbi.nlm.nih.gov/pmc/articles/PMC5538402/

Boosting Autophagy with Exercise

Fast

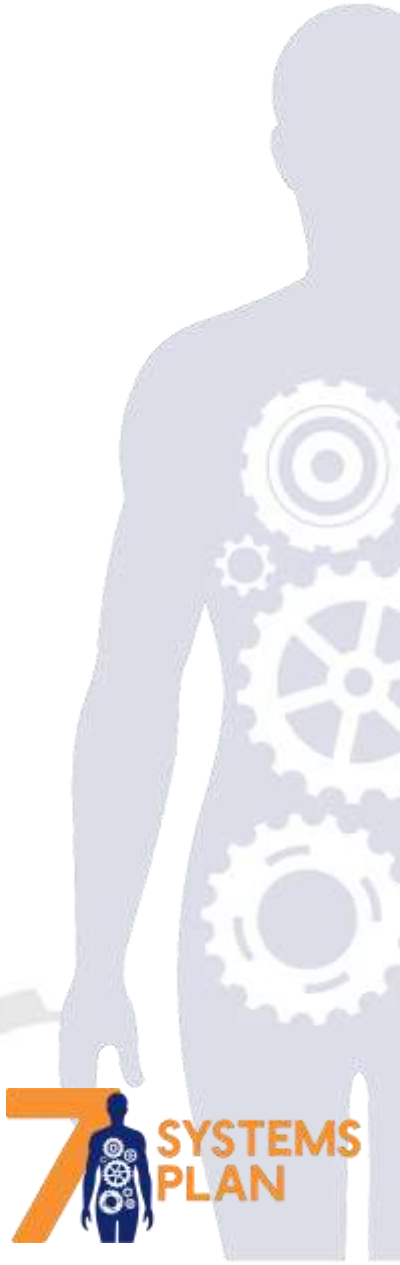
17 hours

+ Exercise

Autophagy activated

My Thursdays

- No breakfast
- No lunch
- Tennis
- **Significant autophagy**
- Eat dinner



7 SYSTEMS PLAN

Action Steps

- Use fasting (under doctor supervision)
- Use time restricted eating (17 and 24)
- Combine with exercise for more benefit

How to Stimulate Autophagy

Deplete store glucose

- Fasting and TRE
- **Calorie restriction**

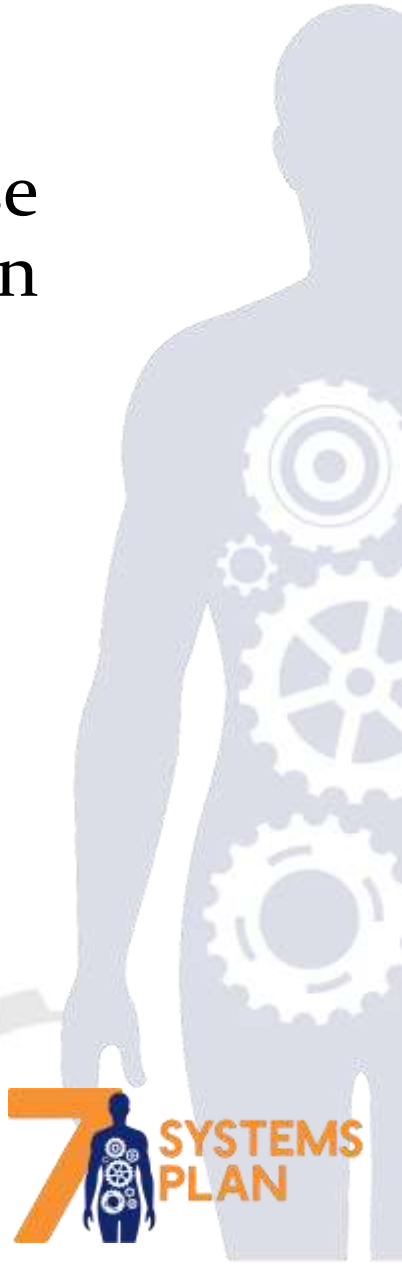
The Health Benefits of Calorie Restriction

SYSTEMS PLAN

mTOR
A Master Determinant of Lifespan and Aging

Mammalian target of rapamycin (mTOR) is a protein kinase that regulates many cellular processes. It tells the cells when to:

- grow
- divide
- and how to survive



SYSTEMS PLAN

Too Much mTOR

- Shorter life
- Cancer
- Many chronic health problems

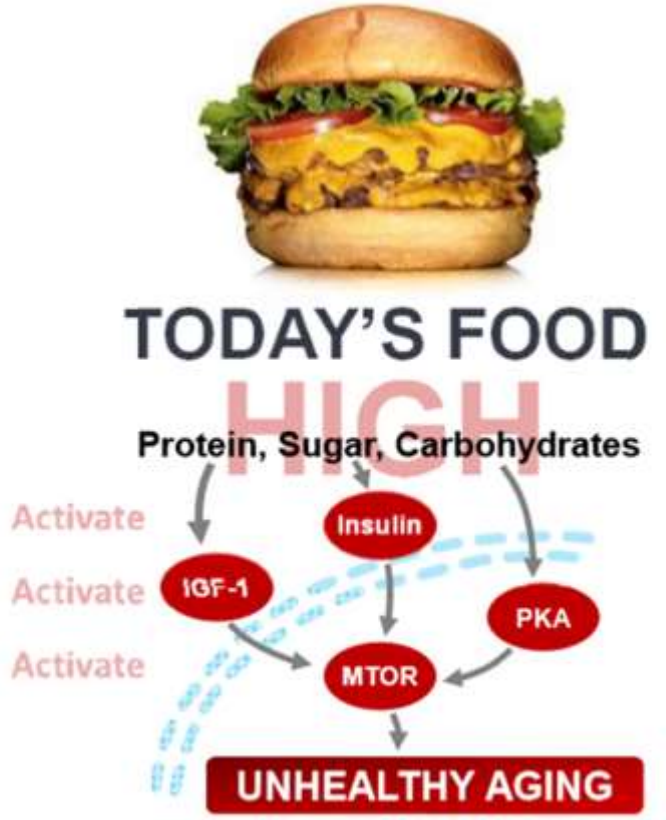
To Little mTOR

- Muscle atrophy
- Delayed healing
- Less insulin sensitivity

SYSTEMS PLAN

High MTOR Causes

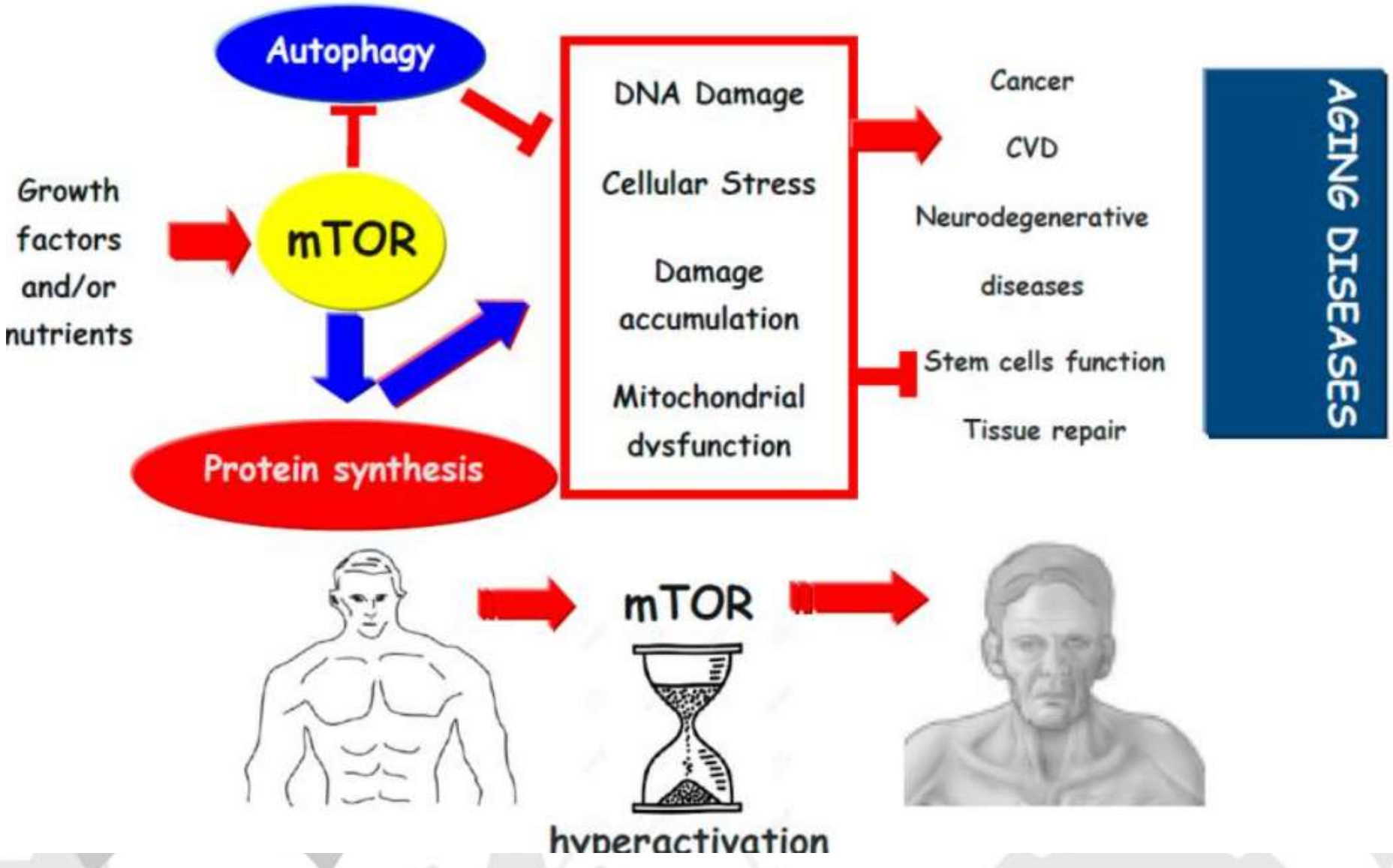
- Oxidative stress
- Mitochondria damage
- Inflammation
- Depleted stem cells
- Decreased autophagy
- Increase zombie cells



SYSTEMS PLAN

The Action of mTOR (Motor)

- The action of mTOR has been described as the engine of a speeding car without brakes.


Autophagy
Growth factors and/or nutrients
mTOR
Protein synthesis
DNA Damage
Cellular Stress
Damage accumulation
Mitochondrial dysfunction
Cancer
CVD
Neurodegenerative diseases
Stem cells function
Tissue repair
AGING DISEASES
mTOR
hyperactivation

A New Antiaging Drug

- **"By targeting a key pathway (mTOR) in cells, this drug has been shown to extend lifespan in animals and could be beneficial to prevent age-related diseases in humans**," Dr. Andrea B. Maier — a professor in healthy aging and dementia research at the Director of the Centre for Healthy Longevity at the National University of Singapore.

7 SYSTEMS PLAN

High mTOR

Low mTOR

Sioux Falls to Mt. Rushmore

Children

Adults

mTOR and Autophagy

- When food is abundant, mTOR activity goes up, prompting the cells in our body to divide (**grow**).
- When mTOR detects that food is scarce, it shifts the body into conservation mode, slowing down cell division and kicking in a process called **autophagy**, meaning eating yourself (**repair, recycle, remove**).

mTOR

Autophagy

Calorie Restriction and Autophagy

- Add image

Too Many Calories

Calorie Restriction

SYSTEMS PLAN

Calorie Restriction Benefits

- Studies show if you eat 1/3 less you may live 24 years longer!
- You will be significantly healthier and stronger.
- By simply restricting calories by 30% you may get up to 30% more quality life.

Calorie Restriction in Primates: Will It Work and How Will We Know?

George S. Roth, PhD, Donald K. Ingram, PhD, and Mark A. Lane, PhD

Dietary caloric restriction is the most robust and reproducible means of slowing aging and extending lifespan and healthspan in short-lived mammals and lower organisms. Numerous aspects of this paradigm have been investigated in laboratories around the world since its inception more than 60 years ago. However, two questions about calorie restriction remain unanswered to this day: (1) By what mechanism does it work? and (2) Will it work in humans? This review will focus on the latter with particular emphasis on evaluation criteria, current studies in primate models, available data, and plans for actual human caloric restriction

age and weight until full 30% restriction was achieved. After weight stabilization, which required a period of slowed growth and maturation in prepubertal animals, food allotments were adjusted when necessary to maintain constant body mass. In addition, although the beneficial response is graduated and biphasic, optimal CR in rodents is generally about 40%.[1] However, health concerns in monkeys at higher levels rendered 30% restriction a more prudent strategy. CR monkeys achieved approximately 20% lower weight than AL fed controls (Figure 1) and maintained their weight throughout the study.

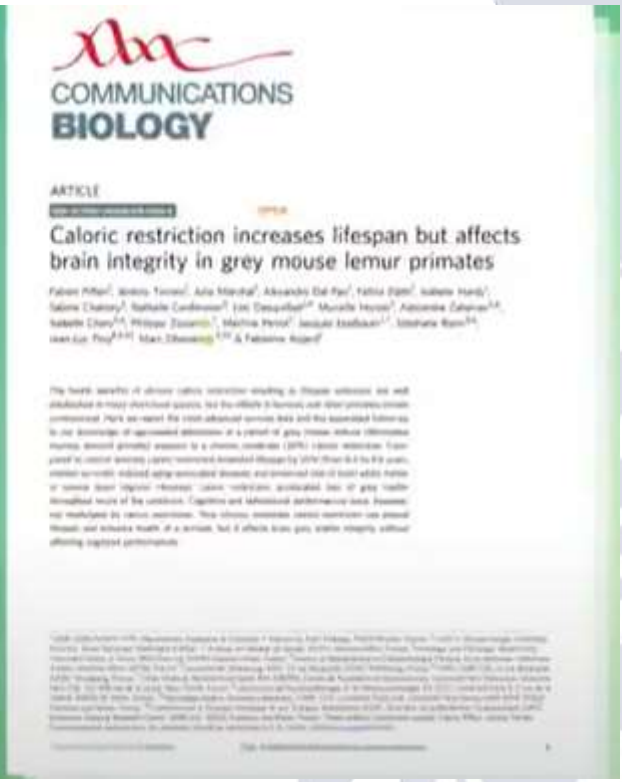
Four Studies

Mortality and Morbidity in Laboratory-maintained Rhesus Monkeys and Effects of Long-term Dietary Restriction

LETTER

Impact of caloric restriction on health and survival in rhesus monkeys from the NIA study

Caloric Restriction Delays Disease Onset and Mortality in Rhesus Monkeys



COMMUNICATIONS BIOLOGY

ARTICLE

Caloric restriction increases lifespan but affects brain integrity in grey mouse lemur primates

SYSTEMS PLAN

Eat when want Diet Calorie Restricted

Source: Reproduced from Life Extension Magazine

Candi

SYSTEMS PLAN

SYSTEMS PLAN

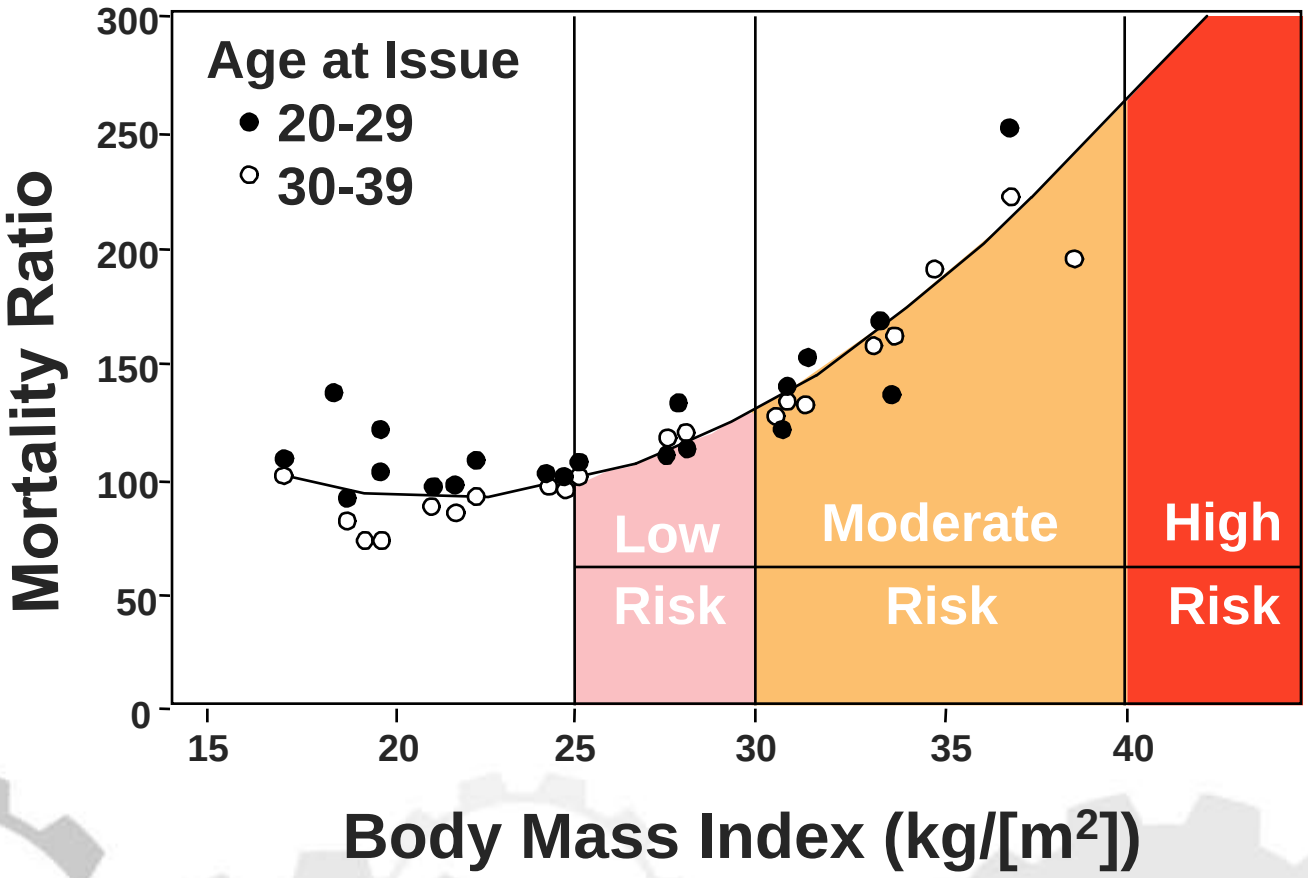
Okinawa

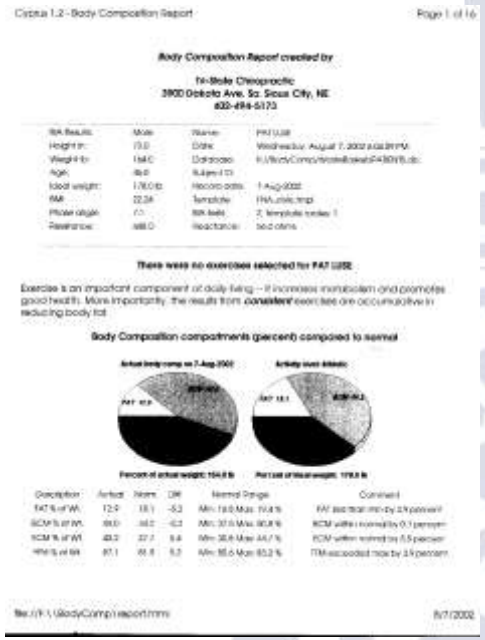
- Most **centenaries** per capita
- Consume 38% less calories than the Japanese

Thinner People Live Longer

- Vilcabama of South America
- Central European Caucasians
- Hunza of the Himalayas
- **Average BMI for centenaries?**

Relationship of BMI To Excess Mortality





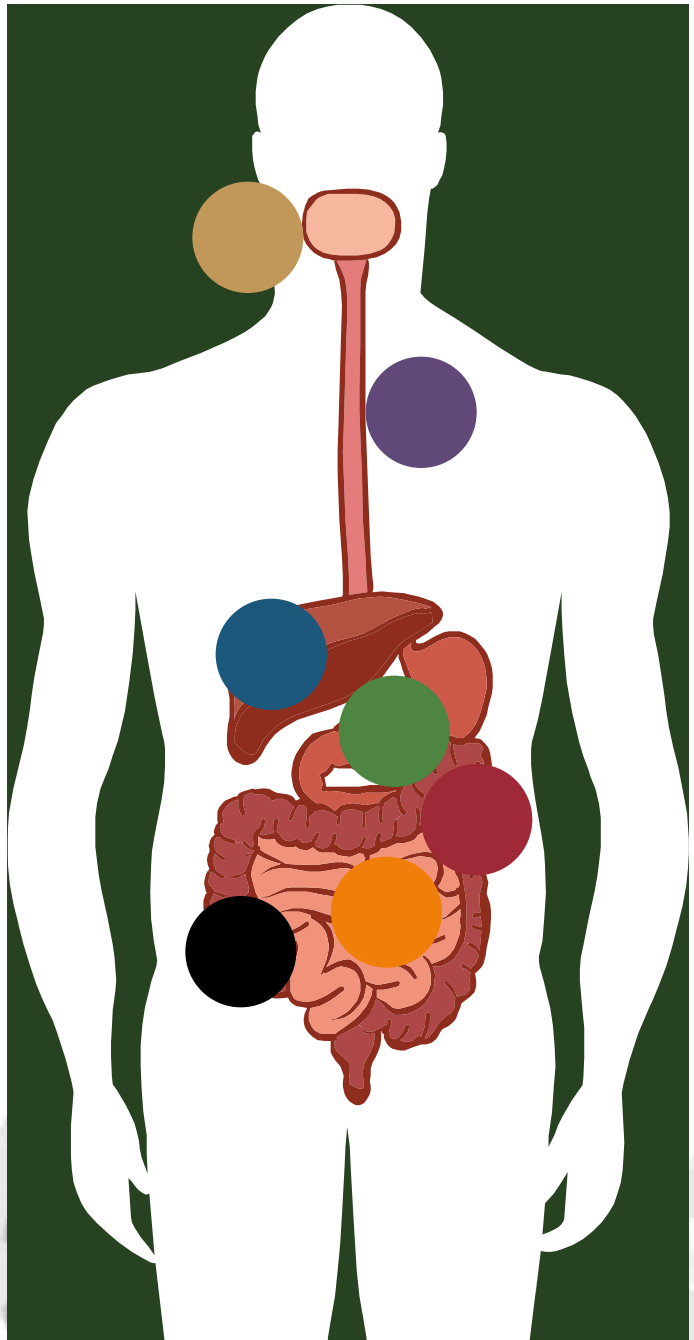
Bray GA. Overweight is risking fate. Definition, classification, prevalence and risks. *Ann NY Acad Sci* 1987;499:14-28.

7 SYSTEMS PLAN

Calorie Restriction Action Steps

- Don’t eat less, eat differently to restrict calories and stimulate autophagy
- Follow the 7 Systems Plan

DIGESTIVE SYSTEM



1. Mouth
2. Esophagus
3. Stomach
4. Liver
5. Pancreas
6. Small Intestine
7. Colon

SYSTEMS PLAN

Your Most Important Organ?

Fitoterapia 82 (2011) 53–66

The intestinal microbiome: A separate organ inside the body with the metabolic potential to influence the bioactivity of botanicals

For many years, it was believed that the main function of the large intestine was the resorption of water and salt and the facilitated disposal of waste materials.

Keywords:
Polyphenols
Gut bacteria
Phytoestrogens
Bioavailability
Degradation
Nutraceuticals

A B S T R A C T

For many years, it was believed that the main function of the large intestine was the resorption of water and salt and the facilitated disposal of waste materials. However, this task definition was far from complete, as it did not consider the activity of the microbial content of the large intestine. Nowadays it is clear that the complex microbial ecosystem in our intestines should be considered as a separate organ within the body, with a metabolic capacity which exceeds the liver with a factor 100. The intestinal microbiome is therefore closely involved in the first-pass metabolism of dietary compounds. This is especially true for botanical supplements, which are now marketed for various health applications. Being of natural origin, their structural building blocks, such as polyphenols, are often highly recognized by the human and especially the intestinal microbial metabolism machinery. Intensive metabolism results in often low circulating levels of the original products, with the consequence that final health effects of botanicals are often related to specific active metabolites which are produced in the body rather than being related to the product's original composition. Understanding how such metabolic processes contribute to the *in situ* exposure is therefore crucial for the proper interpretation of biological responses. A multidisciplinary approach, characterizing the food

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The Problem

Cell Metab. 2014 Nov 4;20(5):779-86

Starving our Microbial Self: The Deleterious Consequences of a Diet Deficient in Microbiota-Accessible Carbohydrates

Erica D. Sonnenburg[1] and Justin L. Sonnenburg[1,*]
[1]Department of Microbiology and Immunology, Stanford University School of Medicine, 259 Campus Drive, Stanford, CA 94305, USA
*Correspondence: jsonnenburg@stanford.edu

The gut microbiota of a healthy person may not be equivalent to a healthy microbiota. It is possible that the Western microbiota is actually dysbiotic and predisposes individuals to a variety of diseases. The asymmetric plasticity between the relatively stable human genome and the more malleable gut microbiome suggests that incompatibilities between the two could rapidly arise. The Western lifestyle, which includes a diet low in microbiota-accessible carbohydrates (MACs), has selected for a microbiota with altered membership and functionality compared to those of groups living traditional lifestyles. Interactions between resident microbes and host leading to immune dysregulation may explain several diseases that share inflammation as a common basis. The low-MAC Western diet results in poor production of gut microbiota-generated short-chain fatty acids (SCFAs), which attenuate inflammation through a variety of mechanisms in mouse models. Studies focused on modern and traditional societies, combined with animal models, are needed to characterize the connection between diet, microbiota composition, and function. Differentiating between

SYSTEMS PLAN

Cell Metab. 2014 Nov 4;20(5):779-86

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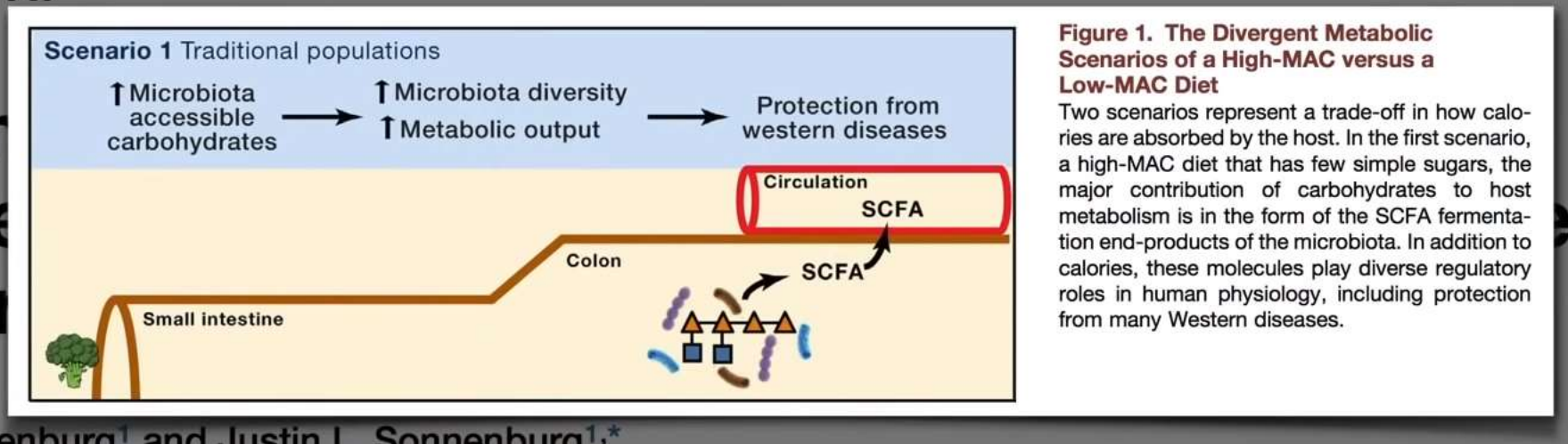

Figure 1. The Divergent Metabolic Scenarios of a High-MAC versus a Low-MAC Diet

Two scenarios represent a trade-off in how calories are absorbed by the host. In the first scenario, a high-MAC diet that has few simple sugars, the major contribution of carbohydrates to host metabolism is in the form of the SCFA fermentation end-products of the microbiota. In addition to calories, these molecules play diverse regulatory roles in human physiology, including protection from many Western diseases.

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Burkitt reported that rural Africans passed stool that was up to five times greater by mass, had intestinal transit times that were more than twice as fast, and ate three to seven times more dietary fiber (60–140 g versus 20 g) than their Western counterparts

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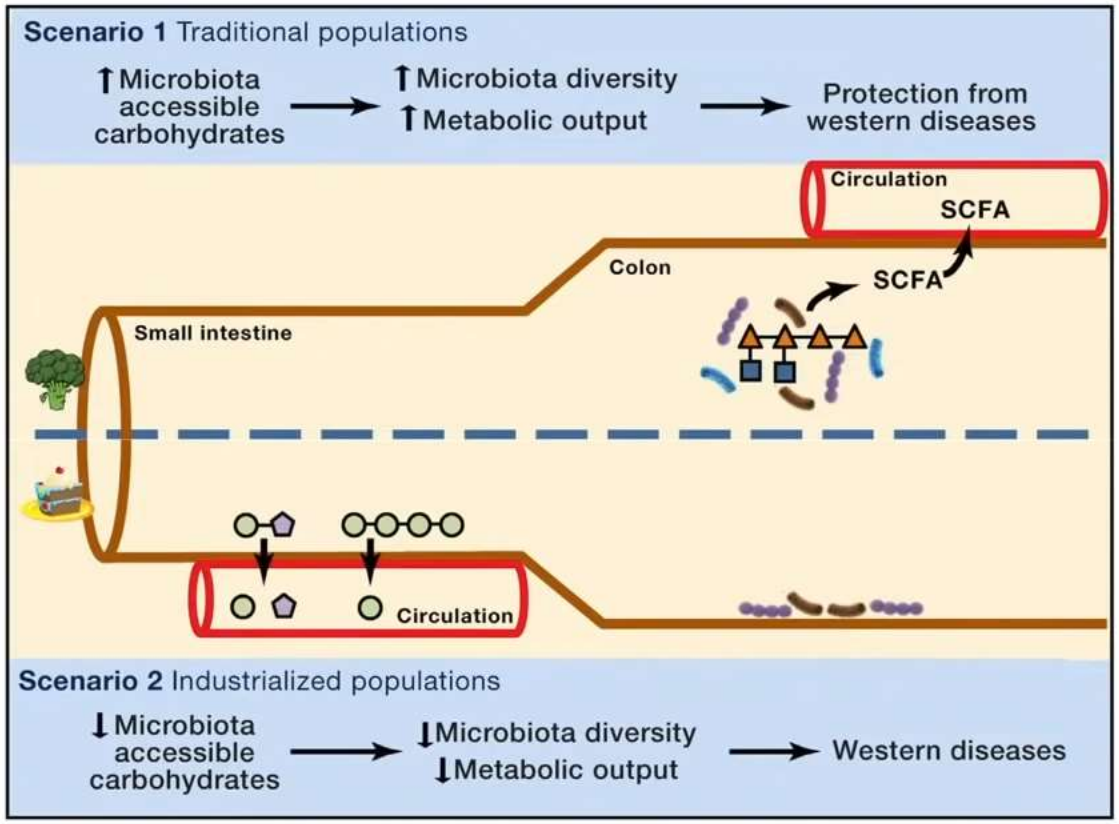

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Starving our Microbial Self: The Deleterious Consequences of a Diet Deficient in Microbiota-Accessible Carbohydrates

dietary plant material, commonly referred to as dietary fiber, which is the most common fuel for the microbiota

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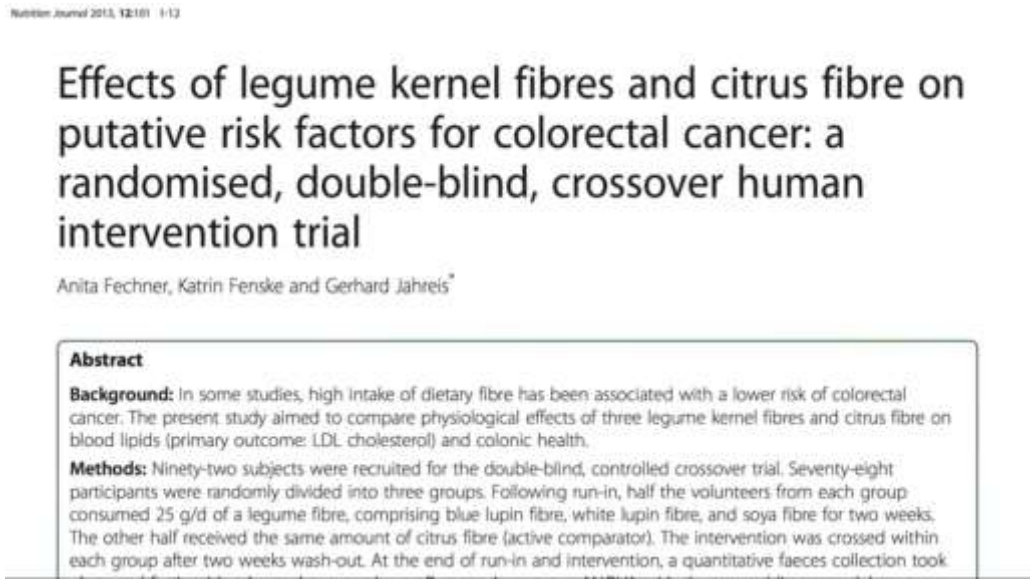
Does Adding Fiber Help?



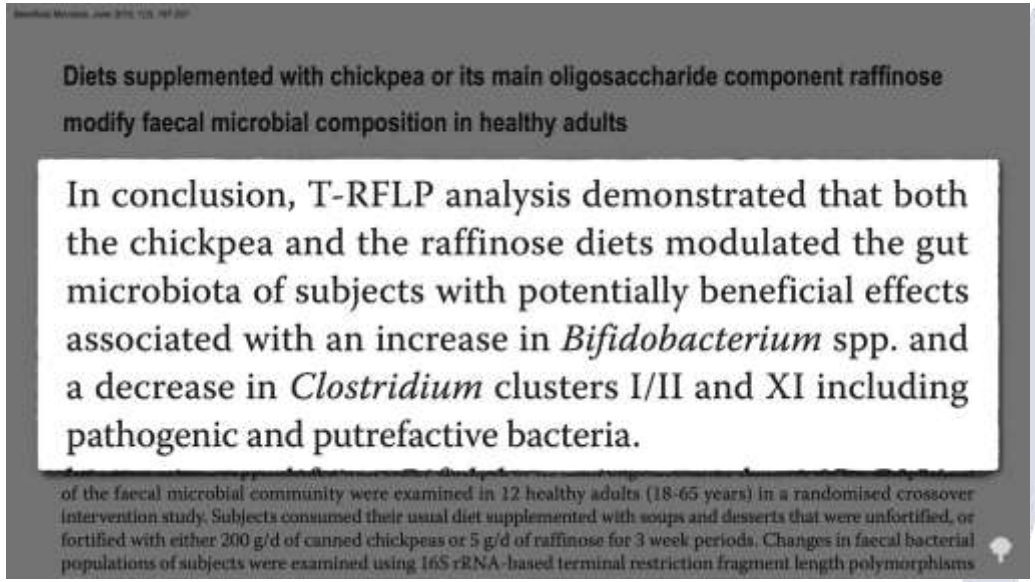
Effects of legume kernel fibres and citrus fibre on putative risk factors for colorectal cancer: a randomised, double-blind, crossover human intervention trial

Anita Fechner, Katrin Fenske and Gerhard Jahreis*

Abstract

Background: In some studies, high intake of dietary fibre has been associated with a lower risk of colorectal cancer. The present study aimed to compare physiological effects of three legume kernel fibres and citrus fibre on blood lipids (primary outcome: LDL cholesterol) and colonic health.

Methods: Ninety-two subjects were recruited for the double-blind, controlled crossover trial. Seventy-eight participants were randomly divided into three groups. Following run-in, half the volunteers from each group consumed 25 g/d of a legume fibre, comprising blue lupin fibre, white lupin fibre, and soya fibre for two weeks. The other half received the same amount of citrus fibre (active comparator). The intervention was crossed within each group after two weeks wash-out. At the end of run-in and intervention, a quantitative faeces collection took

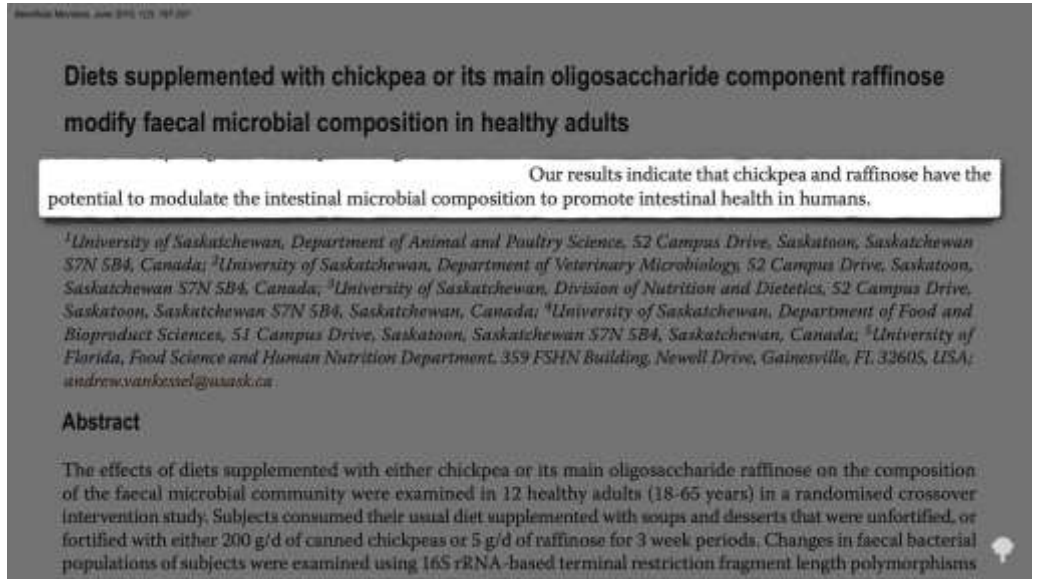


Diets supplemented with chickpea or its main oligosaccharide component raffinose modify faecal microbial composition in healthy adults

In conclusion, T-RFLP analysis demonstrated that both the chickpea and the raffinose diets modulated the gut microbiota of subjects with potentially beneficial effects associated with an increase in *Bifidobacterium* spp. and a decrease in *Clostridium* clusters I/II and XI including pathogenic and putrefactive bacteria.

of the faecal microbial community were examined in 12 healthy adults (18-65 years) in a randomised crossover intervention study. Subjects consumed their usual diet supplemented with soups and desserts that were unfortified, or fortified with either 200 g/d of canned chickpeas or 5 g/d of raffinose for 3 week periods. Changes in faecal bacterial populations of subjects were examined using 16S rRNA-based terminal restriction fragment length polymorphisms

YES- Two Power Foods



Diets supplemented with chickpea or its main oligosaccharide component raffinose modify faecal microbial composition in healthy adults

Our results indicate that chickpea and raffinose have the potential to modulate the intestinal microbial composition to promote intestinal health in humans.

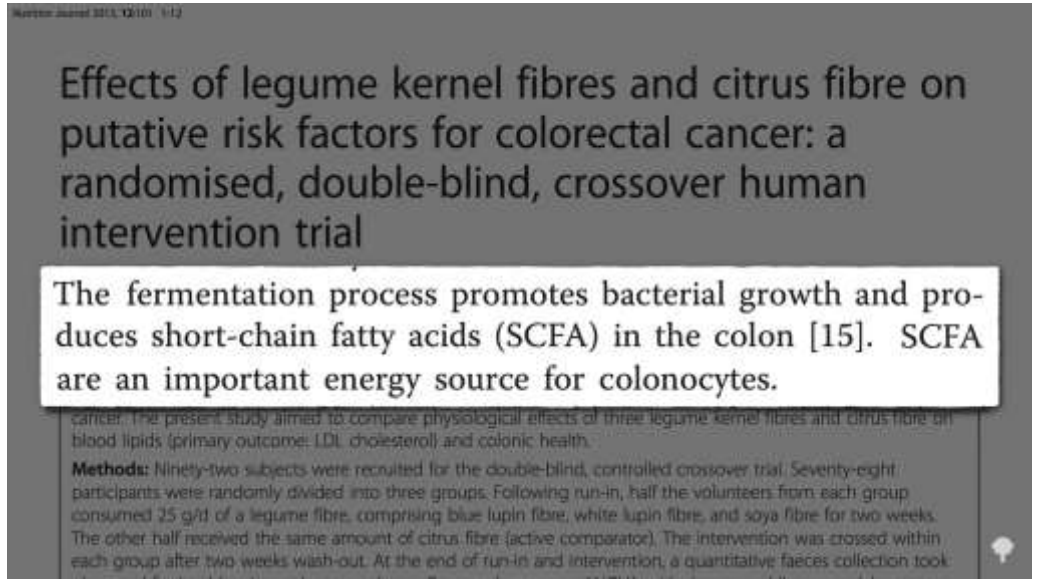
[1]University of Saskatchewan, Department of Animal and Poultry Science, 52 Campus Drive, Saskatoon, Saskatchewan S7N 5B4, Canada; [2]University of Saskatchewan, Department of Veterinary Microbiology, 52 Campus Drive, Saskatoon, Saskatchewan S7N 5B4, Canada; [3]University of Saskatchewan, Division of Nutrition and Dietetics, 52 Campus Drive, Saskatoon, Saskatchewan S7N 5B4, Saskatchewan, Canada; [4]University of Saskatchewan, Department of Food and Bioproduct Sciences, 51 Campus Drive, Saskatoon, Saskatchewan S7N 5B4, Saskatchewan, Canada; [5]University of Florida, Food Science and Human Nutrition Department, 359 FSHN Building, Newell Drive, Gainesville, FL 32605, USA; andrew.vankessel@usask.ca

Abstract

The effects of diets supplemented with either chickpea or its main oligosaccharide raffinose on the composition of the faecal microbial community were examined in 12 healthy adults (18-65 years) in a randomised crossover intervention study. Subjects consumed their usual diet supplemented with soups and desserts that were unfortified, or fortified with either 200 g/d of canned chickpeas or 5 g/d of raffinose for 3 week periods. Changes in faecal bacterial populations of subjects were examined using 16S rRNA-based terminal restriction fragment length polymorphisms

- Chickpeas
- Raffinose (trisaccharide)
  - Beans
  - Cabbage
  - Brussel sprouts
  - Broccoli
  - Asparagus
  - Other vegetables
  - Whole grains

Fiber and Legumes Promote Fermentation



Effects of legume kernel fibres and citrus fibre on putative risk factors for colorectal cancer: a randomised, double-blind, crossover human intervention trial

The fermentation process promotes bacterial growth and produces short-chain fatty acids (SCFA) in the colon [15]. SCFA are an important energy source for colonocytes.

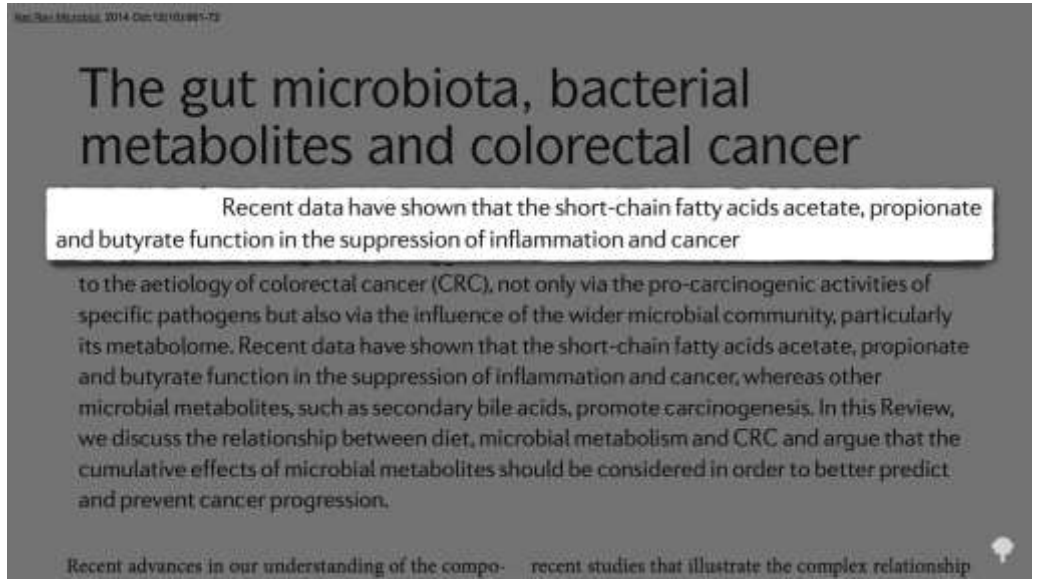
cancer. The present study aimed to compare physiological effects of three legume kernel fibres and citrus fibre on blood lipids (primary outcome: LDL cholesterol) and colonic health.

Methods: Ninety-two subjects were recruited for the double-blind, controlled crossover trial. Seventy-eight participants were randomly divided into three groups. Following run-in, half the volunteers from each group consumed 25 g/d of a legume fibre, comprising blue lupin fibre, white lupin fibre, and soya fibre for two weeks. The other half received the same amount of citrus fibre (active comparator). The intervention was crossed within each group after two weeks wash-out. At the end of run-in and intervention, a quantitative faeces collection took

- Promote bacterial growth
- Provide energy for the colon cells
- Help regulate the immune system
- Produce short chain fatty acids

SYSTEMS PLAN

Short-chain Fatty Acids Produced by Bacteria



The gut microbiota, bacterial metabolites and colorectal cancer

Recent data have shown that the short-chain fatty acids acetate, propionate and butyrate function in the suppression of inflammation and cancer

to the aetiology of colorectal cancer (CRC), not only via the pro-carcinogenic activities of specific pathogens but also via the influence of the wider microbial community, particularly its metabolome. Recent data have shown that the short-chain fatty acids acetate, propionate and butyrate function in the suppression of inflammation and cancer, whereas other microbial metabolites, such as secondary bile acids, promote carcinogenesis. In this Review, we discuss the relationship between diet, microbial metabolism and CRC and argue that the cumulative effects of microbial metabolites should be considered in order to better predict and prevent cancer progression.

Recent advances in our understanding of the compo- recent studies that illustrate the complex relationship

- Suppress inflammation
- Suppress cancer
- Modulate your immune system

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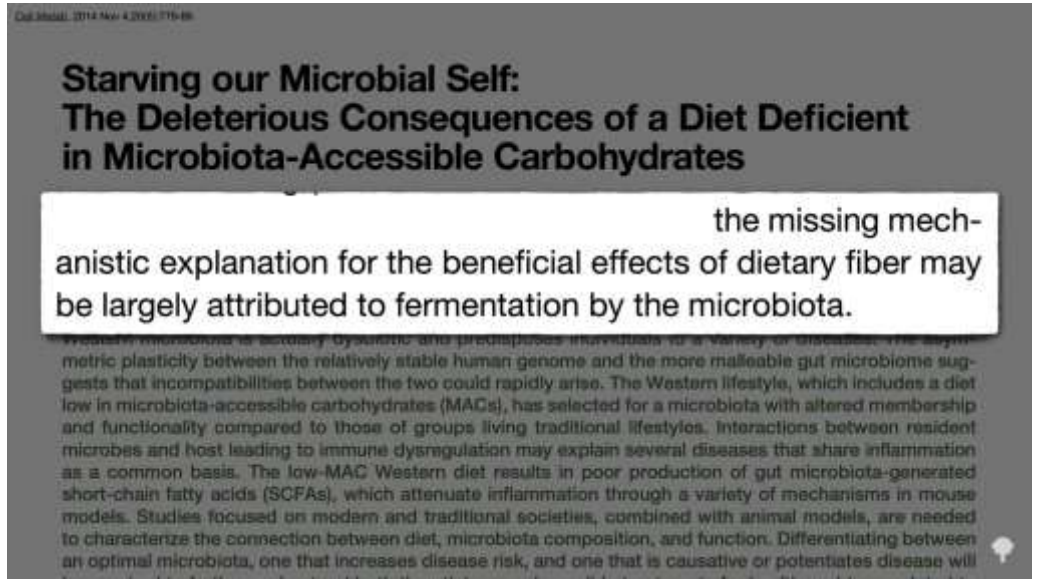
The Fermentation Process Is Essential



Starving our Microbial Self:
The Deleterious Consequences of a Diet Deficient in Microbiota-Accessible Carbohydrates

the missing mechanistic explanation for the beneficial effects of dietary fiber may be largely attributed to fermentation by the microbiota.

metric plasticity between the relatively stable human genome and the more malleable gut microbiome suggests that incompatibilities between the two could rapidly arise. The Western lifestyle, which includes a diet low in microbiota-accessible carbohydrates (MACs), has selected for a microbiota with altered membership and functionality compared to those of groups living traditional lifestyles. Interactions between resident microbes and host leading to immune dysregulation may explain several diseases that share inflammation as a common basis. The low-MAC Western diet results in poor production of gut microbiota-generated short-chain fatty acids (SCFAs), which attenuate inflammation through a variety of mechanisms in mouse models. Studies focused on modern and traditional societies, combined with animal models, are needed to characterize the connection between diet, microbiota composition, and function. Differentiating between an optimal microbiota, one that increases disease risk, and one that is causative or potentiates disease will

The Missing Link- Fiber

- Vegetables and legumes

Meat suppresses bacterial growth

SYSTEMS PLAN


Produced by Tony Spitz

Poop Pills Can Combat Deadly Infections

December 11, 2017 • 35,951 views

Previous Next

Story at-a-glance

- An answer to a serious infection called Clostridium difficile (C. diff.) infection comes from a relatively new therapy called fecal microbiota transplantation (FMT)
- C. diff., a common bacterium in hospitals, is a leading cause of diarrhea in health care today, with older people on medication at greatest risk, and often occurs soon after administration of antibiotics
- FMT is when feces are transferred from a healthy donor to the gastrointestinal tract of a C. diff-infected patient to reintroduce healthy bacteria into their gut, but the pill form offers a noninvasive alternative
- In terms of patient comfort, fewer trial subjects who were given the FMT capsule described the experience as “unpleasant” compared to receiving FMT through the colonoscopy route
- Your gut health, as well as your overall health, are closely interconnected, so “feeding” your microbiome, as well as resisting antibiotics as much as possible, will optimize your microbiome

Papua New Guinea

Papua New Guinea

Ozempic and other Weight Loss Injections

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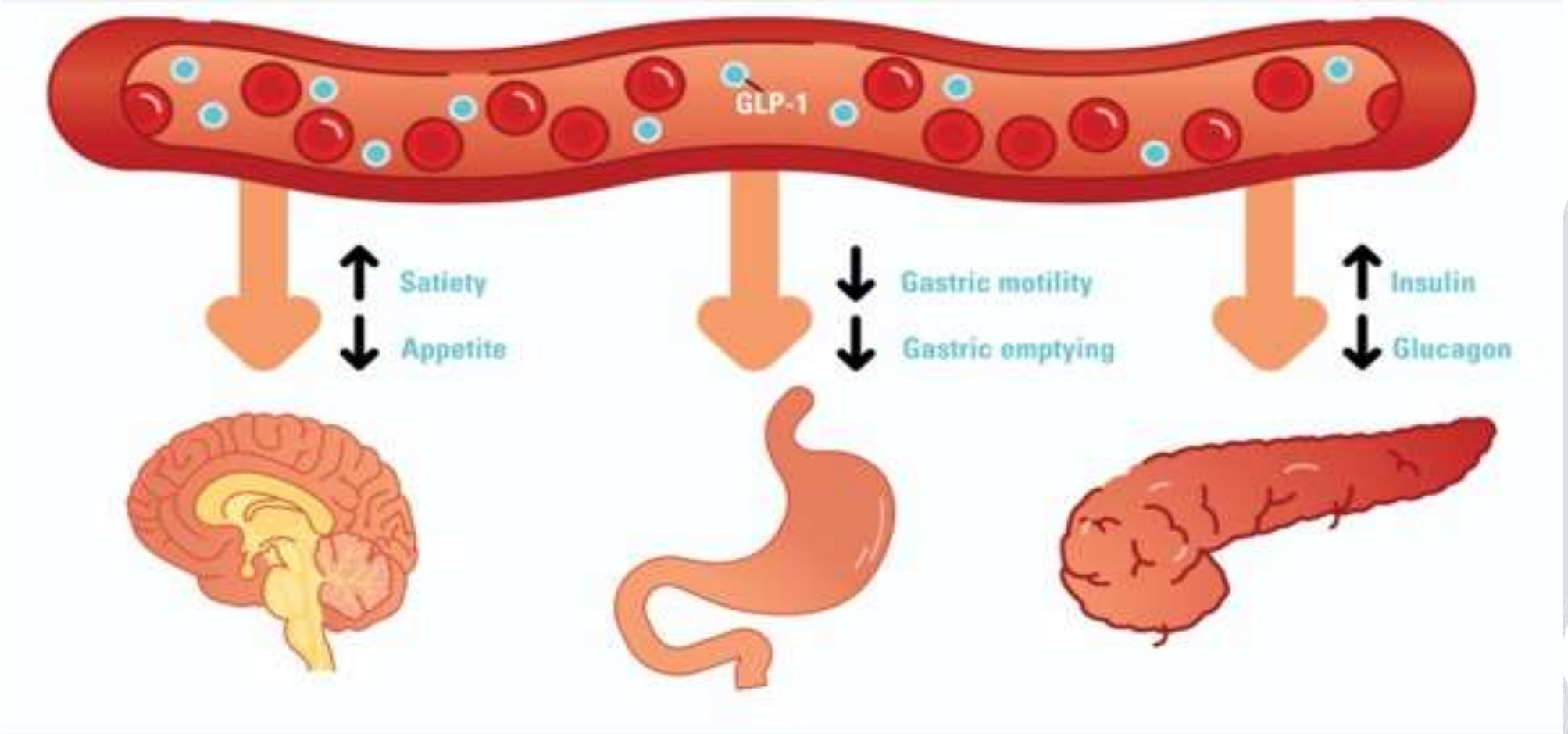
How Ozempic Works



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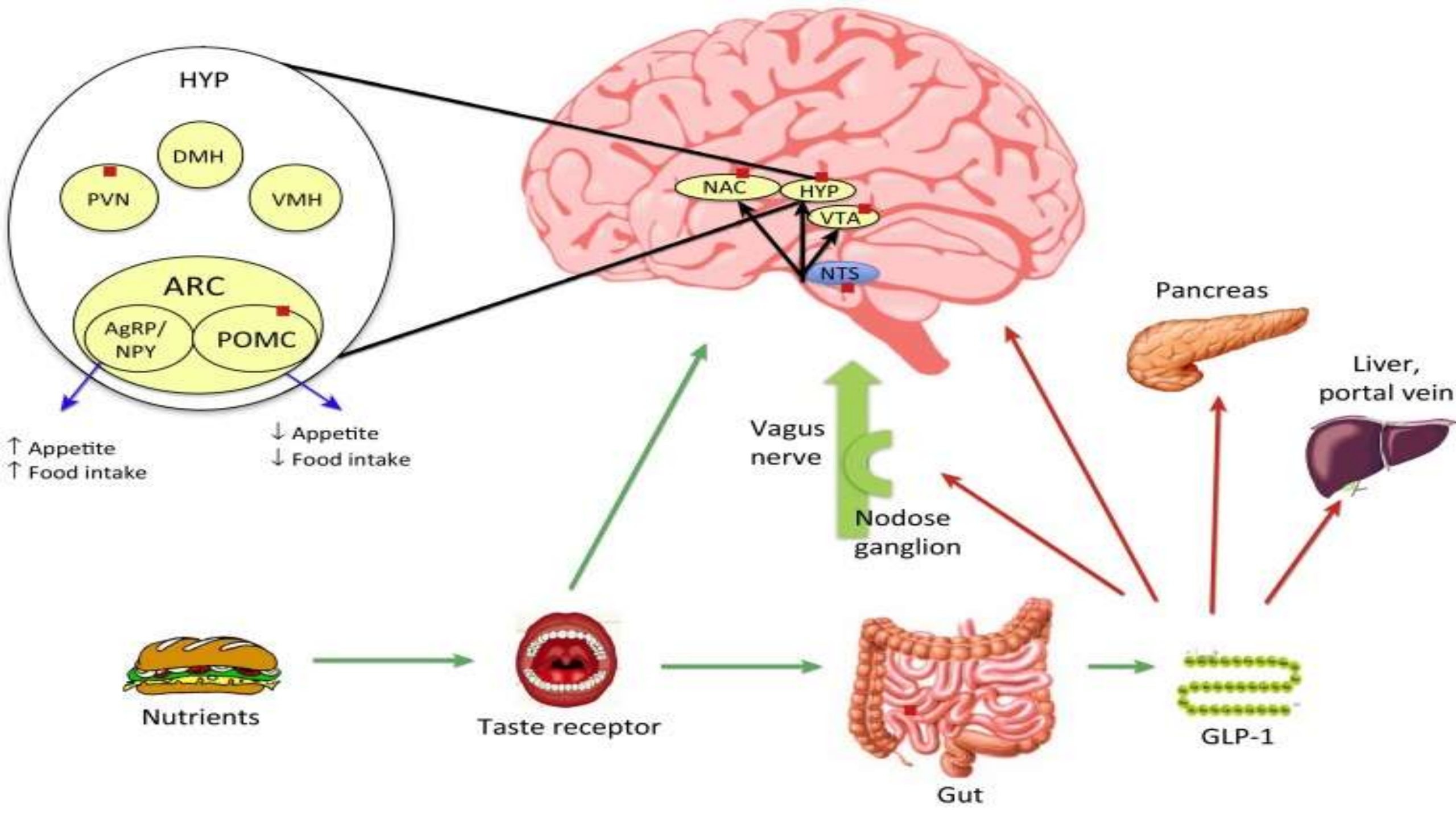
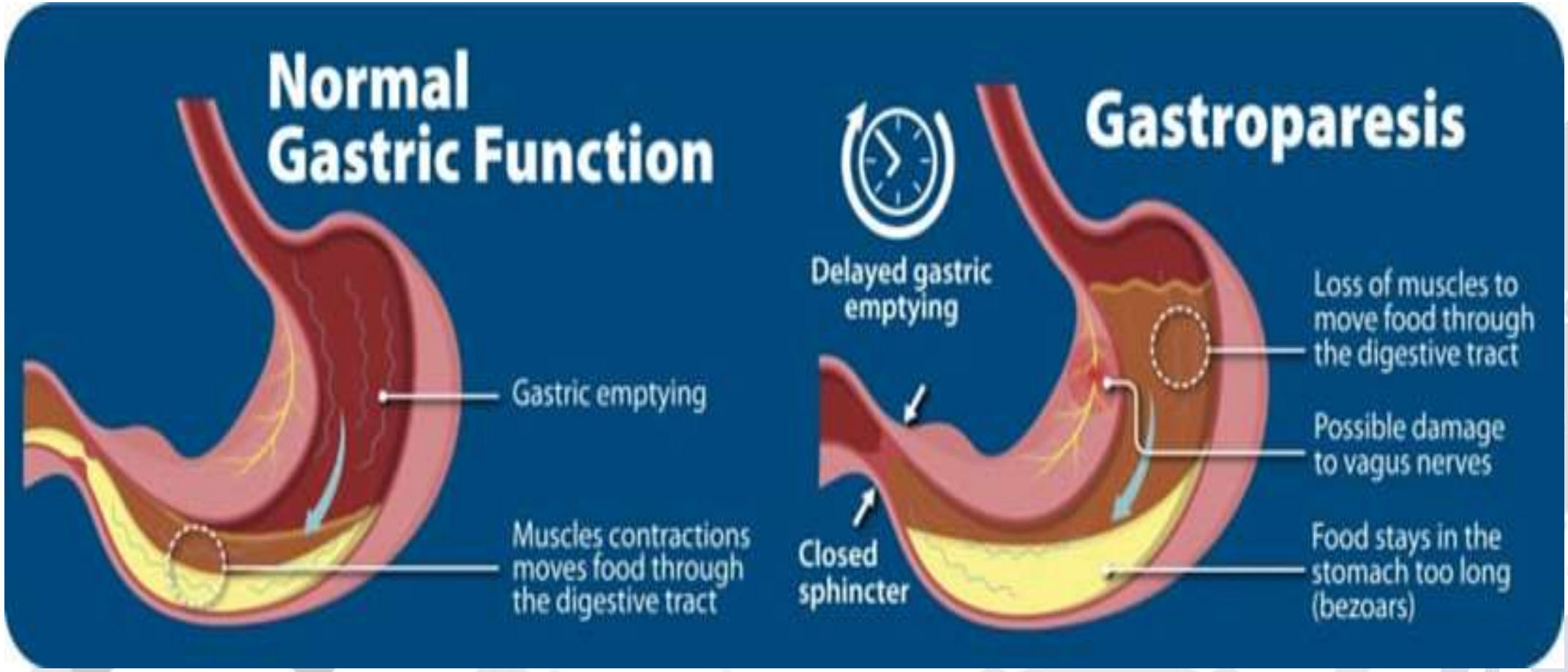

HYP
DMH
PVN
VMH
ARC
AgRP/
NPY
POMC
↑ Appetite
↑ Food intake
↓ Appetite
↓ Food intake
NAC
HYP
VTA
NTS
Vagus
nerve
Nodose
ganglion
Pancreas
Liver,
portal vein
Nutrients
Taste receptor
Gut
GLP-1

Delayed Gastric Emptying



Serious Gastrointestinal Conditions

- Associated with an increased risk of several serious health conditions, including stomach paralysis, pancreatitis and bowel obstruction.
  - 9.09 times higher risk of pancreatitis
  - 4.22 times higher risk of bowel obstruction
  - 3.67 times higher risk of gastroparesis
- Research from the University of British Columbia

Ozempic Linked to Fatal Intestinal Blockages

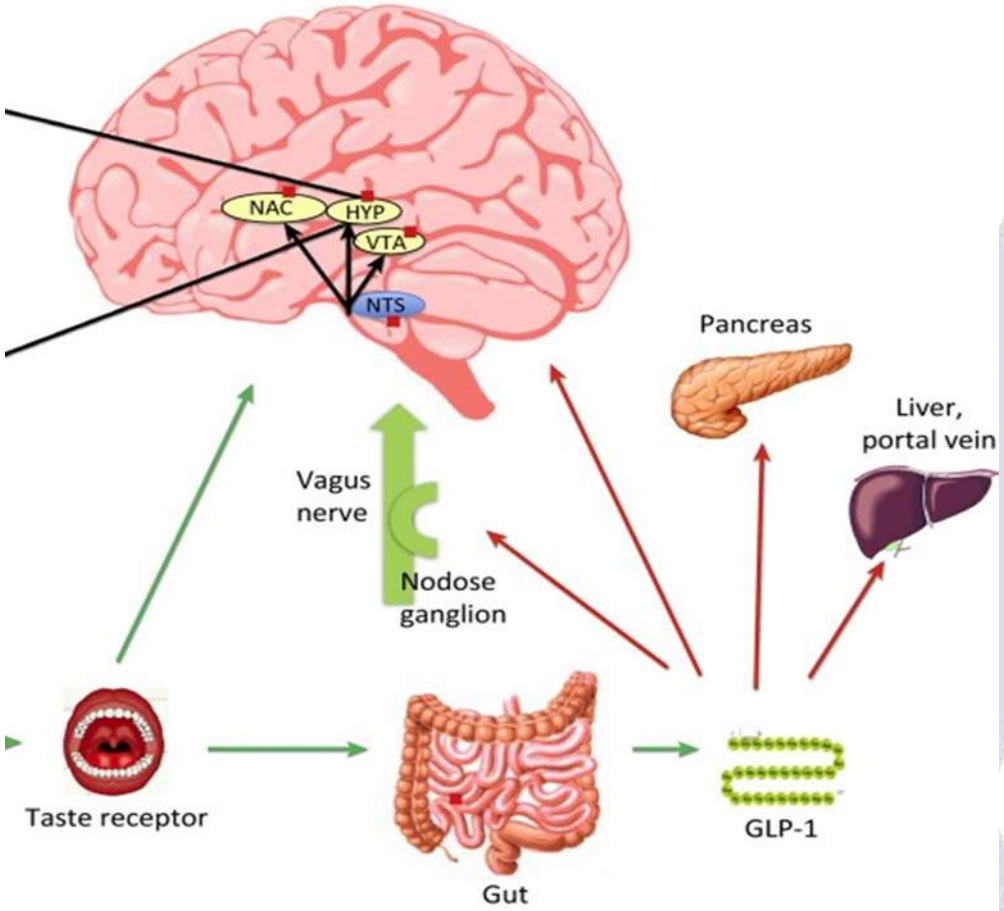
- These trendy weight loss medications cause other significant risks as well and may even cause a potentially fatal intestinal obstruction.

GI Obstruction

- These medications can cause increases in the intestinal length and villus height
- The small intestine may become as inelastic and fibrotic, leading to **long-term** upper intestinal obstruction.

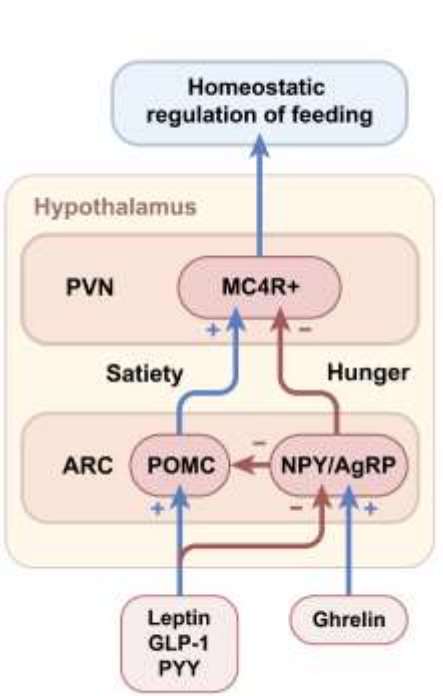
Ozempic may Work via Your Brain

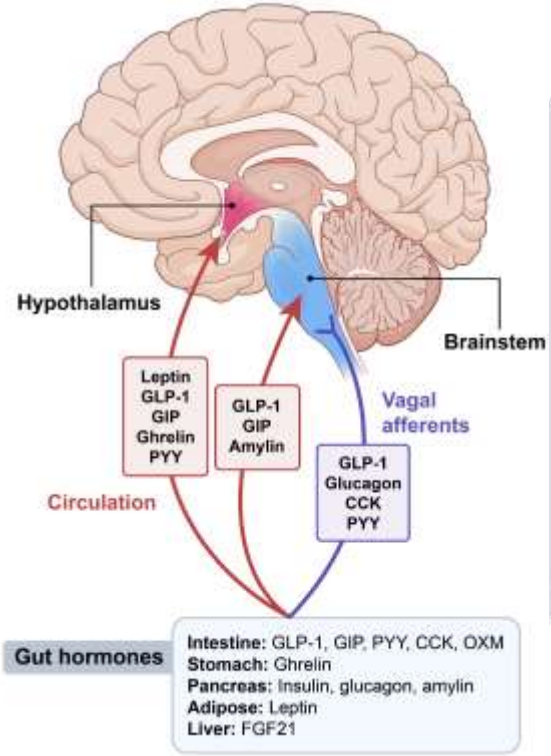
These brain receptors are likely the reason the GLP-1 drugs can curb the desire to eat — but also curb other desires as well. The weight-loss drugs are ultimately drugs for the brain.



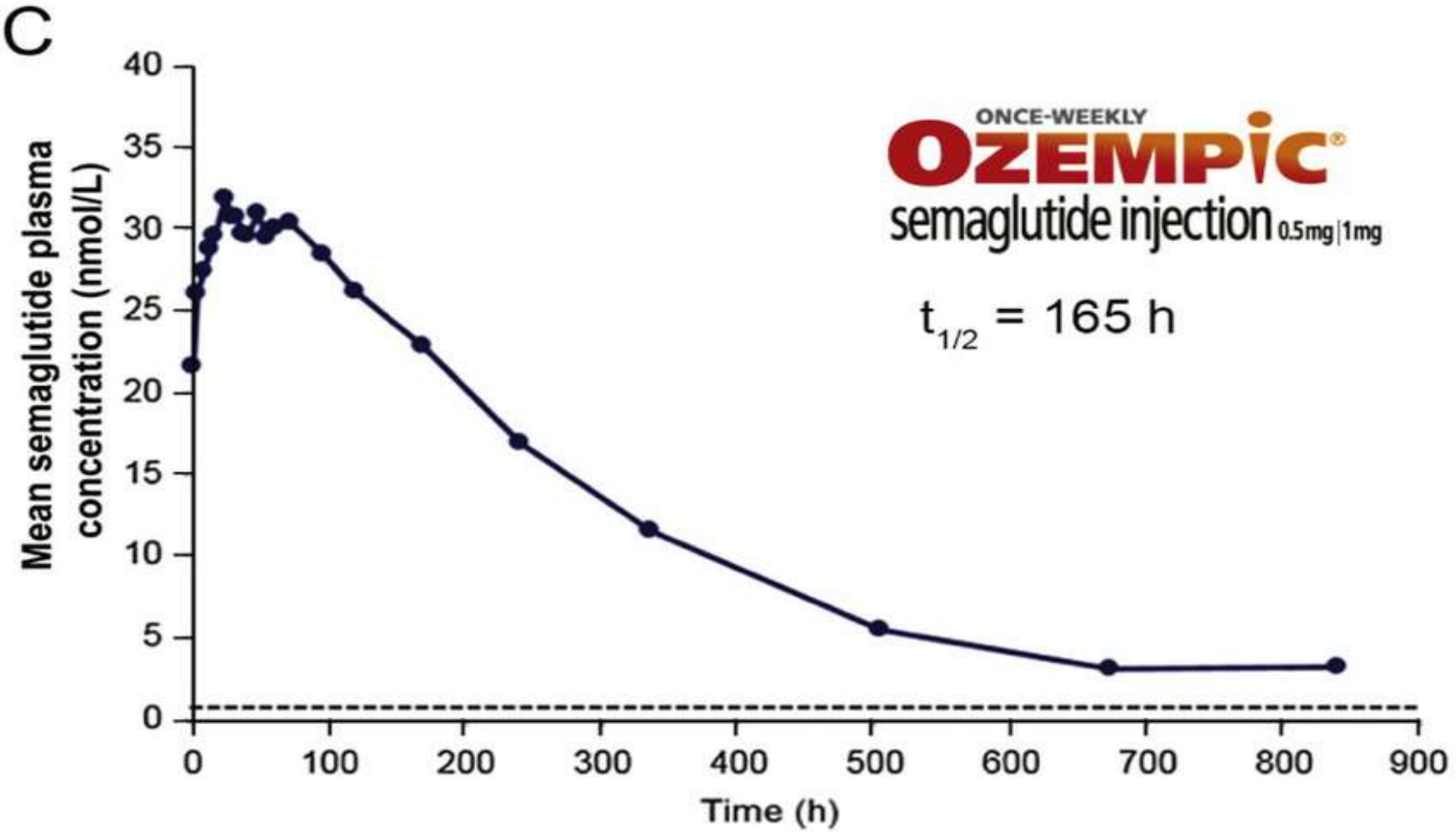
The Atlantic

- Semaglutide's brain effects may explain why many people taking the drugs also **lose the desire** to engage in behaviors like drinking alcohol, shopping and smoking.





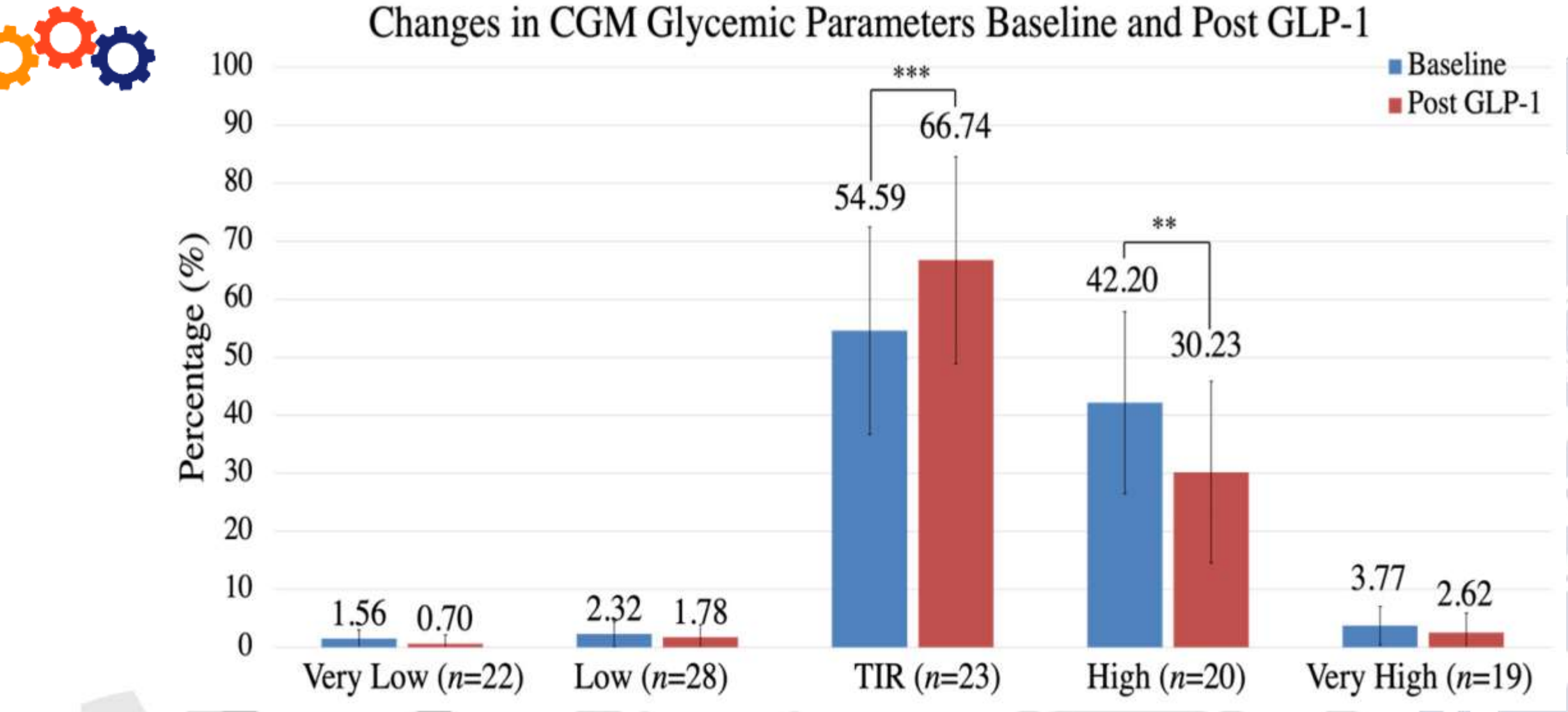
The Journal of Clinical Investigation Insight



ONCE-WEEKLY
OZEMPIC®
semaglutide injection 0.5mg | 1mg

$t_{1/2}$ = 165 h

SYSTEMS PLAN


Changes in CGM Glycemic Parameters Baseline and Post GLP-1
Baseline
Post GLP-1
Percentage (%)
100
90
80
70
60
50
40
30
20
10
0
***
**
1.56
0.70
2.32
1.78
54.59
66.74
42.20
30.23
3.77
2.62
Very Low (n=22)
Low (n=28)
TIR (n=23)
High (n=20)
Very High (n=19)

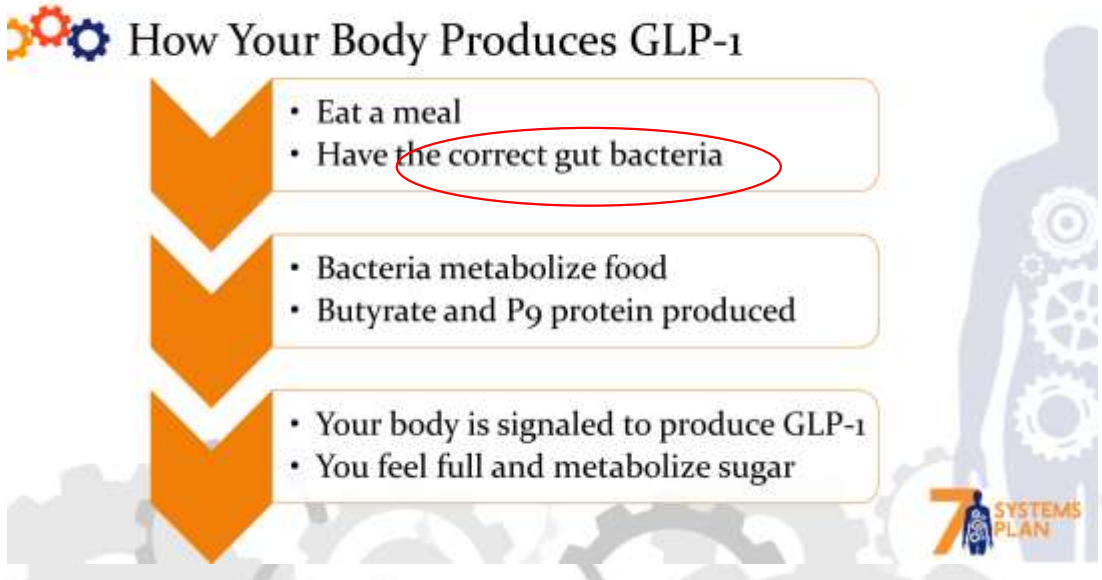
A New Natural Product that Mimics Ozempic

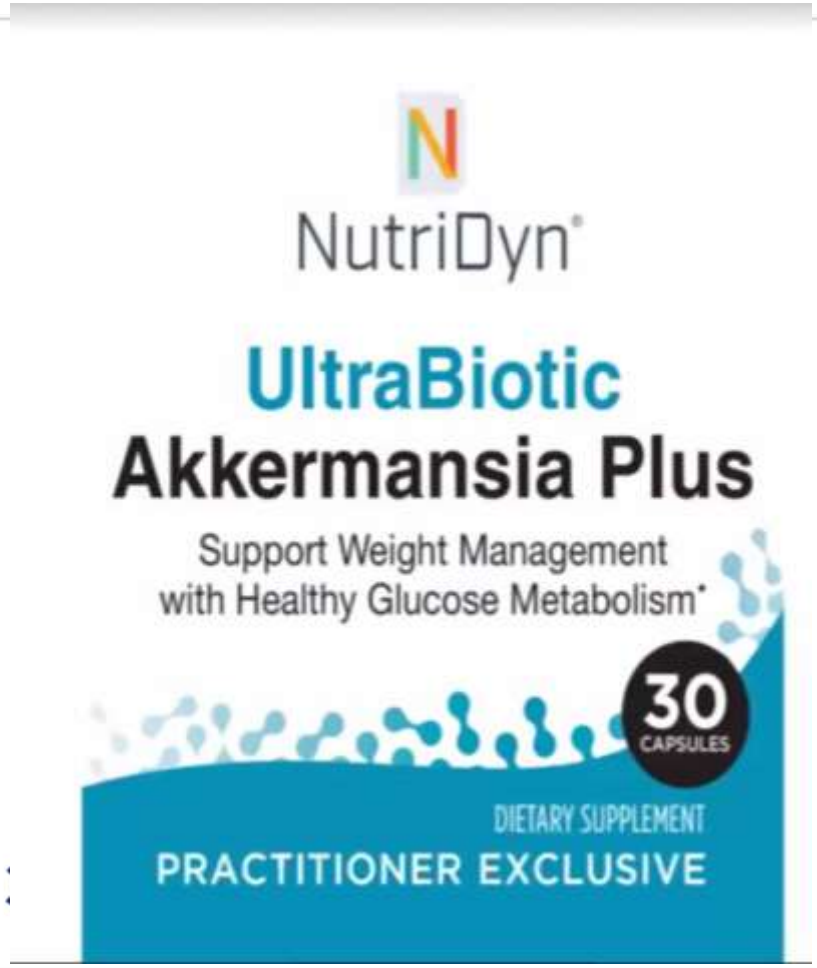
- Similar benefits
- Only good side effects

?

The Missing Link to Produce GLP-1

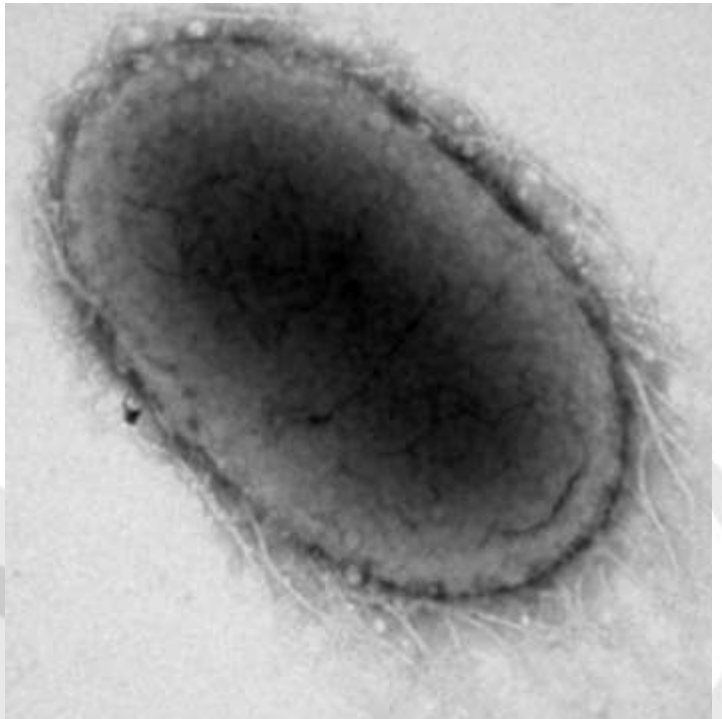
- There are only two probiotic strains that have been shown to be able to stimulate GLP-1, and one them is Akkermansia.





SYSTEMS PLAN

The Probiotic that acts like Ozempic



Akkermansia: glucose control, weight loss

- Additionally, a protein secreted by Akkermansia, P9, and a protein located within the outer membrane of the microbe, Amuc_1100, are presently receiving considerable attention in the research community.
- The P9 protein increases GLP-1 secretion through binding to ICAM2 receptors on L-cells, thereby promoting improved glucose control and weight loss.

Yoon HS, Cho CH, Yun MS, Jang SJ, You HJ, Kim JH, Han D, Cha KH, Moon SH, Lee K, Kim YJ, Lee SJ, Nam TW, Ko G. Akkermansia muciniphila secretes a **glucagon-like peptide-1**-inducing protein that improves glucose homeostasis and ameliorates metabolic disease in mice. Nat Microbiol. 2021 May;6(5):563-573. doi: 10.1038/s41564-021-00880-5. Epub 202 Dropbox promotion 3820962.

SYSTEMS PLAN

UltraBiotic Akkermansia Plus Potential Benefits:

- Supports healthy glucose metabolism
- Supports healthy weight management
- Promotes colon health
- Supports a balanced gut microbiome
- Supports digestive health
- Promotes healthy immune function

Clinically Supported Strains to Boost GLP-1:

- Bifidobacterium animalis
- Lactobacillus rhamnosus GG
- Clostridium butyricum
- Akkermansia muciniphila

The Choice

NutriDyn®

UltraBiotic

Akkermansia Plus

Support Weight Management
with Healthy Glucose Metabolism*

30 CAPSULES

DIETARY SUPPLEMENT

PRACTITIONER EXCLUSIVE

30 CAPSULES Dietary Supplement

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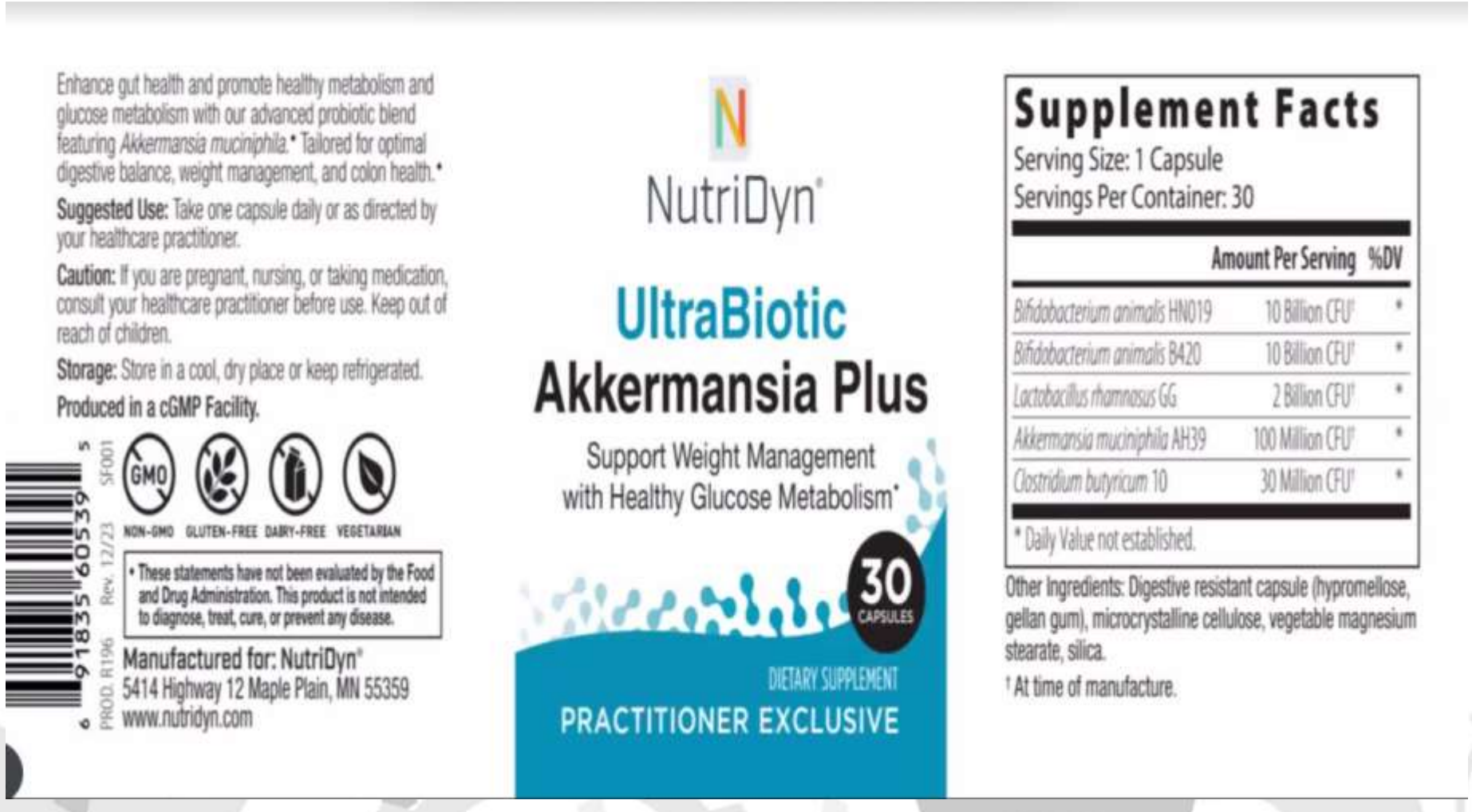
UltraBiotic Akkermansia Plus



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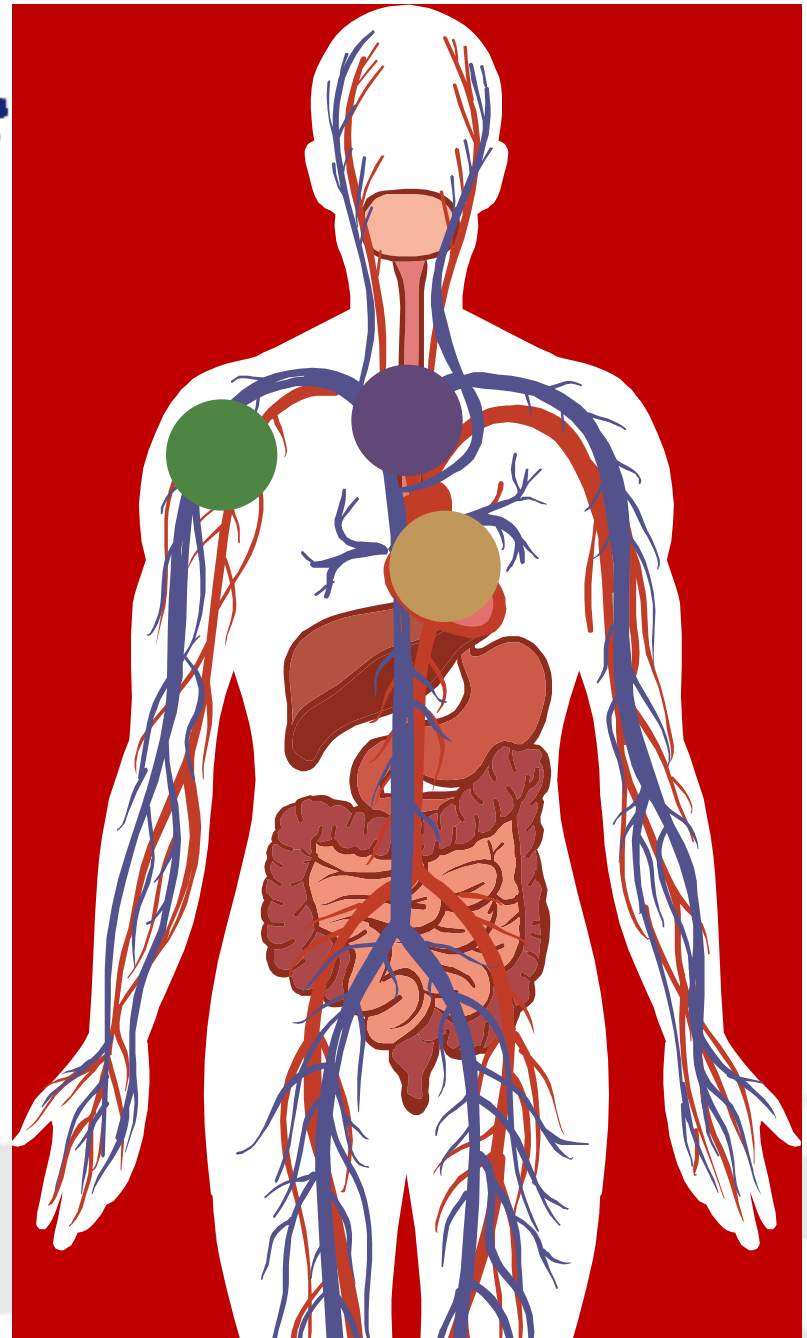
DELIVERY SYSTEM



1. Heart
2. Blood vessels
3. Nutrient Transport-
   LDL, VLDL, Albumin…

The 50% Factor for Longevity

JAMA | Original Investigation

The State of US Health, 1990-2016

Burden of Diseases, Injuries, and Risk Factors Among US States

The US Burden of Disease Collaborators

INTRODUCTION Several studies have measured health outcomes in the United States, but none have provided a comprehensive assessment of patterns of health by state.

OBJECTIVE To use the results of the Global Burden of Disease Study (GBD) to report trends in the burden of diseases, injuries, and risk factors at the state level from 1990 to 2016.

DESIGN AND SETTING A systematic analysis of published studies and available data sources estimates the burden of disease by age, sex, geography, and year.

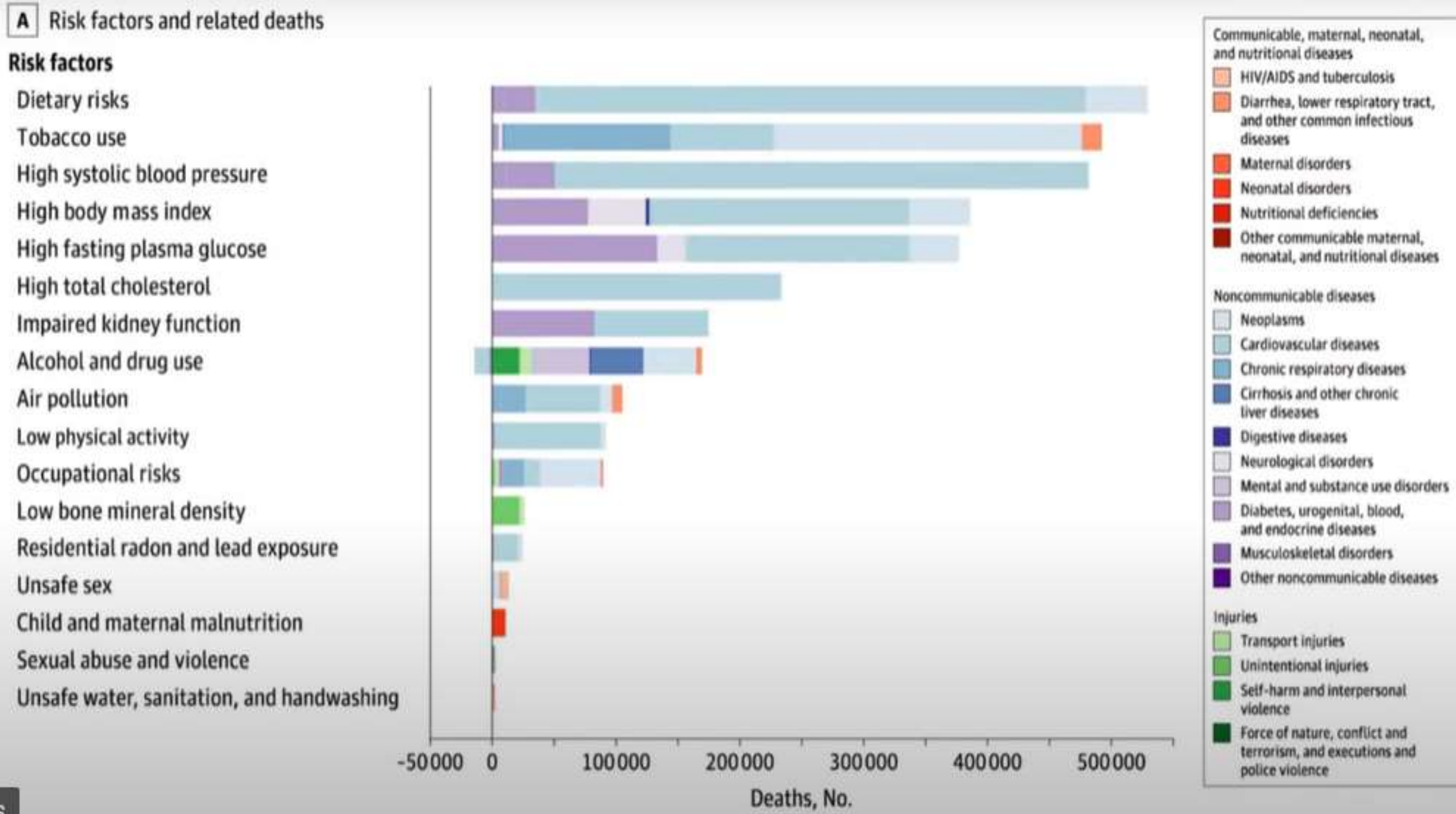
MAIN OUTCOMES AND MEASURES Prevalence, incidence, mortality, life expectancy, healthy life expectancy (HALE), years of life lost (YLLs) due to premature mortality, years lived with disability (YLDs), and disability-adjusted life-years (DALYs) for 333 causes and 84 risk factors

Editorial page 1438

Author Audio Interview

Supplemental content

CME Quiz at jamanetwork.com/learning and CME Questions page 1503


A Risk factors and related deaths
Risk factors
Dietary risks
Tobacco use
High systolic blood pressure
High body mass index
High fasting plasma glucose
High total cholesterol
Impaired kidney function
Alcohol and drug use
Air pollution
Low physical activity
Occupational risks
Low bone mineral density
Residential radon and lead exposure
Unsafe sex
Child and maternal malnutrition
Sexual abuse and violence
Unsafe water, sanitation, and handwashing
-50000
0
100000
200000
300000
400000
500000
Deaths, No.
Communicable, maternal, neonatal, and nutritional diseases
HIV/AIDS and tuberculosis
Diarrhea, lower respiratory tract, and other common infectious diseases
Maternal disorders
Neonatal disorders
Nutritional deficiencies
Other communicable maternal, neonatal, and nutritional diseases
Noncommunicable diseases
Neoplasms
Cardiovascular diseases
Chronic respiratory diseases
Cirrhosis and other chronic liver diseases
Digestive diseases
Neurological disorders
Mental and substance use disorders
Diabetes, urogenital, blood, and endocrine diseases
Musculoskeletal disorders
Other noncommunicable diseases
Injuries
Transport injuries
Unintentional injuries
Self-harm and interpersonal violence
Force of nature, conflict and terrorism, and executions and police violence

Diet and Longevity

Blue Zone Study

7 SYSTEMS PLAN

STATE OF THE ART

REVIEWS

Dan Buettner, BA, and Sam Ske

Food Guidelines

We distilled more than 150 dietary surveys of the world's longest-lived people to discover the secrets of a longevity diet.

These 11 simple guidelines reflect how the world's longest-lived people ate for most of their lives. We make it easy to eat like the healthiest people in the world with the Blue Zones Meal Planner, where you'll find thousands of recipes that follow these guidelines while making plant-slant food delicious and accessible. By adopting some of the healthy eating principles into your daily life, you too can *Live Better, Longer*. Click here to download our free printable of the Blue Zones Food Guidelines so you can post it in your home as a daily reminder.

Abstract

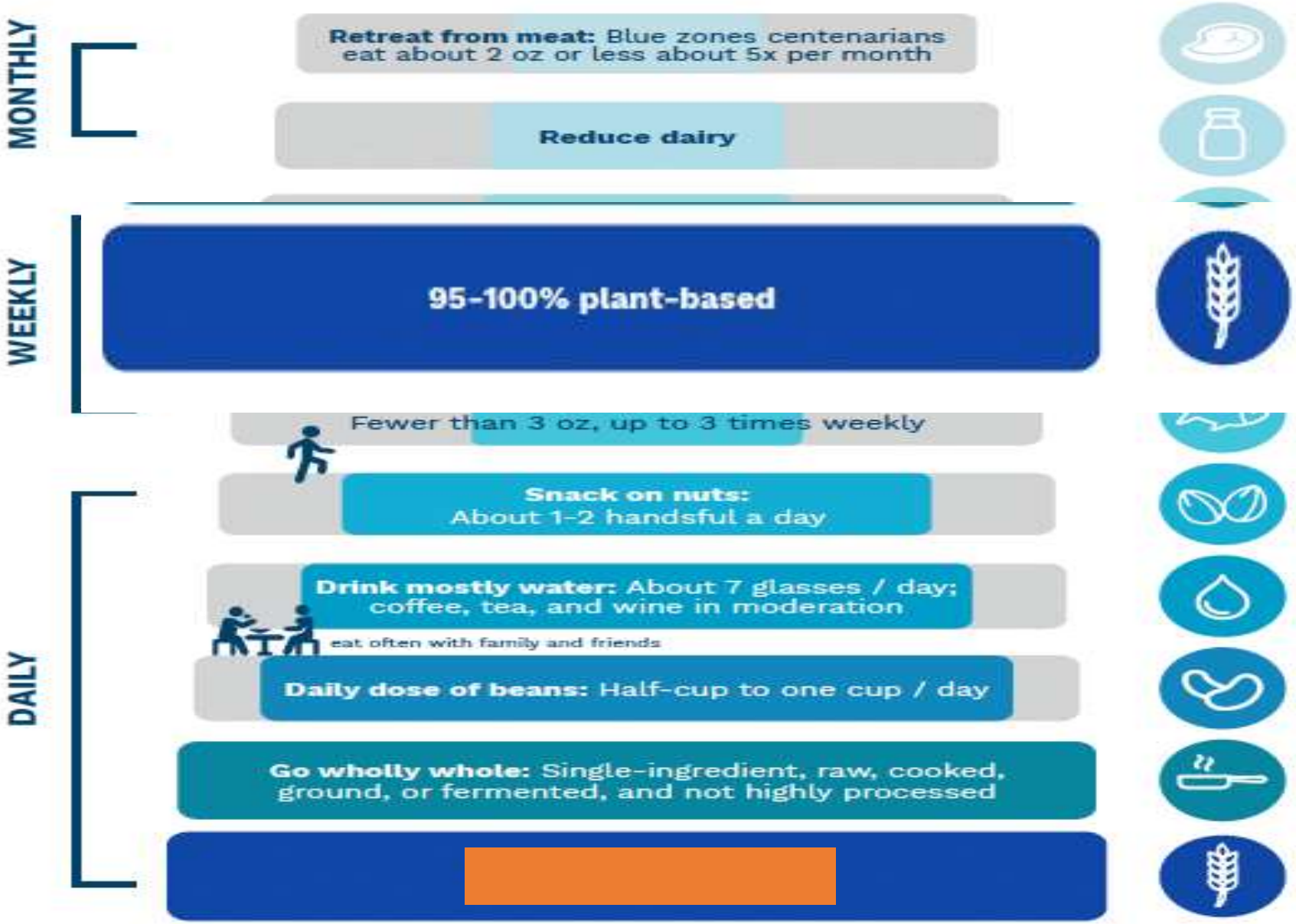
Geograph... Buettner, to uncover the secrets of longevity, evolved into the discovery of

lifestyle. In 2004, Dan Buettner, CEO of Blue Zones LLC, was

...evity. They ...f all Blue Z residents shared 9 specific characteristics. These are calle

BLUE ZONES™

FOOD GUIDELINES



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JOURNAL OF THE AMERICAN COLLEGE OF NUTRITION
https://doi.org/10.1080/07315724.2020.1790442

PERSPECTIVE

Plant-Based Diets for Healthy Aging

Hana Kahleova[a], Susan Levin[a], and Neal D. Barnard[a,b]

[a]Departmen

George Was

pared with the other white Californians. A plant-based diet Health Sciences,

can explain about half of this difference in life-span (8).

ARTICLE HISTORY
Received 24 June 2020
Accepted 29 June 2020

KEYWORDS
Diets; preventative nutrition and chronic disease; general nutrition; aging; plant-based

Lifestyle Characteristics

- Family coherence
- Not smoking
- Moderate and daily physical activity
- Social engagement
- Integration into the community
- **Plant based diet**

these areas share common behavioral and lifestyle characteristics, despite the different race, nationality, and regional characteristics they have. Particularly, the investigators of the Blue Zones reported that "*some lifestyle characteristics, like family coherence, avoidance of smoking, plant-based diet, moderate and daily physical activity, social engagement, where people of all ages are socially active and integrated into the community, are common in all people enrolled in the surveys*" [4]. Clearly, longevity is a complex attribute, determined by

What You Eat

Everything

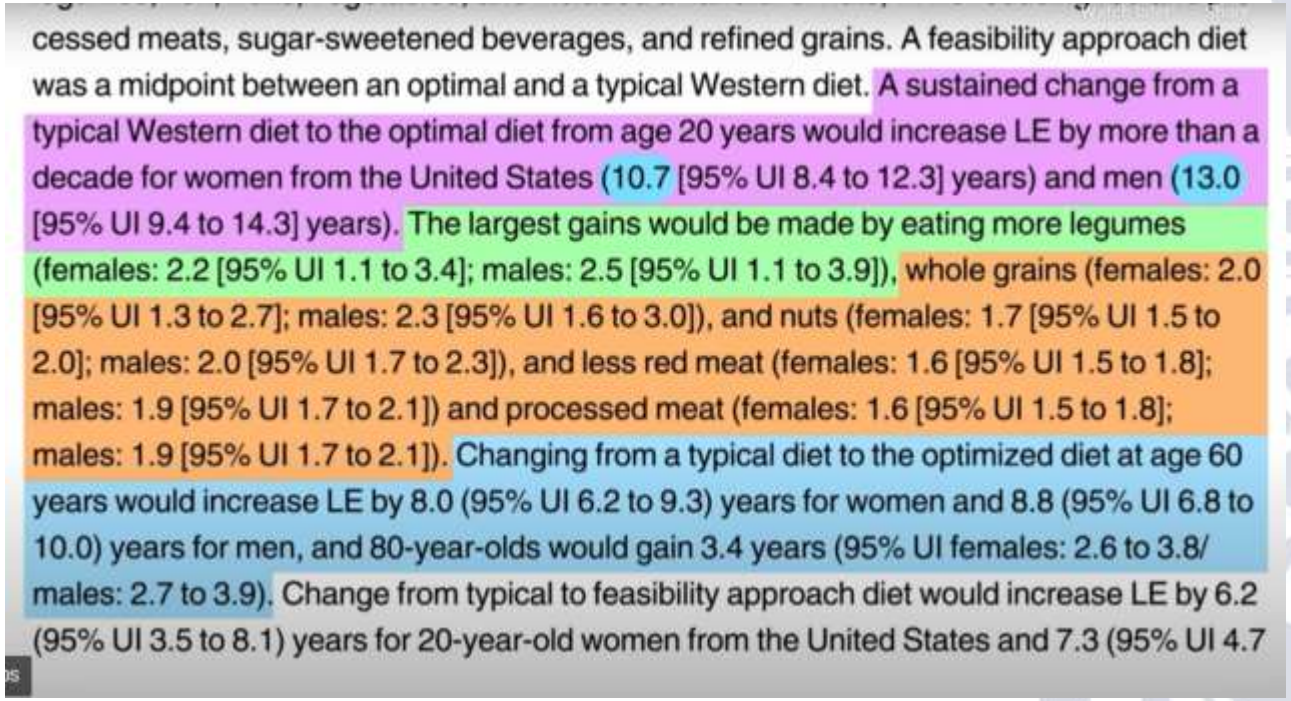
Change Your Diet

Age 20+ 13 years

Age 60+10 years

Age 80+3 years

- Legumes + 2.5
- Whole grains + 2.3
- Nuts + 2.0
- Less red meat + 1.9
- Less processed meat + 1.9



cessed meats, sugar-sweetened beverages, and refined grains. A feasibility approach diet was a midpoint between an optimal and a typical Western diet. A sustained change from a typical Western diet to the optimal diet from age 20 years would increase LE by more than a decade for women from the United States (10.7 [95% UI 8.4 to 12.3] years) and men (13.0 [95% UI 9.4 to 14.3] years). The largest gains would be made by eating more legumes (females: 2.2 [95% UI 1.1 to 3.4]; males: 2.5 [95% UI 1.1 to 3.9]), whole grains (females: 2.0 [95% UI 1.3 to 2.7]; males: 2.3 [95% UI 1.6 to 3.0]), and nuts (females: 1.7 [95% UI 1.5 to 2.0]; males: 2.0 [95% UI 1.7 to 2.3]), and less red meat (females: 1.6 [95% UI 1.5 to 1.8]; males: 1.9 [95% UI 1.7 to 2.1]) and processed meat (females: 1.6 [95% UI 1.5 to 1.8]; males: 1.9 [95% UI 1.7 to 2.1]). Changing from a typical diet to the optimized diet at age 60 years would increase LE by 8.0 (95% UI 6.2 to 9.3) years for women and 8.8 (95% UI 6.8 to 10.0) years for men, and 80-year-olds would gain 3.4 years (95% UI females: 2.6 to 3.8/ males: 2.7 to 3.9). Change from typical to feasibility approach diet would increase LE by 6.2 (95% UI 3.5 to 8.1) years for 20-year-old women from the United States and 7.3 (95% UI 4.7

Recommended Food List

Foods listed in green are recommended. You want to avoid the foods listed in red.

FOODS TO EAT

**FOODS TO BE CAREFUL WITH

Vegetables Low GI	Vegetables Medium GI	Fruit	Oils	Concentrated Proteins	Nuts & Seeds	**Legumes	Grains	Dairy	Beverages	Functional Foods
Cruciferous: broccoli, brussels sprouts, cabbages, cauliflower Greens: leaf greens, bok choy, collard greens, escarole, kale, mustard greens, Swiss chard, watercress, spinach Lettuce/Mixed greens Mushrooms Salsa (sugar-free) Sprouts: alfalfa, broccoli or radish sprouts, bamboo shoots, etc. Squash: spaghetti, summer, yellow, zucchini Other vegetables: artichokes, asparagus, organic celery, chives, cucumbers, dill pickles, eggplants, garlic, green beans, hot peppers, leeks, lentils, mixed vegetable juices, okra, onions, organic sweet bell peppers, radishes, snow peas, organic tomatoes, water chestnuts	Beets Carrots Pumpkins Rutabagas Sweet potatoes or yams Tomatoes Winter squash Organic Yukon Gold Potatoes	Berries: blackberries, blueberries, raspberries, and organic strawberries Organic apples Apricots Cantaloupe Organic cherries Clementine Fresh Figs Organic grapes Honeydew melon Kiwifruits Mango Organic nectarines Oranges Organic peaches Organic pears Plums Tangerines Watermelon Bananas Dried fruit Fruit juices Pineapples	Best: Avocados and Guacamole Olives Good: Extra virgin coconut oil Cold pressed extra virgin olive oil Flaxseed oil Walnut oil Avocado oil Mayonnaise (made with avocado oil) Vegetable and Processed oils Canola oil Hydrogenated oil Margarine Peanut oil Sunflower oil Safflower oil Trans fats Vegetable shortening	Best: Low GI vegetables Tofu Tempeh Soy or veggie burger (read ingredients) Fish (wild caught) Beef (grass-fed) Lamb (grass-fed) Chicken (free-range) Good: Beef-lean Eggs (free-range) Cottage cheese Ricotta Mozzarella Parmesan Processed meat Deli Meat Hot Dogs Pork Sausage Salami Tuna	Note: Walnut Almonds Brazil nuts Macadamia Pecan Pistachios Hazelnuts Seeds: Sunflower Pumpkin Sesame seeds Nut butter: Almond butter Not as good: Peanuts Cashews Peanut butter (no sugar) Nuts with sugar or chocolate Nut butter that contains trans fats or sugar	Beans: black, butter, cannellini, garbanzo, chickpeas, great northern, pinto, kidney, lima, navy, mung, fat free refried, green soy Hummus Bean Soup Lentils: beluga, French, and red variety Peas: split green or yellow peas Baked beans Peanuts Soybean oil	Amaranth, teff, or quinoa Rice: Barley, buckwheat groats, millet Bulgur Popcorn Whole oats: Whole wheat, spelt, or kamut berries Pasta: 100% whole wheat, spelt, kamut, or black bean Crackers Breads: mixed whole-grain or 100% whole-rye Tortillas: Pita whole-wheat or low-carb Flour tortilla Wheat bread White bread Pasta	Butter or ghee Buttermilk Yogurt (plain) Dairy Substitutes: Almond milk (no sugar) Hemp milk (no sugar) Coconut milk (no sugar) All conventional dairy products including milk Processed cheese	Water Coffee Herbal or Green tea Sparkling or Mineral water Alcohol Soda Sugary beverages Fruit juices Enhanced or flavored water Diet/Artificially sweetened drinks	Dynamic Daily Meal Dynamic GI Restore Dynamic Cardio-Metabolic Dynamic Inflam Ease Dynamic GI Integrity Dynamic Detox

**Avoid these foods if you have GI issues, inflammation, auto-immune disease, or diabetes.

Data from NHANES for 37,232 participants

- This study found that berry consumers had:
  - 21% lower risk of all-cause mortality compared to nonconsumers

  The differences for specific categories as follows:
    - 14% lower risk for any berry
    - 21% lower risk for strawberry consumption
    - 31% lower risk for blueberry consumption
    - 31% lower risk for cranberry consumption.

7 Systems Plan Longevity Shake

My Recipe

- 1/3 cup blueberries and water
- 1 scoop functional food (after blended)
- 1 scoop fruits and greens
- 1 scoop of Multi Collagen Renew
- 1 T ground chia and flax seeds
- 1 t wheat germ
- 1 t olive oil
- 1 t apple cyder vinegar
- ½ t beet powder
- ½ t Spirulina (smells bad)
- ¼ t Amla powder
- ¼ t Macha (green tea)


7 SYSTEMS PLAN
COLLAGEN RENEW
UNFLAVORED
BRAGG
ORGANIC
APPLE CIDER VINEGAR
KRETSCHMER
WHEAT GERM
4G PLANT PROTEIN
7 SYSTEMS PLAN
INFLAM-EZE
TROPICAL PUNCH
FRUITS & GREENS
ORGANIC
Mamma Chia
SEED YOUR SOUL
CHIA SEED
NET WT 12 OZ (340 g)
ORGANIC BLACK CHIA
THRIVE
ORGANIC TEA
Matcha
NET WT. 3.5 OZ (100G)
CASCADIAN FA
ORGANIC
BLUEBERRIES
NET WT. 28 OZ (1 LB 12 OZ) 793g | KEEP FROZEN
wellmade
BY THRIVE MARKET
Organic traditions
AMLA BERRY POWDER
Adaptogenic vitality herb | High in vitamin C with iron | Aka Indian gooseberry
ORGANIC
Spirulina Powder
superfood supplement
VEGAN
ETHICALLY SOURCED
GLUTEN-FREE

2 min

The #1 Nutrient to Add to Your Diet for Longevity?

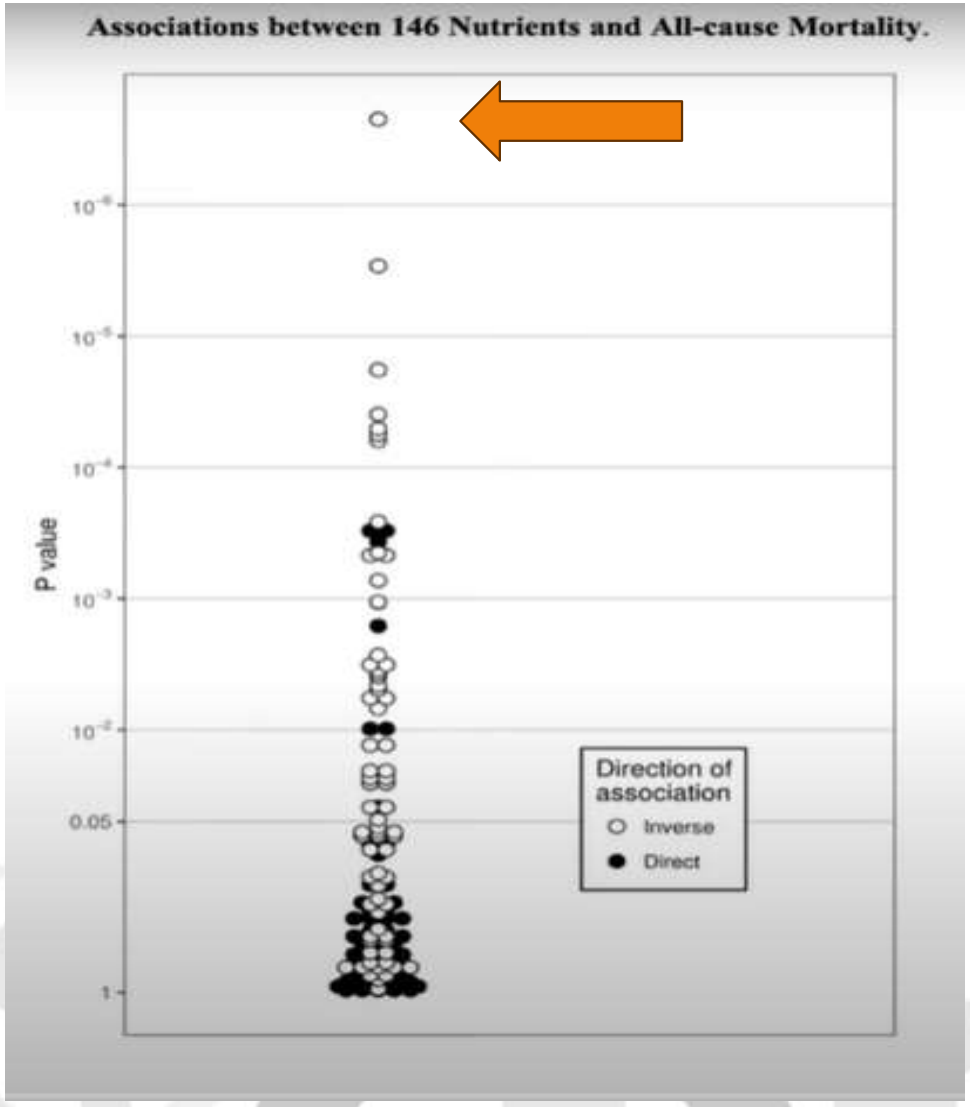
SYSTEMS PLAN

The #1 Nutrient to Add to Your Diet for Longevity?

You produce less as you get older

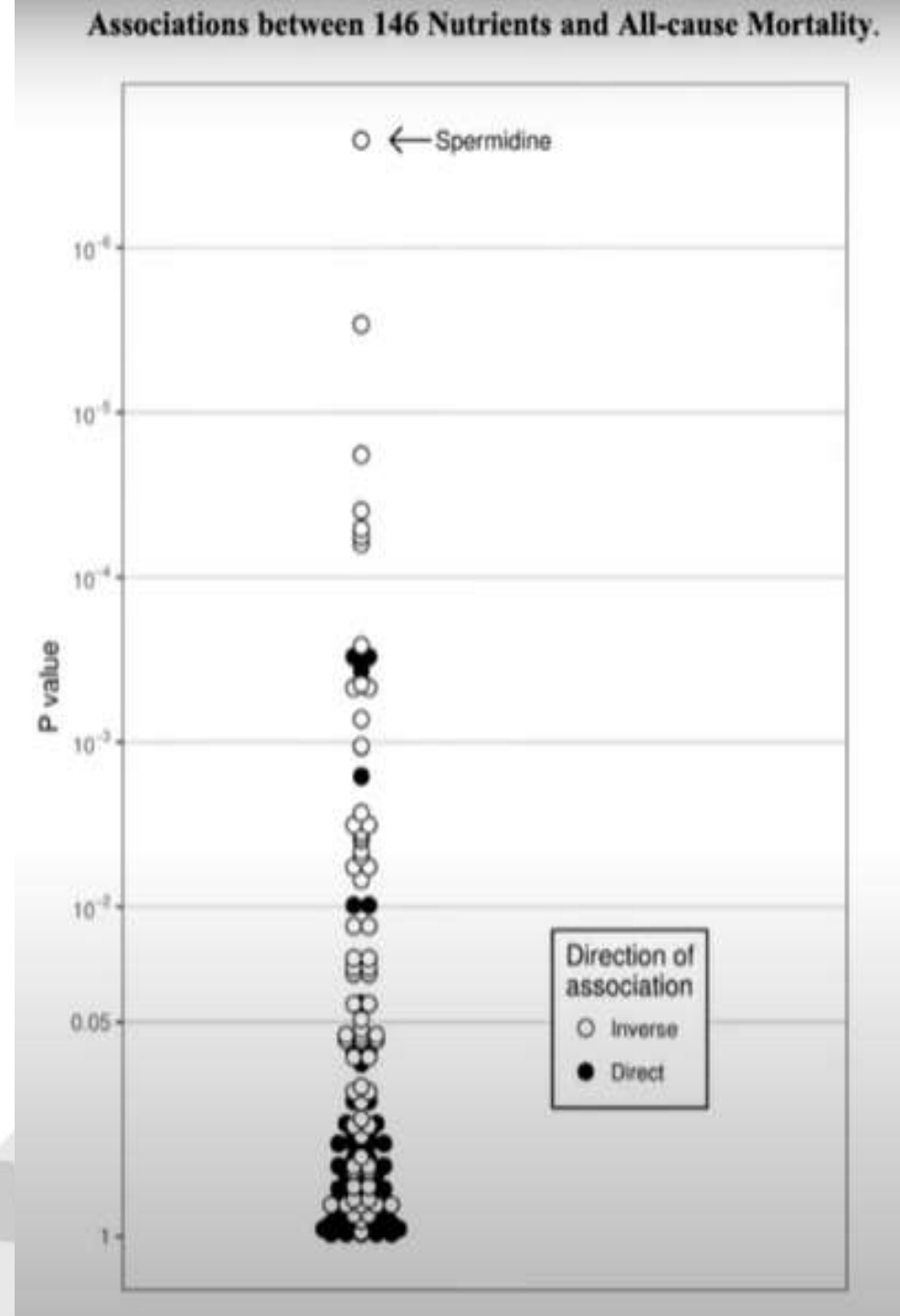
Extends life in mice 25%

Stimulates autophagy



SYSTEMS PLAN

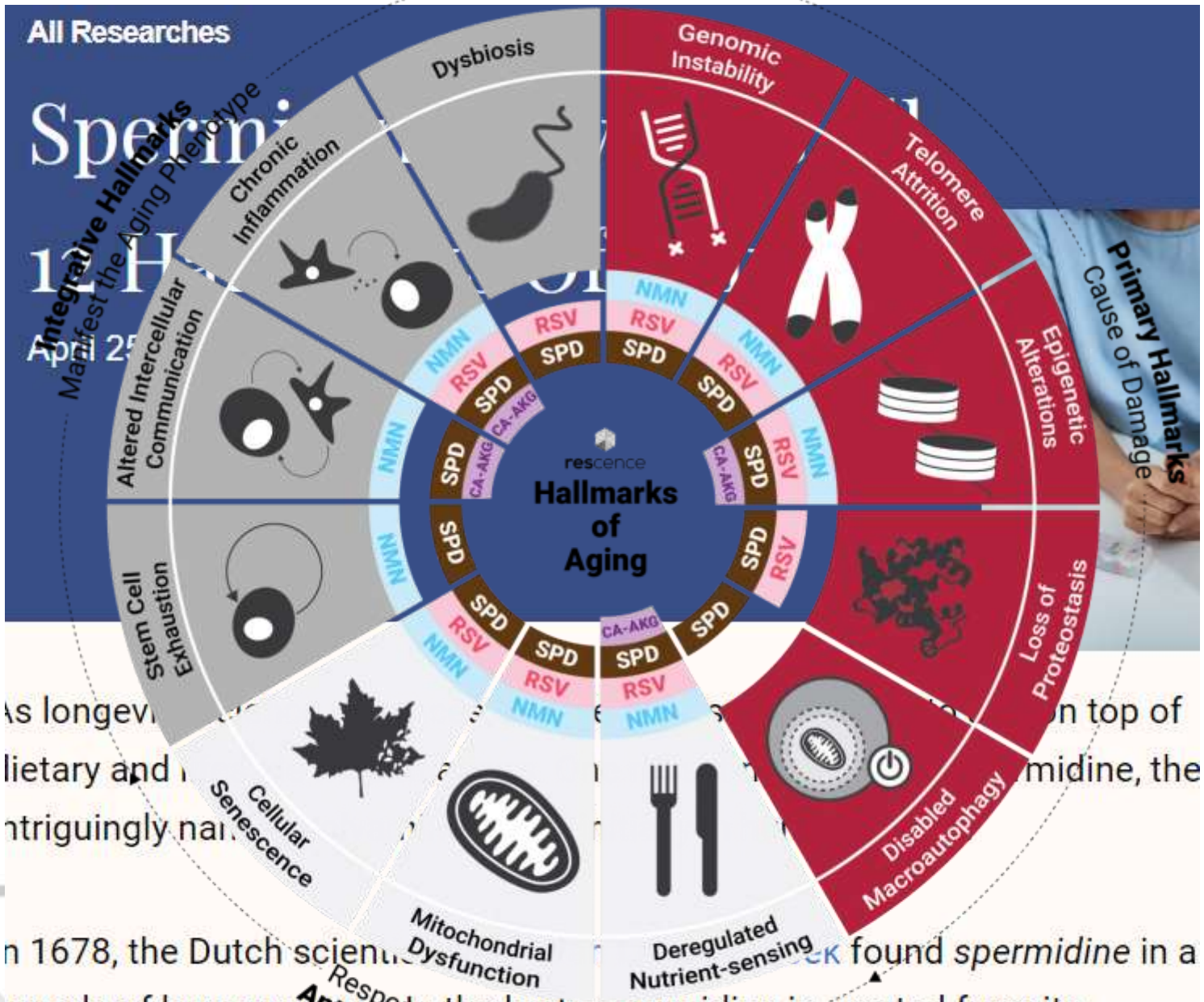
the region, were available for review. For this analysis, we defined the baseline as the year of the first detailed dietary assessment (1995) involving 829 women and men aged 45–84 y with a follow-up of 20 y (1995–2015; **Supplemental Figure 1**). The study protocol conformed to the Declaration of Helsinki and was approved by the local ethics committees (Bolzano and Verona). Participants gave their written informed consent and did not receive financial compensation. Participant characteristics were



Spermidine

- Spermidine alters the composition and function of gut microbiota, and intake is linked with a lower risk of obesity.
- The compound leads to:
  - significant weight loss
  - improved insulin resistance
  - alleviation of metabolic endotoxemia
  - enhanced intestinal barrier function.

Gut Microbes. 2020; 12(1): 1832857

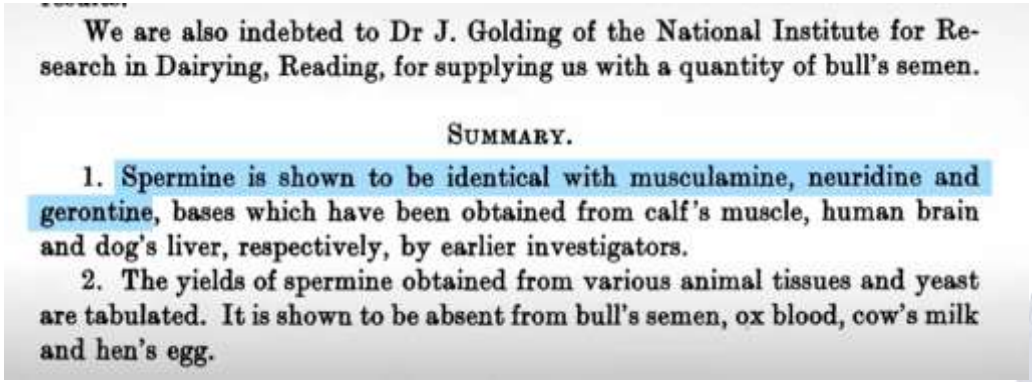


As longev… …n top of
lietary and … …midine, the
ntriguingly na…

n 1678, the Dutch scient… …found *spermidine* in a
ample of human sperm. In the body, spermidine is created from its
precursor, putrescine, which is the precursor for another polyamine called

Where was Spermidine Originally Found?

- The polyamine was first isolated from seminal fluid in 1870 - and simply named after it. They are in all cells.
- A polyamine is an organic compound having more than two amino groups.
- Polyamines are essential elements of cells from all species.
- They are required for optimum cell growth.



We are also indebted to Dr J. Golding of the National Institute for Research in Dairying, Reading, for supplying us with a quantity of bull's semen.

SUMMARY.

1. Spermine is shown to be identical with musculamine, neuridine and gerontine, bases which have been obtained from calf's muscle, human brain and dog's liver, respectively, by earlier investigators.
2. The yields of spermine obtained from various animal tissues and yeast are tabulated. It is shown to be absent from bull's semen, ox blood, cow's milk and hen's egg.

DOI: 10.1089/rej.2012.1349

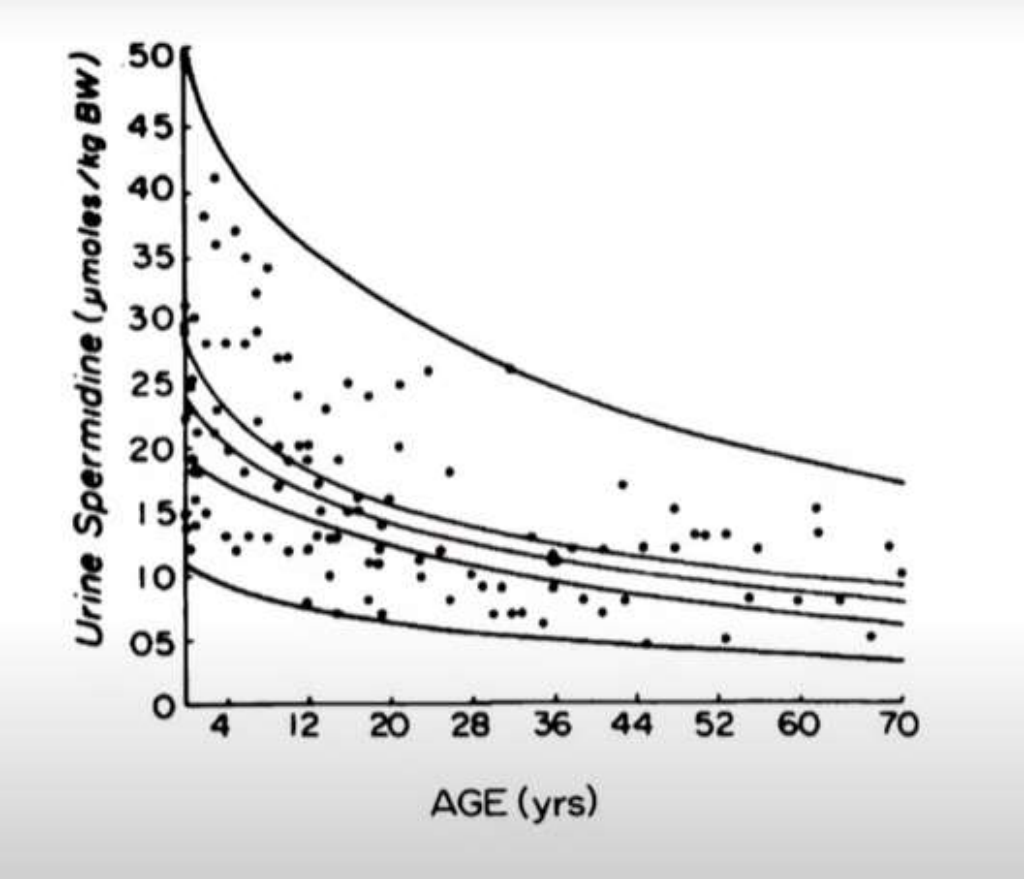
Spermidine and Spermine Are Enriched in Whole Blood of Nona/Centenarians

Stefania Pucciarelli,[1] Benedetta Moreschini,[1] Daniela Micozzi,[1] Giusi S. De Fronzo,[1] Francesco M. Carpi,[1] Valeria Polzonetti,[1] Silvia Vincenzetti,[2] Fiorenzo Mignini,[3] and Valerio Napolioni[1]

Abstract

Polyamines (putrescine, spermidine, and spermine) are a family of molecules that derive from ornithine through a decarboxylation process. They are essential for cell growth and proliferation, stabilization of negative charges of DNA, RNA transcription, translation, and apoptosis. Recently, it has been demonstrated that exogenously ad-

We Produce Less as We Age



of synthetic spermidine, or prebiotics and probiotics that drive microbial polyamine synthesis in the intestine.

In sum, in our view, spermidine is synthesized by our organism in sufficient quantities during youth, but not in old age. Thus, one may argue that, as we age, spermidine evolves to the status of a vitamin, and thus has to be supplemented from external sources to secure the maintenance of autophagic flux required for organismal homeostasis.

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Spermidine

A novel autophagy inducer and longevity elixir

(Bardócz et al., 1993; Okamoto et al., 1997). Because spermine and spermidine are not enzymatically degraded in the alimentary tract, oral spermine and spermidine are absorbed quickly from intestinal lumen and distributed to all organs and tissues (Bardocz

Frank Ma

Institute of Molecular Biosciences; University of Graz; Graz, Austria; Institut Gustave Roussy; Villejuif, France;

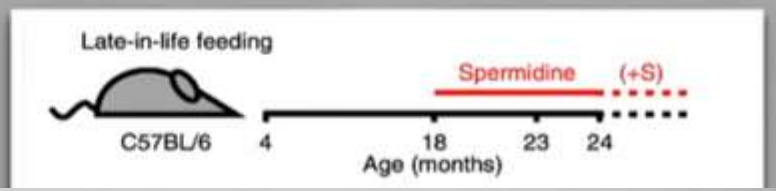
University Paris Sud; Villejuif, France

Spermidine is a ubiquitous polycation

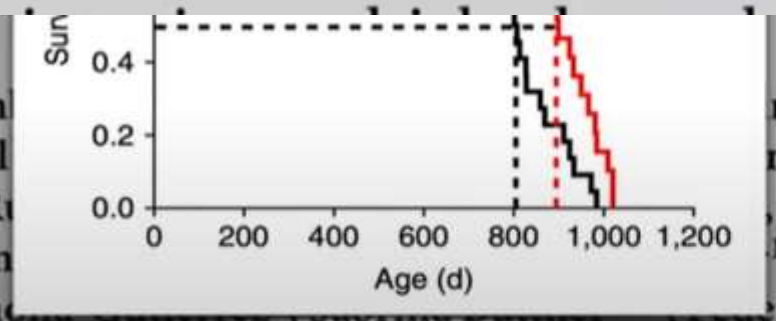
it retarded necrotic cell death. In a

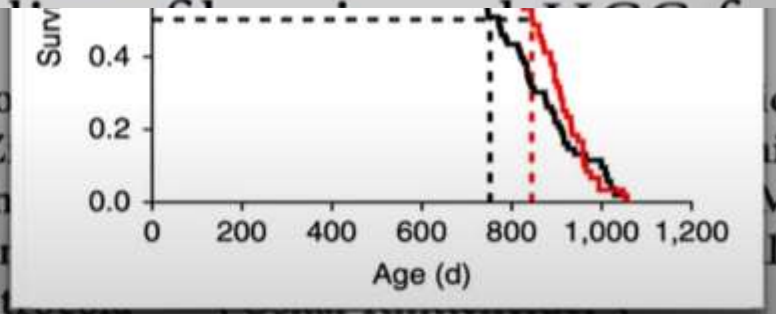
Start Late in Life- Still Extends Life

nature medicine



tered spermidine can extend lifespan in mice, we determined that life extension of up to 25% can be produced by lifelong





Tobias Eisen[illegible]na Schro[illegible]c[1],
Tobias Pendl[illegible]ndreas Z[illegible]ing Tong[8],
Christoph Ru[illegible], Angelin[illegible]Magnes[9],
Gert Trausin[illegible][10], Zehar[illegible]ler[13],
Didac Carm[illegible]rico Piet[illegible]
Emilie Schrepfer[20,21], Patrick Rockenfeller[1,22], Corinna Simonini[3], Alexandros Rahn[6], Marion Horsch[23],
Kristin Moreth[23], Johannes Rockers[23–25], Helmut Fuchs[23], Valerie Gailus-Durner[23], Frauke Neff[23,26],

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The Best Sources

#2- Soy beans

- A staple of veggie cooking, **soya beans** - in the form of tofu, tempeh, miso or vegan milks
  - **20.7mg/100g**

Nursing Home-Wheatgerm in a Roll

92 subjects

- Dinner roll
- Dinner roll with wheat germ (3.3 mg spermidine)

Results:

- Improved mild dementia by 2 points
- Far more than any antidementia drug

In the implementation of the study, the 92 subjects were divided into two random groups. One group received a grain roll with wheat germ (Schalkmühle, Ilz, Austria; 1075 mg/kg spermidine) for breakfast 6 times a week (roll A). Each roll A contained 3.3 mg of spermidine after baking. To scrutinize the success of spermidine, the second group received rolls baked with wheat bran (Schafler Mühle, Feistritz, Austria; 115 mg/kg spermidine) instead of wheat germ (roll B).

The most substantial improvement in test performance for the group with higher spermidine substitution was found in the group of subjects with mild dementia with an increase of 2.23 ($p=0.026$) in the Mini Mental test. The improvement by more than 2 points is way beyond all available antidementia treatments so far. In a comparable study over the

Food Sources of Spermidine

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Recommended Food List

Foods listed in green are recommended. You want to avoid the foods listed in red.

FOODS TO EAT

**FOODS TO BE CAREFUL WITH

Vegetables Low GI	Vegetables Medium GI	Fruit	Oils	Concentrated Proteins	Nuts & Seeds	**Legumes	Grains	Dairy	Beverages	Functional Foods
Cruciferous: broccoli, brussels sprouts, cabbages, cauliflower Greens: beet greens, bok choy, collard greens, escarole, kale, mustard greens, Swiss chard, watercress, spinach Lettuce/Mixed greens Mushrooms Salsa (sugar-free) Sprouts: alfalfa, broccoli or radish sprouts, bamboo shoots, etc. Squash: spaghetti, summer, yellow, zucchini Other vegetables: artichokes, asparagus, organic celery, chives, cucumbers, dill pickles, eggplants, garlic, green beans, hot peppers, kelp, leeks, reduced vegetable juices, okra, onions, organic sweet bell peppers, radishes, snow peas, organic tomatoes, water chestnuts	Beets Carrots Pumpkins Rutabagas Sweet potatoes or yams Turnips Winter squash Organic Yukon Gold Potatoes	Berries: blackberries, blueberries, raspberries, and organic strawberries Organic apples Apricots Cantaloupe Organic cherries Clementine Fresh Figs Organic grapes Honeydew melons Kiwifruits Mango Organic nectarines Oranges Organic peaches Organic pears Plums Tangerines Watermelon Bananas Dried fruit Fruit juices Pineapples	Best: Avocados and Guacamole Oils Good: Extra virgin coconut oil Cold pressed extra virgin olive oil Flaxseed oil Walnut oil Avocado oil Mayonnaise (made with avocado oil) Vegetable and Processed oils Canola oil Hydrogenated oil Margarine Peanut oil Sunflower oil Safflower oil Trans fats Vegetable shortening	Best: Low GI vegetables Tofu Tempeh Soy or veggie burger (read ingredients) Fish (wild caught) Beef (grass-fed) Lamb (grass-fed) Chicken (free-range) Good: Beef liver Eggs (free-range) Cottage cheese Ricotta Mozzarella Parmesan Processed meat Deli Meat Hot Dogs Pork Sausage Salami Tuna	Nuts: Walnut Almonds Brazil nuts Macadamia Pecan Pistachios Hazelnuts Seeds: Sunflower Pumpkin Sesame seeds Nut butter: Almond butter Not as good: Peanuts Cashews Peanut butter (no sugar) Nuts with sugar or chocolate Nut butter that contains toxic fats or sugar	Beans: black, butter, cannellini, garbanzo, chickpeas, great northern, pinto, kidney, lima, navy, mung, fat free refried, green soy Hummus Bean Soup Lentils: beluga, French, and red variety Peas: split green or yellow peas Baked beans Peanuts Soybean oil	Amaranth, teff, or quinoa Rice: Barley, buckwheat groats, millet Bulgar Popcorn Whole oats Whole wheat, spelt, or kamut berries Pasta: 100% whole wheat, spelt, kamut, or black beans Crackers Breads: rolled whole-grain or 100% whole-rye Tortilla or Pita: whole-wheat or low-carb Flour tortilla Wheat bread White bread Pasta	Butter or ghee Buttermilk Yogurt (plain) Dairy Substitutes: Almond milk (no sugar) Hemp milk (no sugar) Coconut milk (no sugar) All conventional dairy products including milk Processed cheese	Water Coffee Herbal or Green teas Sparkling or Mineral water Alcohol Soda Sugary beverages Fruit juices Enhanced or flavored water Diet/Artificially sweetened drinks	Dynamic Daily Meal Dynamic GI Restore Dynamic Cardio-Metabolic Dynamic Inflam-Eze Dynamic GI Integrity Dynamic Detox

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Take 1T of wheat germ per day.

7SystemsPlan.com

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ORIGINAL INVESTIGATION

Ten Years of Life

Is It a Matter of Choice?

Gary E. Fraser, MB, ChB, PhD; David J. Shavlik, MSPH

Background: Relative risk estimates suggest that effective implementation of behaviors commonly advocated in preventive medicine should increase life expectancy, although there is little direct evidence.

Objective: To test the hypothesis that choices regarding diet, exercise, and smoking influence life expectancy.

vail, 3.96–4.86 years) in women, giving them perhaps the highest life expectancy of any formally described population. Commonly observed combinations of diet, exercise, body mass index, past smoking habits, and hormone replacement therapy (in women) can account for differences of up to 10 years of life expectancy among Adventists. A comparison of life expectancy when these factors take high-risk compared with low-risk values shows independent effects that vary between 1.06 and

Translational Stroke Research
https://doi.org/10.1007/s12975-020-00788-y

COMMENTARY

Effects of Lifestyle Factors on Cognitive Resilience: Commentary on "What This Sunny, Religious Town in California Teaches Us About Living Longer"

Prativa Sherchan[1] · Fayth Miles[2,3] · Michael Orlich[4] · Gary Fraser[3] · John H. Zhang[1,5,6] · Konrad Talbot[3,7] ·

stories about the city of Loma Linda in California, one of the five original "blue zones" in the world, areas or populations with documented high longevity. Loma Linda was labeled as a

"blue zone" based upon research conducted at Loma Linda University on long-lived Seventh-day Adventist populations, as detailed below. A majority of the people in Loma Linda belong to the Seventh-day Adventist faith, which advocates

focus of numerous epidemiological studies examining the relationship between healthy living and health outcomes.

Three long-term studies focused on this population have explored the effects of lifestyle and diet on disease outcomes

Adventist vegetarian men and women have expected ages at death of 83.3 and 85.7 years, respectively. These are 9.5 and 6.1 years, respectively, greater than those of the 1985 California population in a uni-

variate analysis. When vegetarians are forced to take me

Loma Linda University, Loma Linda, CA 92350, USA

incidence of these diseases to be lower in Adventists com-

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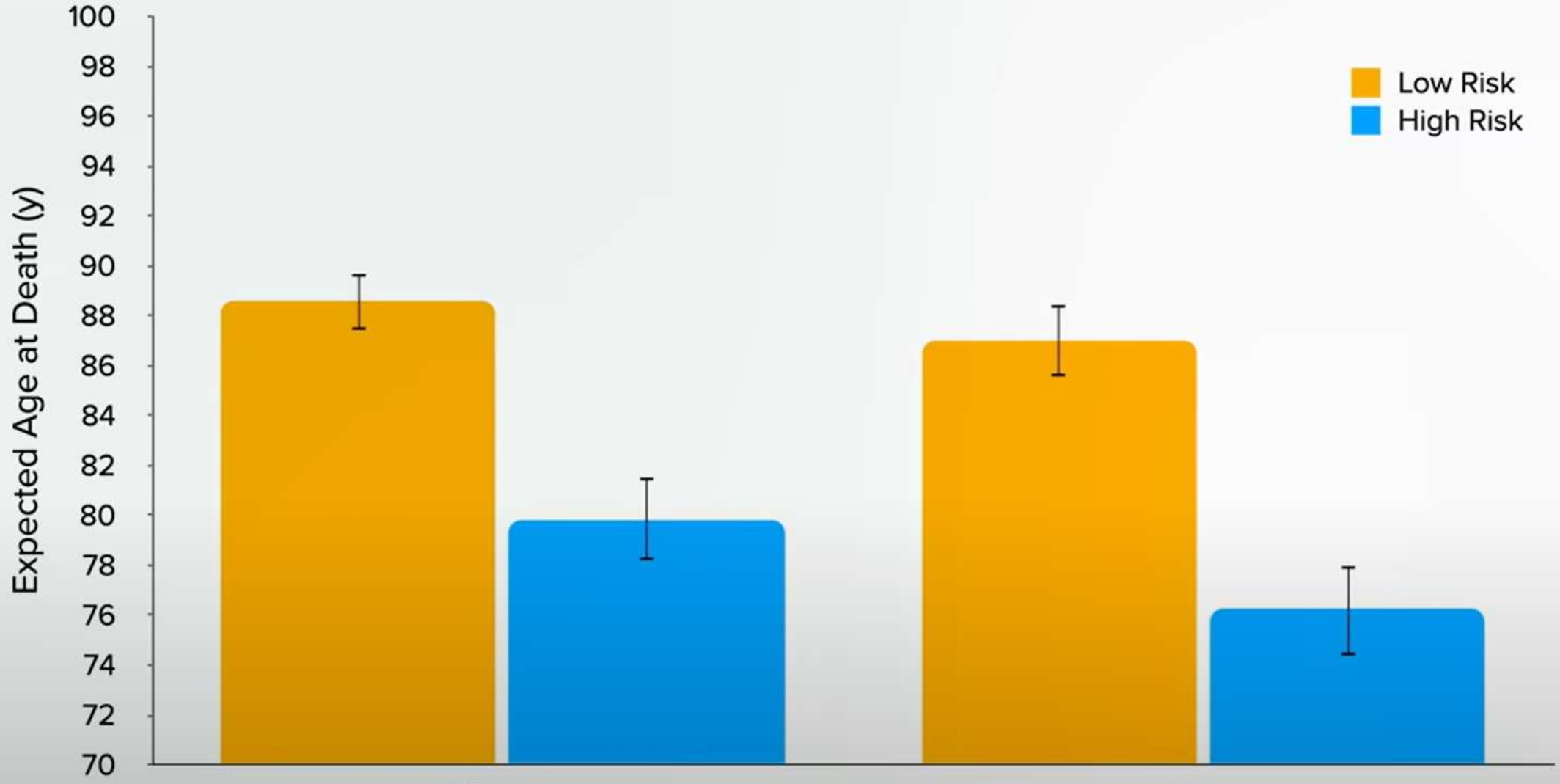
Arch Intern Med. 161(13):1645-52.

Expected Ages at Death in Men & Women



Difference (95% Confidence Interval), y	Women	Men
	8.7	10.8

Better Quality of Life

Substantial gains in life expectancy would only be worthwhile if they were also accompanied by a longer period of good-quality life. Although our data cannot directly address quality of life, it was previously shown[34] that the vegetarian Adventists took less medication and had fewer overnight hospital stays, surgical procedures, and x-ray examinations during the previous year. Vegetarians also had a reduced prevalence of several chronic diseases[29] that may degrade the quality of life. The re-

- Less medications
- Less hospital stays
- Less surgical procedures
- Less x-rays
- Less chronic disease

7 SYSTEMS PLAN

Research

JAMA Internal Medicine | Original Investigation

Association Between Plant and Animal Protein Intake and Overall and Cause-Specific Mortality

self-reported health status. Replacement of 3% energy from animal protein with plant protein was inversely associated with overall mortality (risk decreased 10% in both men and women) and cardiovascular disease mortality (11% lower risk in men and 12% lower risk in

diets to overall health, a comprehensive analysis of long-term cause-specific mortality in association with the intake of plant protein and animal protein has not been reported.

OBJECTIVE To examine the associations between overall mortality and cause-specific mortality and plant protein intake.

DESIGN, SETTING, AND PARTICIPANTS This prospective cohort study analyzed data from 416 104 men and women in the US National Institutes of Health–AARP Diet and Health Study from 1995 to 2011. Data were analyzed from October 2018 through April 2020.

EXPOSURES Validated baseline food frequency questionnaire dietary information, including

3% Less Meat

Replace with Plant Protein

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CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of

The report on aging and health published by the World Health Organization (WHO) in 2015 defines healthy aging as "the process of developing and maintaining the functional ability that enables wellbeing in older age" and

Rosario Ortolá, MD, PhD,[a,b] Ellen A Struijk, PhD,[a,b] Esther García-Esquinas, MD, PhD,[a,b]

Deficit Accumulation Index. At each wave, unhealthy aging was measured using a 52-item DAI with 4 domains: functional impairments, self-reported health/vitality, mental health, and morbidities/use of health services. The overall and domain-

BACKGROUND: Animal and vegetable-based proteins differ on their effect on many health outcomes, but

CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

CLINICAL SIGNIFICANCE

- Higher intake of vegetable protein was associated with less deficit accumulation.

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Fernando Rodríguez-Artalejo, MD, PhD; Esther López-García, PhD

vant. In addition, substitution of 1% of energy from vegetable protein for an equal amount of total animal protein, dairy protein, or meat protein also led to significantly less deficit accumulation.

BACKGROUND: Animal and vegetable-based proteins differ on their effect on many health outcomes, but

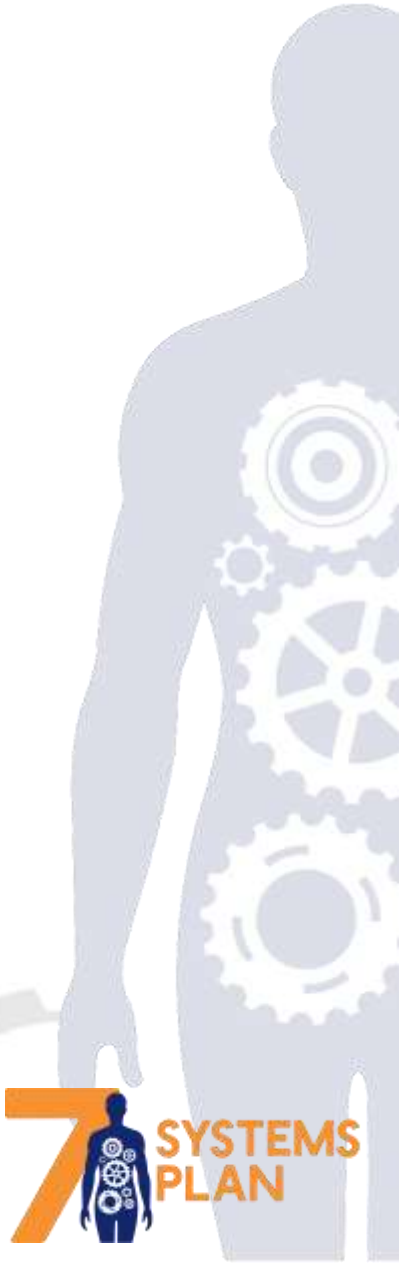
Saturated Fat Problem?

are attributable only to protein per se. One might think that the beneficial associations observed for vegetable protein could also be the result of the observed reduction in fat intake accompanying the increase in vegetable protein (Supplemental Table 3 in Supplementary material 1). However, adjustment for change in fat intake did not materially modify the association. Besides, consistently with the distri-

Beneficial Because:

with occasional meat consumption. In addition, it is not clear if the beneficial health effects are because of an avoidance of deleterious effects associated with overconsumption of calories and meat or to a genuine health promotion of plants and their bioactive ingredients, or possibly both together.

- Less calories
- Harmful ingredients in meat (AGEs)
- Healthy bioactive ingredients in plants



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7 Reasons to Eat Less Meat

1. Longer life
2. IGF-1
3. AGEs
4. Antibiotics
5. Dioxins
6. Plastics
7. Calories

What to do With Meat

- Eat meat
  - Less often
  - In smaller amounts
- Use more plant protein
  - Legumes, vegetables, whole grains
- Use healthy meat
  - Wild caught fish
  - Grass fed meat
  - Free range

A New Hormone to Extend Life

ELSEVIER

Biochimica et Biophysica Acta 1492 (2000) 203–206

BBA

www.elsevier.com/locate/bba

Short sequence-paper

Identification of a novel FGF, FGF-21, preferentially expressed in the liver[1]

Tetsuya Nishimura, Yuhki Nakatake, Morichika Konishi, Nobuyuki Itoh *

We isolated cDNA encoding a novel FGF (210 amino acids) from mouse embryos. As this is the 21st documented FGF, we tentatively term it FGF-21. FGF-21 has a hydrophobic amino terminus (~30 amino acids), which is a typical signal sequence, and appears to be a

Abstract

We isolated cDNA encoding a novel FGF (210 amino acids) from mouse embryos. As this is the 21st documented FGF, we tentatively term it FGF-21. FGF-21 has a hydrophobic amino terminus (~30 amino acids), which is a typical signal sequence, and appears to be a secreted protein. The expression of FGF-21 mRNA in mouse adult tissues was examined by Northern blotting analysis. FGF-21 mRNA was most abundantly expressed in the liver, and also expressed in the thymus at lower levels. We also isolated human cDNA encoding FGF-21 (209 amino acids). Human FGF-21 is highly identical (~75% amino acid identity) to mouse FGF-21. Among human FGF family members, FGF-21 is most similar (~35% amino acid identity) to FGF-19.

Keywords: FGF-21; Fibroblast growth factor; Liver; Gene family; cDNA

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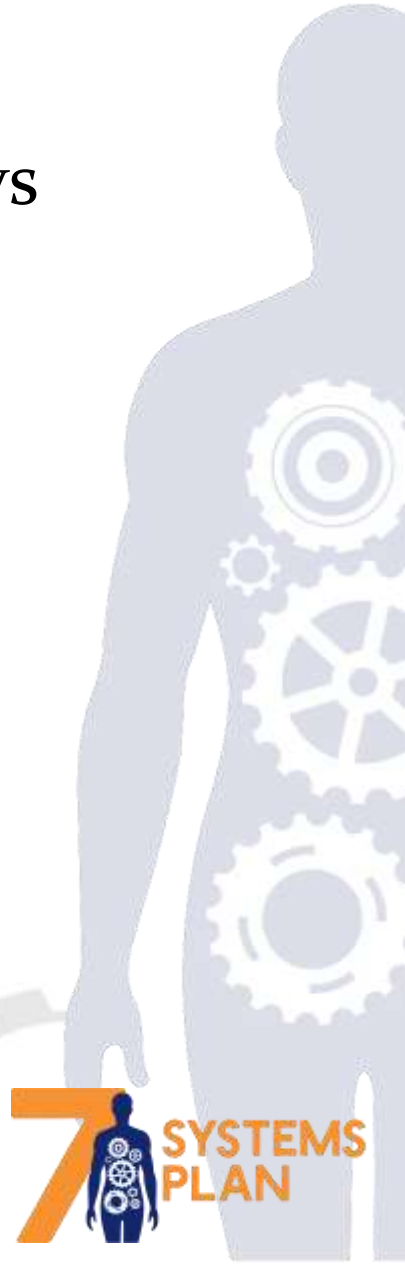
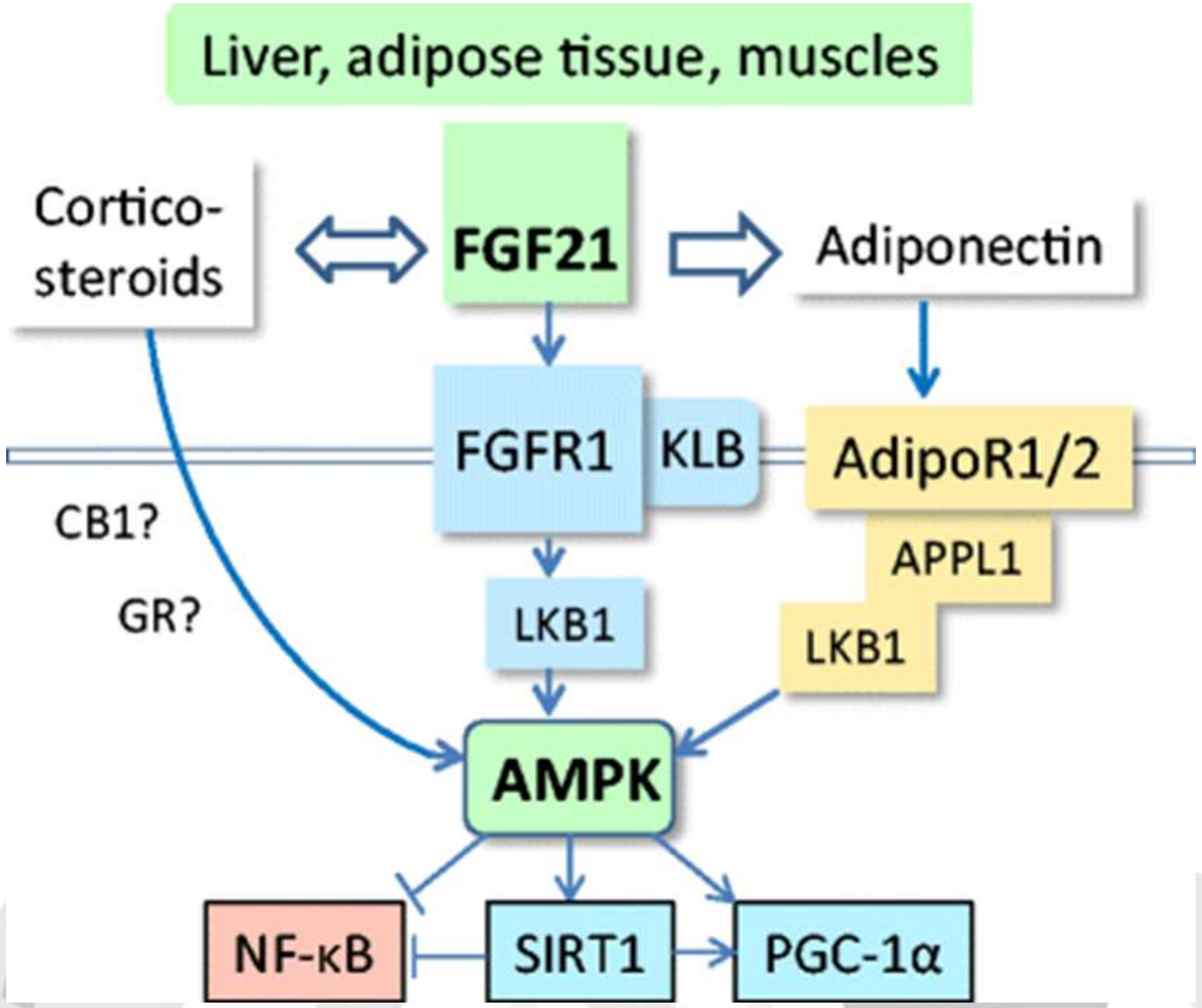
Fibroblast Growth Factor 21 (FGF21)

- A hormone that regulates important metabolic pathways
- FGF21 can:
  - regulate carbohydrate and fat metabolism
  - maintain energy during fasting
  - **improve cellular aging**
  - **increase weight loss**




Liver, adipose tissue, muscles
Cortico-steroids
FGF21
Adiponectin
FGFR1
KLB
AdipoR1/2
CB1?
GR?
APPL1
LKB1
LKB1
AMPK
NF-κB
SIRT1
PGC-1α

eLIFE
elife.elifesciences.org

RESEARCH ARTICLE

The starvation hormone, fibroblast growth factor-21, extends lifespan in mice

Yuan Zhang[1], Yang Xie[2], Eric D Berglund[3], Katie Colbert Coate[4], Tian Teng He[5], Takeshi Katafuchi[1], Guanghua Xiao[2], Matthew J Potthoff[4], Wei Wei[1], Yihong Wan[1], Ruth T Yu[6], Ronald M Evans[6], Steven A Kliewer[7]*, David J Mangelsdorf[4]*

[1]Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, United States; [2]Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, United States; [3]Hypothalamic Research, University of Texas Southwestern Medical Center, Dallas, United States; [4]Department of Pharmacology, Howard Hughes Medical Institute, University of Texas Southwestern Medical Center, Dallas, United States; [5]Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, United States; [6]Gene Expression Laboratory, Howard Hughes Medical Institute, Salk Institute for Biological Studies, San Diego, United States; [7]Departments of Molecular Biology and Pharmacology, University of Texas Southwestern Medical Center, Dallas, United States

Abstract Fibroblast growth factor-21 (FGF21) is a hormone secreted by the liver during fasting that elicits diverse aspects of the adaptive starvation response. Among its effects, FGF21 induces hepatic fatty acid oxidation and ketogenesis, increases insulin sensitivity, blocks somatic growth and causes bone loss. Here we show that transgenic overexpression of FGF21 markedly extends lifespan in mice without reducing food intake or affecting markers of NAD+ metabolism or AMP kinase and mTOR signaling. Transcriptomic analysis suggests that FGF21 acts primarily by blunting the growth hormone/insulin-like growth factor-1 signaling pathway in liver. These findings raise the possibility that FGF21 can be used to extend lifespan in other species.

DOI: 10.7554/eLife.00065.001

***For correspondence:** steven.kliewer@utsouthwestern.edu

DE GRUYTER

Horm Mol Biol Clin Invest 2015; aop

Mark F. McCarty*

Practical prospects for boosting hepatic production of the "pro-longevity" hormone FGF21

DOI 10.1515/hmbci-2015-0057
Received October 25, 2015; accepted November 20, 2015

Keywords: ATF4; bilirubin; FGF21; FXR; GLP-1; glucagon; PPARα; vegan.

Abstract: Fibroblast growth factor-21 (FGF21), produced

drugs, elevated lipolysis, moderate-protein vegan diets, growth hormone, and bile acids may have potential to

duced primarily by hepatocytes and adipocytes, FGF21 activates hybrid receptors comprised of an isoform of the FGF receptor and the transmembrane protein βKlotho,

In recent years, fibroblast growth hormone-21 (FGF21) has emerged as a key agent for promotion of metabolic and vascular health, leanness, and longevity [1–5]. Pro-

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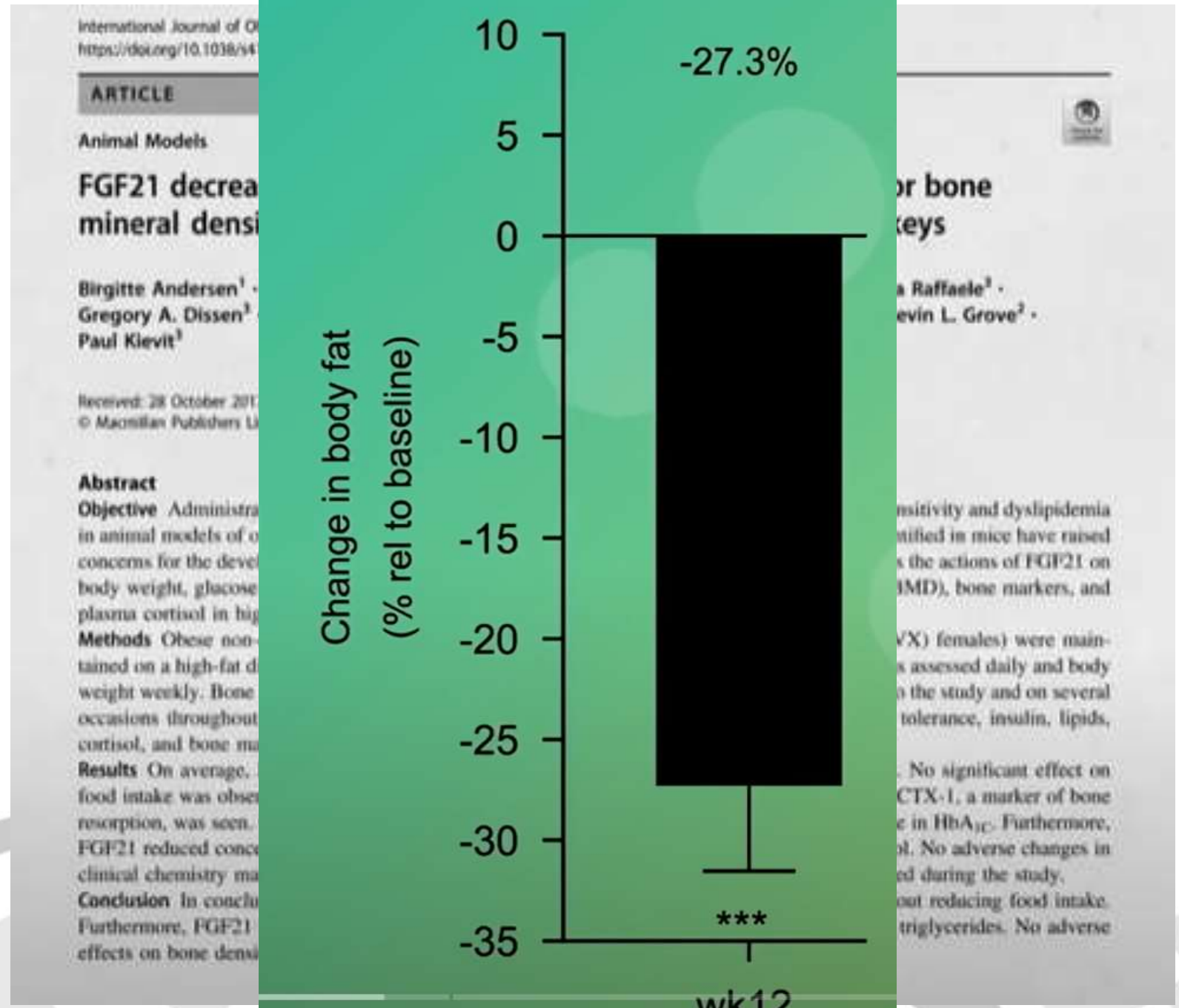
ARTICLE
Animal Models
Abstract
Change in body fat
(% rel to baseline)
10
5
0
-5
-10
-15
-20
-25
-30
-35
-27.3%
***
wk12

eLIFE
RESEARCH ARTICLE

The starvation hormone, fibroblast growth factor-21, extends lifespan in mice

In this report, we demonstrate that chronic exposure of mice to the starvation hormone, FGF21, increases median survival time by ~30% and ~40% in males and females, respectively, without decreasing food intake. The increase in lifespan extension is comparable to that achieved by caloric restriction

University of Texas Southwestern Medical Center, Dallas, United States; [a]Department

may limit its utility as a therapeutic agent. We conclude that FGF21 could potentially be used as a hormone therapy to extend lifespan in mammals.

Abstract Fibroblast growth factor-21 (FGF21) is a hormone secreted by the liver during fasting

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PERSPECTIVE

FOCUS ON AGING

nature medicine

Can aging be 'drugged'?

Celine E Riera[1–3] & Andrew Dillin[1–3]

The engines that drive the complex process of aging are being identified by model-organism research, thereby providing potential targets and rationale for drug studies. Several studies of small molecules have already been completed in animal models with the hope of finding an elixir for aging, with a few compounds showing early promise. What lessons can we learn from drugs currently being tested, and which pitfalls can we avoid in our search for a therapeutic for aging? Finally, we must also ask whether an elixir for aging would be applicable to everyone, or whether we age differently, thus potentially shortening lifespan in some individuals.

As a positive outcome of medical progress and the modern lifestyle, life is generally now prolonged in developed countries. The number of centenarians keeps rising worldwide, and since the mid-1970s a new category of centenarians has appeared: the supercentenarians, who are individuals over the age of 110 (www.grg.org). However, a downside of this increased longevity is the rise in the incidence of age-associated diseases, such as cardiovascular and metabolic disorders, cancer and neurodegenerative disorders[1]. By 2025, it is anticipated that more than 20% of Europeans will be 65 or older (Public health report, European Commission; http://ec.europa.eu/health/ageing/policy/index_en.htm). Similarly, in the US, it is predicted that Americans aged 65 or older will number nearly 89 million in 2050, more than doubling the number of older adults in the US in 2010 (Centers for Disease Control and Prevention (CDC); http://www.cdc.gov/aging/index.html). The aging population will have profound effects on public health, social services, and welfare systems.

chronic diseases, including cardiovascular, cerebrovascular and neurodegenerative diseases; metabolic syndromes; and most prevalent forms of cancer[2]. Conceptually, aging is viewed as a general decline in cell and tissue function that is associated with an increase in low-grade inflammation and a deficiency in the adaptive immune response, thus increasing the susceptibility to disease, and ultimately leading to tissue failure and death[3]. The development of one chronic disease of aging is generally not an isolated event; there is a high incidence of chronic diseases and co-morbidities in the elderly. Therefore, it is crucial to define the molecular events required to boost the body's natural defenses, such as by identifying coping mechanisms that target the threats posed to an organism's cells and tissues.

We present here a broad overview of the progress achieved in animal research to identify drugs that extend lifespan and healthy aging, as well as the current understanding of the mode of action of these drugs. We also argue that the lessons learned in animal models provide an important cornerstone of the process of targeting human aging, but we also raise concerns about therapies that will work for all, as the heterogeneity of human aging remains a largely unexplored area of research.

Existing pharmacology

Multiple drugs have elicited major interest in aging research through their ability to activate signaling networks involved in aging (**Table 1**). An initiative from the US National Institute of Aging (Intervention Testing Program, ITP) tests compounds that may hold the promise of altering lifespan in mice[4]. We discuss some of the current therapies under investigation below.

Rapamycin. Rapamycin was identified by the ITP program to be a

Curr Hypertens Rep (2017) 19: 28
DOI 10.1007/s11906-017-0730-5

The Potential Role of Fibroblast Growth Factor 21 in Lipid Metabolism and Hypertension

man. The idea of one drug that can treat obesity, diabetes, dyslipidemia, and hypertension all at once might have seemed impossible a few years ago but is now a tantalizing and exciting prospect.

DE GRUYTER

Horm Mol Biol Clin Invest 2017; 30(1): 20160034

Review

Albert Pérez-Martí, Viviana Sandoval, Pedro F. Marrero, Diego Haro* and Joana Relat*

Nutritional regulation of fibroblast growth factor 21: from macronutrients to bioactive dietary compounds

DOI 10.1515/hmbci-2016-0034

effects. The objective of this review is to compile exist-

To date, the pharmacological use of FGF21 is limited due to its half-life of around 1–2 h. In order to improve the

a promising therapeutic candidate for the treatment of obesity. FGF21 is predominantly produced by the liver but also by other tissues, such as white adipose tissue (WAT), brown adipose tissue (BAT), skeletal muscle, and pancreas in response to different stimuli such as cold and different nutritional challenges that include fast-

blast growth factor 21; obesity.

Introduction

Fibroblast growth factor 21 (FGF21) increases energy

Cell Metabolism
Clinical and Translational Report

A Long-Acting FGF21 Molecule, PF-05231023, Decreases Body Weight and Improves Lipid Profile in Non-human Primates and Type 2 Diabetic Subjects

Saswata Talukdar,[1,*] Yingjiang Zhou,[1] Dongmei Li,[1] Michelle Rossulek,[1] Jennifer Dong,[1] Veena Somayaji,[1] Yan Weng,[1]

in obese non-human primates (NHPs). When administered to overweight/obese subjects with T2DM, PF-05231023 caused a significant decrease in body weight and circulating atherogenic lipids. Importantly, despite these favorable changes, we

SUMMARY

Moller, 2014; Owen et al., 2014b; Reitman, 2013). The metabolic

DE GRUYTER Hormone Molecular Biology and Clinical Investigation. 2017; 20170002

Review

Junichiro Sonoda[1] / Mark Z. Chen[2] / Amos Baruch[3]

FGF21-receptor agonists: an emerging therapeutic class for obesity-related diseases

[1] Molecular Biology, Genentech, Inc., South San Francisco, CA 94080, USA, Phone: 650-467-2482, E-mail: junichis@gene.com
[2] Molecular Biology, Genentech, Inc., South San Francisco, CA 94080, USA
[3] Biomarker Development, Genentech, Inc., South San Francisco, CA 94080, USA

Abstract:
Fibroblast growth factor 21 (FGF21) analogs and FGF21 receptor agonists (FGF21RAs) that mimic FGF21 ligand activity constitute the new "FGF21-class" of anti-obesity and anti-diabetic molecules that improve insulin

At least nine different FGF21-class molecules have been tested in phase 1 or phase 2 clinical studies. Seven of them are modified FGF21 proteins: LY2405319, LY3025876, LY3084077, BMS986036, BMS986171, PF05231023 and AMG876. The other two are antibody-based receptor agonists: BFKB8488A and NGM313 (Figure 2). So far,

molecules, their molecular designs and the preclinical and clinical activities. These molecules include modified FGF21 as well as agonistic antibodies against the receptor for FGF21, namely the complex of FGF receptor 1 (FGFR1) and the obligatory coreceptor βKlotho (KLB). In addition, a novel approach to increase endogenous FGF21 activity by inhibiting the FGF21-degrading protease fibroblast activation protein (FAP) is discussed.

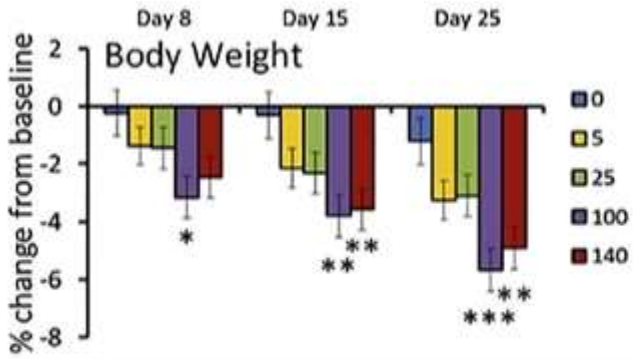
Keywords: monoclonal antibodies, NAFLD, obesity, therapeutics, type 2 diabetes
DOI: 10.1515/hmbci-2017-0002
Received: January 26, 2017; **Accepted:** February 13, 2017

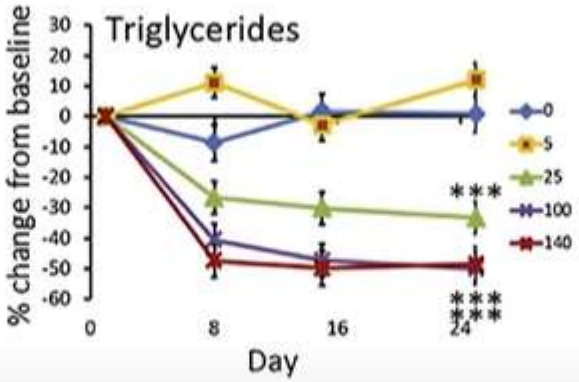
Introduction

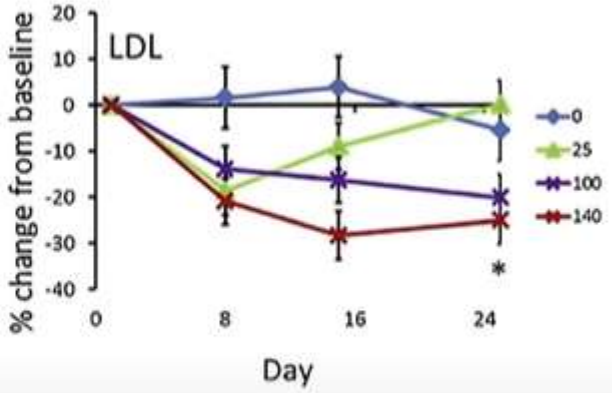
Weight

Triglycerides

LDL







*p < 0.05, **p < 0.01, ***p < 0.001 on day 25 compared with placebo

Received: 31 October 2016 | Revised: 24 May 2017 | Accepted: 25 May 2017
DOI: 10.1111/dom.13023

WILE

ORIGINAL ARTICLE

Once-weekly administration of a long-acting fibroblast growth factor 21 analogue modulates lipids, bone turnover markers, blood pressure and body weight differently in obese people with hypertriglyceridaemia and in non-human primates

PF-05231023 was associated with unfavourable changes in vital signs that pose potential safety concerns for chronic treatment with

[1]Pfizer Inc., Cambridge, Massachusetts, USA
[2]Pfizer Inc., Groton, Connecticut, USA

Present address
Saswata Talukdar, Merck Research Laboratories, South 630 Gateway Blvd, South San Francisco, CA 94080, USA.

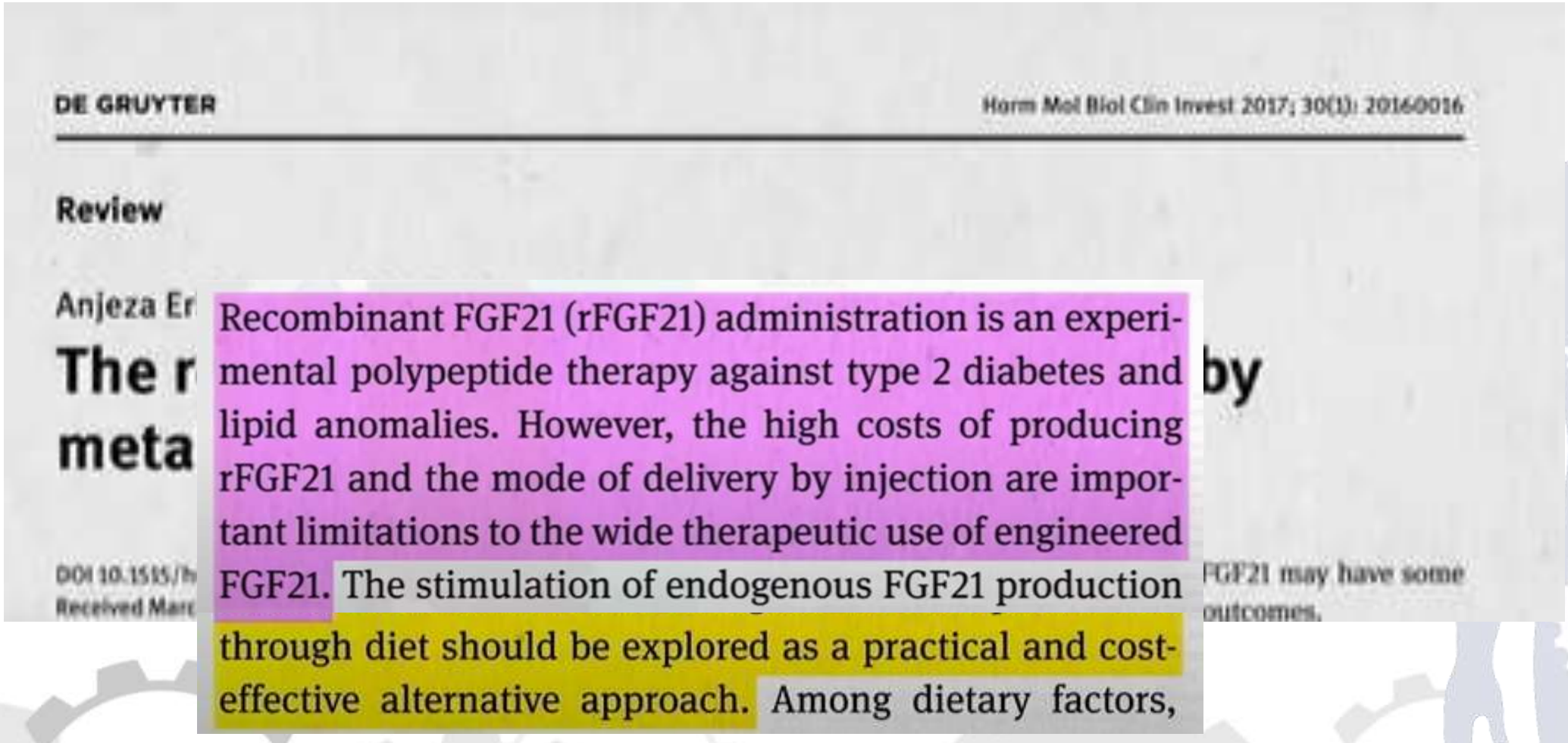
Correspondence
Roberto A. Calle MD, Internal Medicine Research Unit, Pfizer Inc., 1 Portland Street,

Aims: To assess the safety, tolerability, pharmacokinetics and pharmacodynamics of PF-05231023, a long-acting fibroblast growth factor 21 (FGF21) analogue, in obese people with hypertriglyceridaemia on atorvastatin, with or without type 2 diabetes.

Methods: Participants received PF-05231023 or placebo intravenously once weekly for 4 weeks. Safety (12-lead ECGs, vital signs, adverse events [AEs], laboratory tests) and longitudinal weight assessments were performed. Blood samples were collected for pharmacokinetic and pharmacodynamic analyses. Cardiovascular safety studies were also conducted in telemetered rats and mon-

SYSTEMS PLAN

How About Using Food or Lack Thereof



DE GRUYTER

Horm Mol Biol Clin Invest 2017; 30(1): 20160016

Review

Anjeza Er

The r … by

meta

Recombinant FGF21 (rFGF21) administration is an experimental polypeptide therapy against type 2 diabetes and lipid anomalies. However, the high costs of producing rFGF21 and the mode of delivery by injection are important limitations to the wide therapeutic use of engineered FGF21. The stimulation of endogenous FGF21 production through diet should be explored as a practical and cost-effective alternative approach. Among dietary factors,

DOI 10.1515/h…

Received Marc…

…FGF21 may have some …outcomes.

SYSTEMS PLAN

Nature Reviews Endocrinology | Published online 20 November 2015; doi:10.1038/nrendo.2015.202

METABOLISM

Fasting induces FGF21 in humans

A new study shows that circulating levels of FGF21 are markedly increased by fasting in humans and are part of the late stages of the body's adaptive response to starvation—a protective mechanism that evolved to aid survival in periods of famine.

In contrast to mice, in which levels of FGF21 are rapidly increased by fasting, previous studies in humans have either demonstrated no increase or only a modest increase in levels of FGF21 in response to fasting. "We felt that a conclusive fasting study needed to be performed in healthy individuals to definitively answer whether FGF21 was a fasting-induced hormone in humans and to understand what happens to levels of FGF21 during fasting," explains joint-lead investigator Pouneh Fazeli.

The researchers serially measured levels of FGF21 in 11 healthy male and female volunteers (aged 22.4–48.3 years; BMI 22.7–29.3 kg/m²) during a 10-day fast. Although decreased in the early phase of the fast, levels of FGF21 at day 10 were fourfold higher than those at day 0. Induction of FGF21 was associated with decreased thermogenesis of brown adipose tissue (measured by PET/MRI) and reduced levels of adiponectin, and occurred after the ketogenic response. Furthermore, FGF21 induction closely correlated with the release of markers of tissue breakdown (serum transaminases) and with weight loss.

"Our study definitively establishes FGF21 as a fasting-induced hormone in humans," states co-lead investigator Matthew Steinhauser. "By measuring FGF21 levels serially over a full 10-day fast in healthy volunteers, we now know why previous studies in humans reported inconsistent results, namely that FGF21 is induced in the majority of individuals, but only after a long-term fast."

On the basis of beneficial metabolic effects elicited by FGF21 treatment in mice (prevention of diet-induced obesity and improved glucose tolerance), FGF21 mimetics are being developed to treat metabolic diseases such as type 2 diabetes mellitus. "Our finding that the function of FGF21 might be highly dependent on an individual's nutritional status could be an important consideration as these potential drugs are developed," cautions Steinhauser.

David Holmes

ORIGINAL ARTICLE Fazeli, P. K. et al. FGF21 and the late adaptive response to starvation in humans. J. Clin. Invest. http://dx.doi.org/10.1172/JCI83349

SYSTEMS PLAN

Review
Complications
Diabetes Metab J 2016;40:22-31
http://dx.doi.org/10.4093/dmj.2016.40.1.22
pISSN 2233-6079 · eISSN 2233-6087

dmj
DIABETES & METABOLISM JOURNAL

Fibroblast Growth Factor 21 Protects against Atherosclerosis via Fine-Tuning the Multiorgan Crosstalk

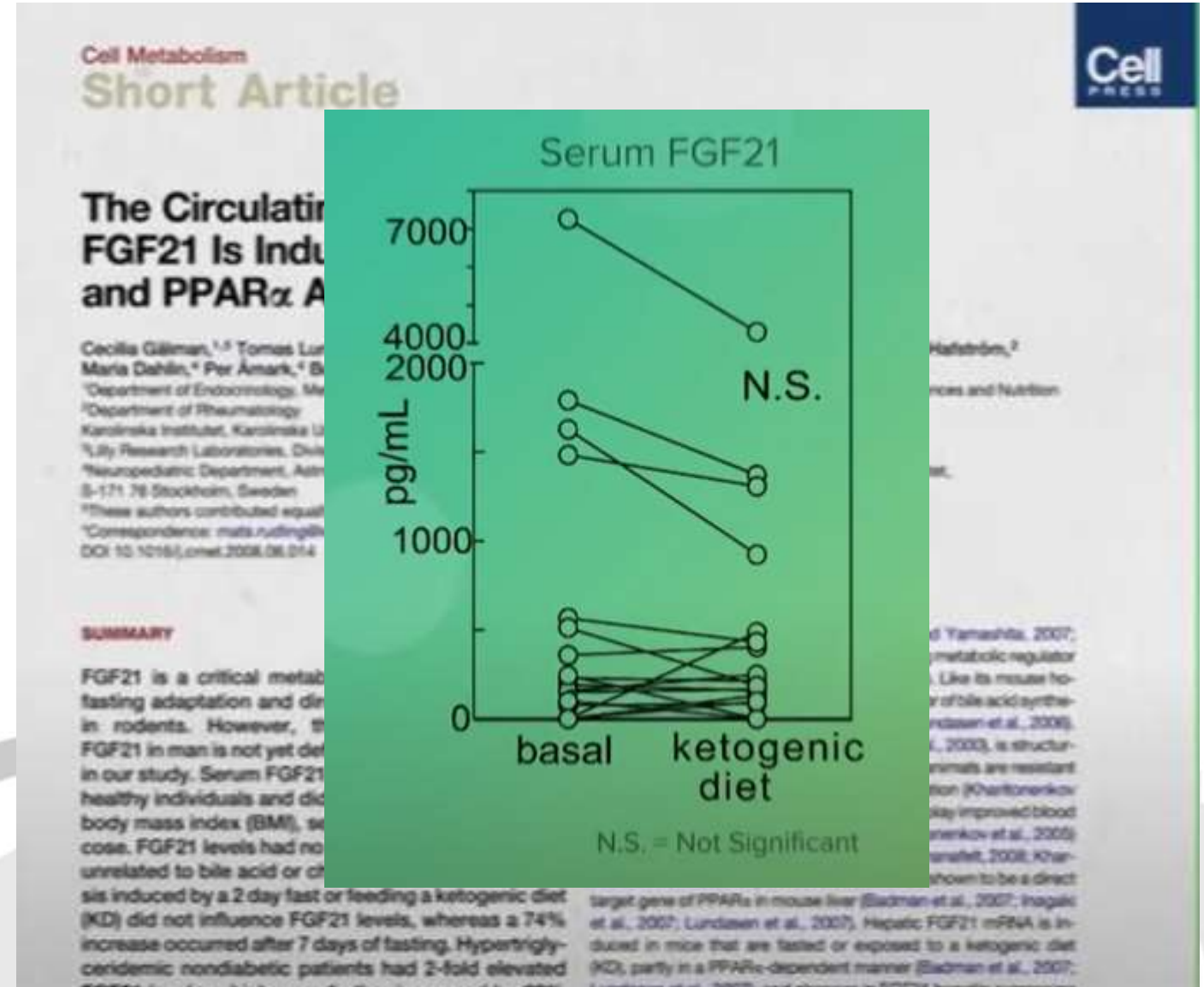
Leigang Jin[1,2], Zhuofeng Lin[3], Aimin Xu[1,2,4]

[1]State Key Laboratory of Pharmaceutical Biotechnology, [2]Department of Pharmacology and Pharmacy, the University of Hong Kong, Hong Kong

tabolism [2]. Physiologically, FGF21 expression is markedly increased in response to fasting/starvation, and elevated FGF21

by genetic depletion of FGF21, but is attenuated upon replenishment with recombinant FGF21. However, the blood vessel is not the direct target of FGF21, and the antiatherosclerotic activity of FGF21 is attributed to its actions in adipose tissues and liver. In adipocytes, FGF21 promotes secretion of adiponectin, which in turn acts directly on blood vessels to reduce endothelial dysfunction, inhibit proliferation of smooth muscle cells and block conversion of macrophages to foam cells. Furthermore, FGF21 suppresses cholesterol biosynthesis and attenuates hypercholesterolemia by inhibiting the transcription factor sterol regulatory

Ketogenic Diets



ORIGINAL ARTICLE

Endocrine Research

Circulating Fibroblast Growth Factor 21 Is Induced by Peroxisome Proliferator-Activated Receptor Agonists But Not Ketosis in Man

Constantinos Christodoulides, Pamela Dyson, Dennis Sprecher, Kostas Tsintzas, and Fredrik Karpe

Oxford Centre for Diabetes, Endocrinology, and Metabolism (C.C., P.D., F.K.), Churchill Hospital, Oxford OX3 7LJ, United Kingdom; National Institute for Health Research, Oxford Biomedical Research Centre

A 3-month ketogenic diet was associated with a 42% decline in plasma FGF21 levels.

Context: Murine fibroblast growth factor (FGF) 21 is a nutritionally regulated hormone secreted by the liver principally in response to peroxisome proliferator-activated receptor-α (PPARα) activation, which plays a critical role in regulating metabolism during ketosis. FGF21 is also a PPARγ target gene in mouse adipose tissue. Little information is available on FGF21 functions in humans.

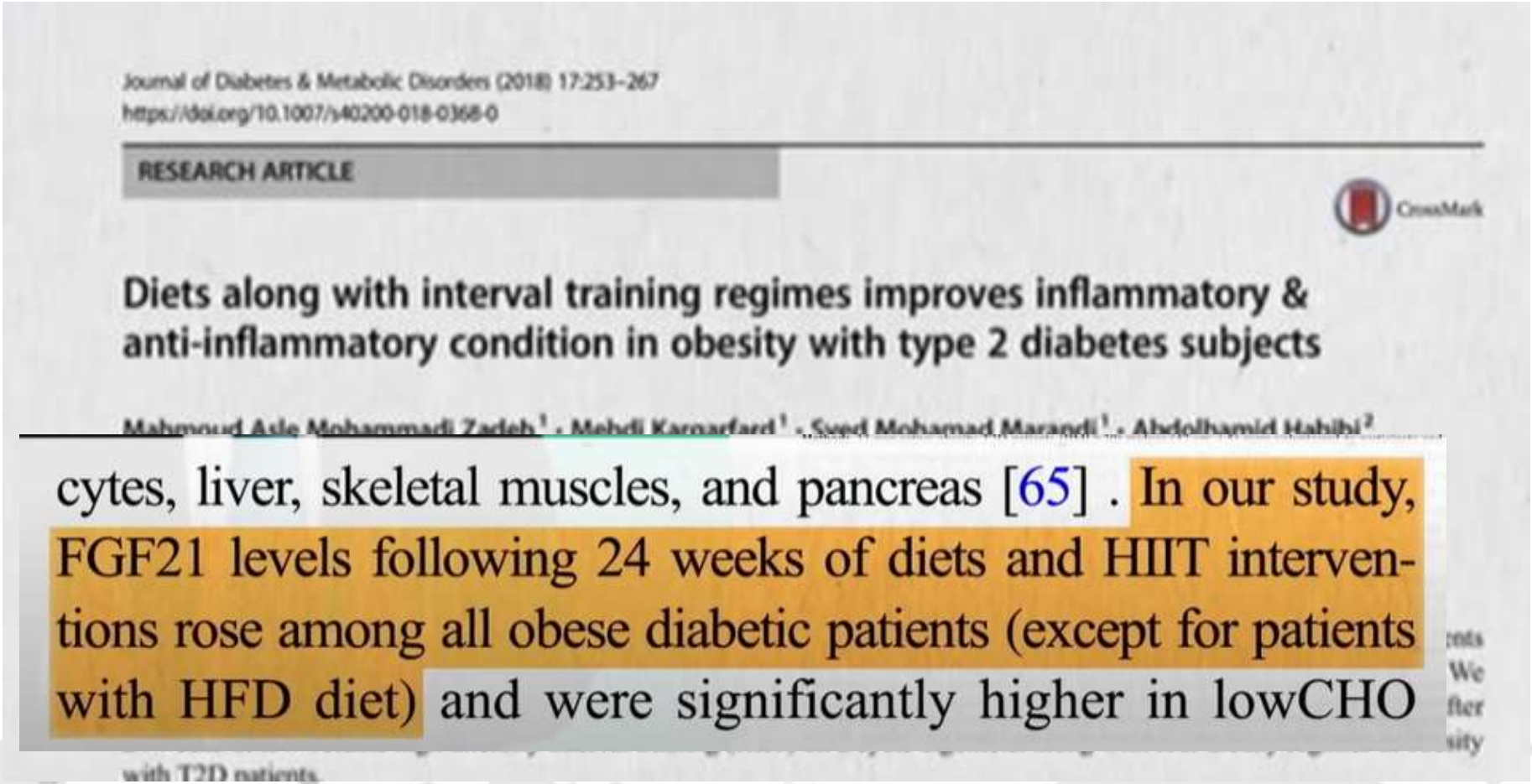
Objective: The aim of the study was to measure plasma FGF21 during fasting, ketogenic diet, and PPAR agonist treatment in humans.

Design and Setting: We conducted a prospective study involving three patient groups at two university hospitals.

Patients: Eight healthy male volunteers underwent a 48-h period of starvation followed by 24-h refeeding (group 1); seven obese individuals were allocated to a low-carbohydrate diet for 3 months (group 2); and three groups of healthy, overweight or obese male volunteers received

7 SYSTEMS PLAN

High Fat Diets



Journal of Diabetes & Metabolic Disorders (2018) 17:253–267
https://doi.org/10.1007/s40200-018-0368-0

RESEARCH ARTICLE

Diets along with interval training regimes improves inflammatory & anti-inflammatory condition in obesity with type 2 diabetes subjects

Mahmoud Asle Mohammadi Zadeh[1] · Mehdi Kargarfard[1] · Syed Mohamad Marandi[1] · Abdolhamid Habibi[2]

cytes, liver, skeletal muscles, and pancreas [65] . In our study, FGF21 levels following 24 weeks of diets and HIIT interventions rose among all obese diabetic patients (except for patients with HFD diet) and were significantly higher in lowCHO

OPEN ACCESS Freely available online

PLOS one

Exercise Increases Serum Fibroblast Growth Factor 21 (FGF21) Levels

Daniel Cuevas-Ramos[1], Paloma Almeda-Valdés[1], Clara Elena Meza-Arana[2], Griselda Brito-Córdova[1], Francisco J. Gómez-Pérez[1], Roopa Mehta[1], Jorge Oseguera-Moguel[3], Carlos A. Aguilar-Salinas[1]*

1 Department of Endocrinology and Metabolism, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico, 2 Department of Internal Medicine, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico, 3 Department of Cardiology, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico

Abstract

Background: Fibroblast growth factor 21 (FGF21) increases glucose uptake. It is unknown if FGF21 serum levels are affected by exercise.

Methodology/Principal Findings: This was a comparative longitudinal study. Anthropometric and biochemical evaluation

Thus, increased FGF21serum levels may be an additional mechanism by which exercise improves carbohydrate and lipid metabolism in the medium term.

Conclusions: Serum FGF21 levels significantly increased after two weeks of physical activity. This increment correlated positively with clinical parameters related to the adrenergic and lipolytic response to exercise.

Trial Registration: ClinicalTrials.gov NCT01512368

Citation: Cuevas-Ramos D, Almeda-Valdés P, Meza-Arana CE, Brito-Córdova G, Gómez-Pérez FJ, et al. (2012) Exercise Increases Serum Fibroblast Growth Factor 21 (FGF21) Levels. PLoS ONE 7(5): e38022. doi:10.1371/journal.pone.0038022

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Competing Interests: The authors have declared that no competing interests exist.

* E-mail: caguilarsalinas@yahoo.com

SYSTEMS PLAN

Physiology International, Volume 106 (1), pp. 70–80 (2019)
DOI: 10.1556/2060.106.2019.01

Effects of aerobic versus resistance training on serum fetuin-A, fetuin-B, and fibroblast growth factor-21 levels in male diabetic patients

A Keihanian[1], H Arazi[1], M Kargarfard[2]

[1]Department of Exercise Physiology, Faculty of Sport Sciences, University of Guilan, Rasht, Iran

group (ATG; $n = 11$), or a control group ($n = 11$). The ATG completed 30–45 min of aerobic running training at 65%–75% of the maximum heart rate. The RTG completed three sets of 10 repetitions maximum of leg press, bench press, knee extension, seated cable row, knee flexion, military press, and calf rise. Blood samples were taken before

The aim of this study was to compare the effects of 8 weeks of aerobic versus resistance training programs on serum fetuin-A, fetuin-B, and fibroblast growth factor-21 (FGF-21) levels in males with type 2 diabetes mellitus. Participants ($n = 34$) were randomly assigned to a resistance training group (RTG; $n = 12$), an aerobic training

Both training groups increased HDL (RTG: 21.2% and ART: 22.6%) and FGF-21 (RTG: 42.2% and ART: 25.1%; $p < 0.05$), and both achieved greater increase compared to the CG ($p < 0.05$). In addition, differences were found between the RTG and the ATG in

(42.2% vs. 25.1%), respectively. Aerobic and resistance exercise training significantly decreased serum fetuin-A, and fetuin-B, and increased FGF-21 levels in males with type 2 diabetes mellitus. However, more significant alterations in serum factors were observed from resistance training. Thus, resistance training may be considered a more suitable training strategy.

Keywords: exercise training, hepatokines, insulin, glucose, type 2 diabetes

Protein, Longevity and FGF21

DRI

DIETARY REFERENCE INTAKES

FOR

RDA for Men	
19–30 years	0.80 g/kg/d or 56 g/d of protein
31–50 years	0.80 g/kg/d or 56 g/d of protein

Panel on Macronutrients, Panel on the Definition of Dietary Fiber, Subcommittee on Upper Reference Levels of Nutrients

Most Men Consume Over 100G/day

ABLE 1

ends in protein intake by age and sex from NHANES, 2001–2014[1]

otein intake sex	Age, y	*n*	2001–2014	2001–2002	2003–2004	2005–2006	2007–2008	2009–2010	2011–2012	2013–2014	*β*	SE	*P*
otein, g/d													
Combined	2–3	3208	53.3 ± 0.6	52.9 ± 1.2	55.9 ± 1.7	51.9 ± 1.6	52.4 ± 2.2	54.1 ± 1.1	53.2 ± 1.1	52.7 ± 1.4	−0.12	0.25	0.6405
	4–8	6311	61.6 ± 0.5	63.5 ± 0.9	65.7 ± 1.6	60.3 ± 1.4	57.8 ± 0.9	61.1 ± 1.1	63.2 ± 0.7	59.7 ± 1.6	−0.54	0.25	0.0302
Females	9–13	3333	65.0 ± 0.9	64.2 ± 1.8	67.2 ± 2.1	66.0 ± 2.6	65.9 ± 2.1	63.6 ± 1.9	62.6 ± 3.7	66.1 ± 2.1	−0.24	0.46	0.6115
	14–18	3430	63.9 ± 0.8	63.7 ± 1.6	67.0 ± 1.6	64.9 ± 2.0	63.1 ± 2.2	64.2 ± 2.2	66.4 ± 2.5	58.7 ± 2.2	−0.65	0.38	0.0859
	19–30	3429	70.3 ± 0.8	71.8 ± 1.8	72.3 ± 2.3	69.6 ± 2.1	69.6 ± 1.7	67.7 ± 1.9	71.1 ± 1.9	70.3 ± 2.1	−0.31	0.38	0.4212
	31–50	5724	70.8 ± 0.6	69.5 ± 1.6	68.9 ± 1.7	74.7 ± 1.7	69.8 ± 1.5	70.3 ± 1.3	69.6 ± 1.6	72.9 ± 1.5	0.25	0.30	0.3981
	51–70	5287	66.8 ± 0.7	64.3 ± 1.1	66.6 ± 2.8	67.3 ± 2.0	65.1 ± 1.8	67.6 ± 1.6	66.6 ± 1.3	69.0 ± 1.1	0.50	0.29	0.0902
	≥71	2821	58.1 ± 0.6	56.3 ± 1.6	58.8 ± 1.1	57.0 ± 1.8	56.6 ± 1.2	59.8 ± 1.7	59.1 ± 1.4	59.1 ± 1.8	0.41	0.30	0.1635
	≥80	1247	56.2 ± 0.8	54.0 ± 1.8	55.8 ± 2.3	53.2 ± 1.4	55.1 ± 1.7	57.1 ± 2.2	57.8 ± 2.3	60.0 ± 2.2	0.93	0.39	0.0203
Males	9–13	3274	78.6 ± 1.1	80.2 ± 3.6	82.2 ± 2.7	75.0 ± 2.9	81.1 ± 3.7	74.2 ± 1.7	78.8 ± 1.5	78.3 ± 2.5	−0.49	0.53	0.3629
	14–18	3664	97.3 ± 1.5	94.5 ± 3.7	97.6 ± 4.3	105.4 ± 3.2	92.1 ± 2.1	98.5 ± 4.1	90.5 ± 5.3	100.8 ± 4.2	−0.05	0.78	0.9477
	19–30	3869	106.3 ± 1.2	104.4 ± 4.1	108.8 ± 2.5	108.2 ± 3.3	104.1 ± 3.2	102.7 ± 3.2	105.9 ± 2.4	109.5 ± 3.2	0.16	0.62	0.7944
	31–50	5675	105.6 ± 0.8	103.1 ± 2.2	105.9 ± 2.1	111.1 ± 2.1	104.1 ± 2.5	106.5 ± 2.4	107.4 ± 1.9	101.2 ± 1.7	−0.22	0.38	0.5603
	51–70	5190	91.5 ± 0.8	88.4 ± 2.3	88.4 ± 2.2	93.1 ± 2.4	91.6 ± 2.5	95.1 ± 1.8	90.9 ± 2.5	92.0 ± 1.3	0.58	0.38	0.1316
	≥71	2765	75.8 ± 0.8	74.0 ± 1.4	72.3 ± 2.7	76.7 ± 1.6	72.6 ± 2.7	73.2 ± 1.9	80.7 ± 1.7	79.8 ± 1.8	1.15	0.35	0.0015
	≥80	1123	71.2 ± 1.1	69.4 ± 2.0	67.9 ± 3.0	71.7 ± 1.8	69.7 ± 3.2	67.2 ± 2.5	76.9 ± 2.6	73.8 ± 3.7	1.02	0.57	0.0755

7 SYSTEMS PLAN

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Cell Reports
Article

Decreased Consumption of Branched-Chain Amino Acids Improves Metabolic Health

Luigi Fontana,[1,2,3,16,*] Nicole E. Cummings,[4,5,8,16] Sebastian I. Arriola Apelo,[4,5] Joshua C. Neuman,[4,5,7] Ildiko Kasza,[9] Brian A. Schmidt,[4,5] Edda Cava,[1,2] Francesco Spelta,[1,10] Valeria Tosti,[1,10] Faizan A. Syed,[4,5] Emma L. Baar,[4,5] Nicola Veronese,[1,11] Sara E. Cottrell,[4,5,12] Rachel J. Fenske,[4,5,7] Beatrice Bertozzi,[1] Harpreet K. Brar,[4,5] Terri Pietka,[1] Arnold D. Bullock,[13] Robert S. Figenshau,[13] Gerald L. Andriole,[13] Matthew J. Merrins,[4,5,14] Caroline M. Alexander,[8] Michelle E. Kimple,[4,5,6,7,15] and Dudley W. Lamming[4,5,6,7,15,*]

[1]Division of Geriatrics and Nutritional Sciences, Washington University in St. Louis, St. Louis, MO 63130, USA
[2]Department of Clinical and Experimental Sciences, University of Brescia Medical School, 25121 Brescia, Italy

Decrease Protein

	Protein restricted (n=19)	within-group *p*	Control (n=19)	within-group *p*	Among-group *p*
Energy Intake (kcal/d)					
Baseline	2621 ± 410.9		2464 ± 611.3		
Follow-up	2856 ± 198.6		2367 ± 444.8 (102.1)		
Δ Energy Intake	**235 ± 510.3**	0.06	**-96 ± 347.4**	0.24	**0.03**
Total Protein (g)					
Baseline	111.5 ± 16.7		101.0 ± 15.0		
Follow-up	63.8 ± 2.2		95.1 ± 16.2		
Δ Protein	**-47.6 ± 16.2**	**<0.0001**	**-5.9 ± 11.5**	0.04	**<0.0001**

Table 2. A Human Clinical Trial of Protein Restriction: Blood Parameters

	Protein-Restricted	Within-Group (p)	Control	Within-Group (p)	Among-Group (p)
FGF21 (pg/ml)					
Baseline	131.55 ± 101.62		231.08 ± 244.61		
Follow-up	260.33 ± 172.67		223.43 ± 143.76		
Δ FGF21	128.78 ± 155.25	0.003	−7.64 ± 176.06	0.86	0.02

SYSTEMS PLAN

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CellPress

Decrease protein
Consumed 300 calories more per day
Lost 2 pounds more body fat

Cell Reports
Article

Table 2. A Human Clinical Trial of Protein Restriction: Blood Parameters

	Protein-Restricted	Within-Group (p)	Control	Within-Group (p)	Among-Group (p)
FGF21 (pg/ml)					
Baseline	131.55 ± 101.62		231.08 ± 244.61		
Follow-up	260.33 ± 172.67		223.43 ± 143.76		
Δ FGF21	128.78 ± 155.25	0.003	−7.64 ± 176.06	0.86	0.02

Amino Acids Improves Metabolic Health

ble 1. A Human Clinical Trial of Protein Restriction: Physical Parameters

mass (kg)	Protein-Restricted	Within-Group (p)	Control	Within-Group (p)	Among-Group (p)
eline	33.24 ± 11.91		31.07 ± 11.83		
ow-up	31.86 ± 11.09		30.72 ± 11.45		
at mass	−1.37 ± 1.55	0.001	−0.36 ± 1.02	0.15	0.02

asza,
lotka,
der,

[3]Department of Clinical and Experimental Sciences, University of Brescia Medical School, 25121 Brescia, Italy

Play down protein to play up metabolism?

Timo D. Müller[1] and Matthias H. Tschöp[1,2]

[1]Institute for Diabetes and Obesity, Helmholtz Center Munich, Munich, Germany. [2]Division of Metabolic Diseases, Department of Medicine, Technische Universität München, Munich, Germany.

Who among us hasn't fantasized about a diet that allows ingestion of a surfeit of calories that are burned off effortlessly by ramping up energy expenditure? In this issue of the *JCI*, research led by Christopher Morriso

with our cellular metabolism will be required. Laeger et al. show that the expression and secretion of the weight-reducing hormone fibroblast growth factor 21 (FGF21) is regulated by dietary proteins and not, as has been heretofore assumed, simply triggered by reduced caloric intake. This study not only sheds new light on the role of FGF21 in systems metabolism, but also on the ways our bodies cope with the ever-changing availability of different dietary macronutrients.

ither low
both. In
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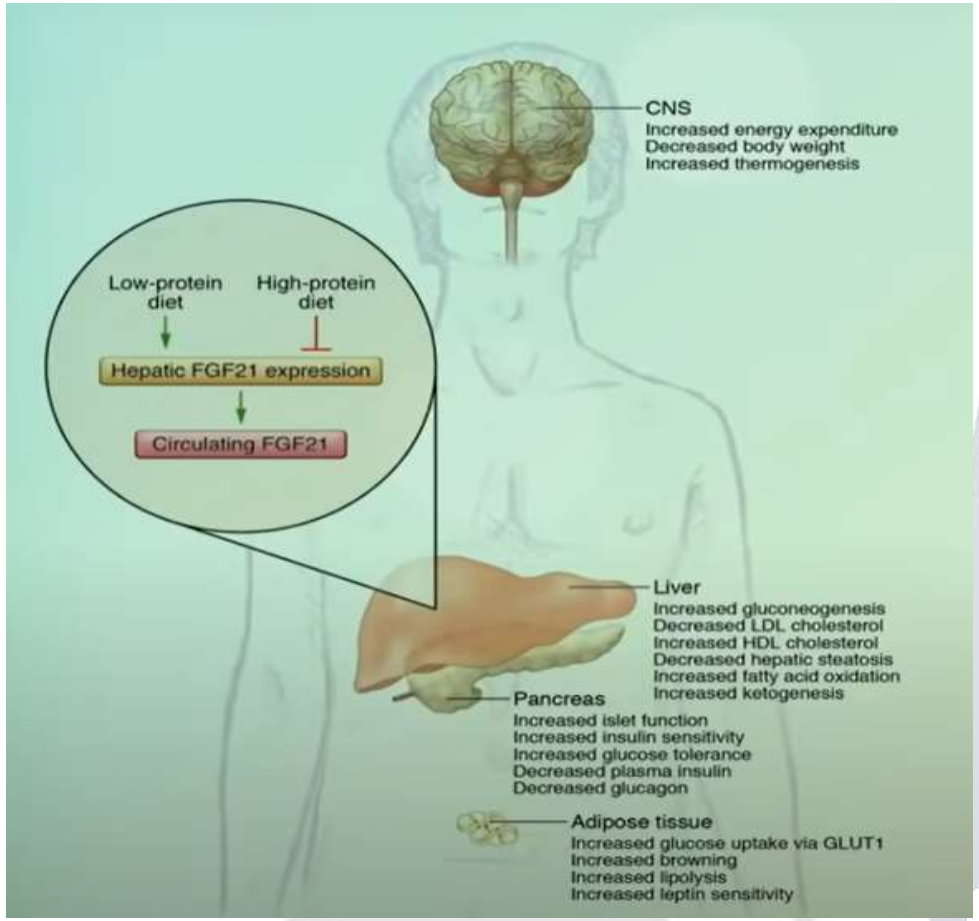
at were
energy restricted but not protein restricted showed decreased levels of FGF21. Importantly, Laeger et al. corroborated this observation in humans by demonstrating increased FGF21 levels in participants of a clinical study that were fed a LP diet.

Next, Laeger et al. assessed FGF21 levels upon fasting and refeeding and observed that the fasting-induced increase in FGF21 is potentiated by refeeding with

Protein

- Low protein diet ↑ liver production of FGF21
- High protein diet ↓ liver production of FGF21



SYSTEMS PLAN

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Cell Reports
Article

Decreased Consumption of Branched-Chain Amino Acids Improves Metabolic Health

Luigi Fontana,[1,2,3,16,*] Nicole E. Cummings,[4,5,6,16] Sebastian I. Arriola Apelo,[4,5] Joshua C. Neuman,[4,5,7] Ildiko Kasza,[8] Brian A. Schmidt,[4,5] Edda Cava,[1,9] Francesco Spelta,[1,10] Valeria Tosti,[1,10] Faizan A. Syed,[4,5] Emma L. Baar,[4,5] Nicola Veronese,[1,11] Sara E. Cottrell,[4,5,12] Rachel J. Fenske,[4,5,7] Beatrice Bertozzi,[1] Harpreet K. Brar,[4,5] Terri Pietka,[1]

branched-chain amino acids. Our human clinical trial data suggests that even a quite modest PR regimen may have significant clinical benefits. In the long term, further investigation of the

[7]Interdisciplinary Graduate Program in Nutritional Sciences, University of Wisconsin-Madison, Madison, WI 53706, USA
[8]McArdle Laboratory for Cancer Research, University of Wisconsin-Madison, Madison, WI 53705, USA
[9]Department of Experimental Medicine, Sapienza University of Rome, 00185 Rome, Italy
[10]Department of Medicine, University of Verona, 37129 Verona, Italy
[11]Division of Geriatrics, Department of Medicine, University of Padova, 35122 Padova, Italy
[12]Rural and Urban Scholars in Community Health Program, University of Wisconsin-Madison, Madison, WI 53706, USA
[13]Division of Urology, Washington University School of Medicine in St. Louis, St. Louis, MO 63110, USA

The Journal of Clinical Investigation RESEARCH ARTICLE

A liver stress-endocrine nexus promotes metabolic integrity during dietary protein dilution

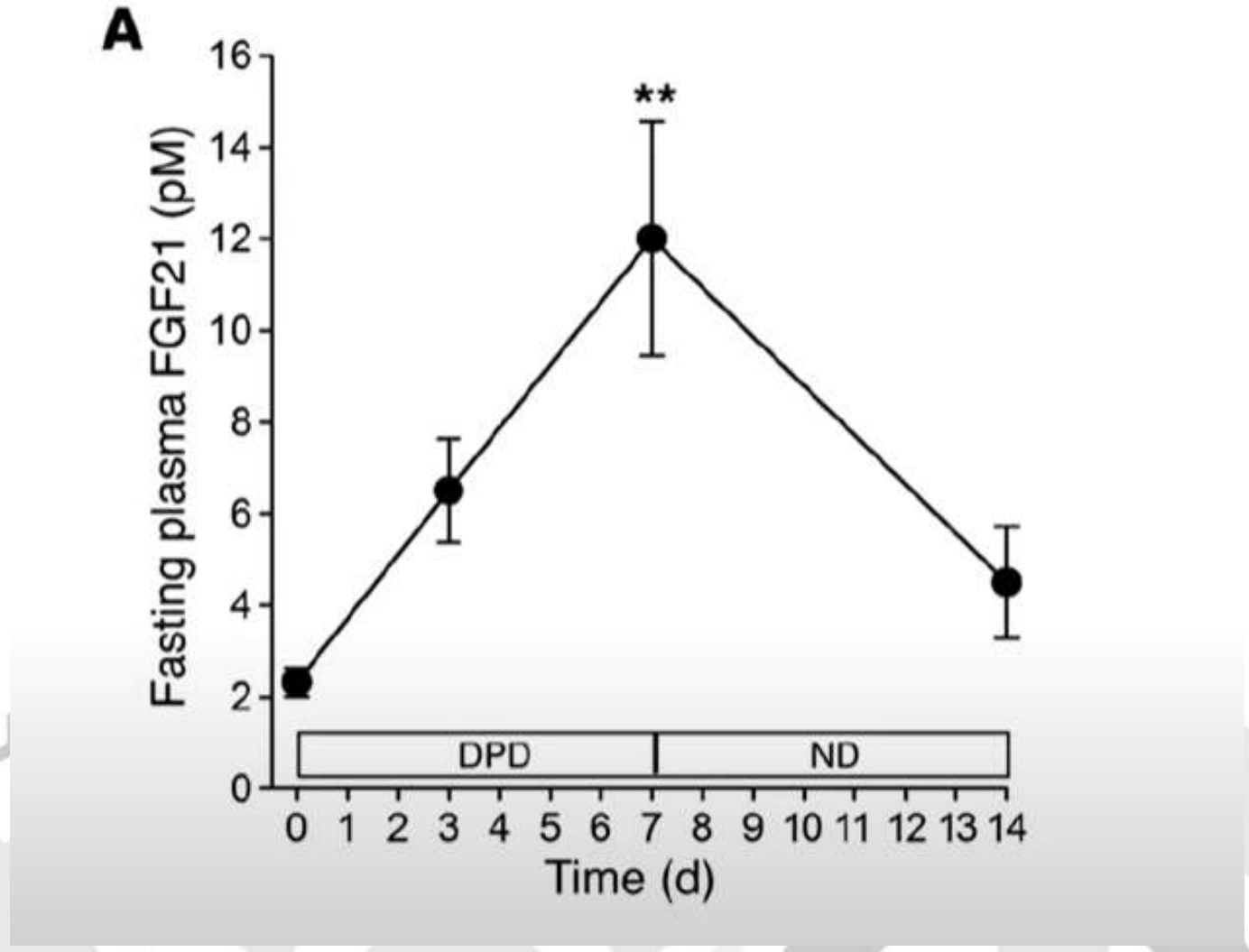
Adriano Maida,[1] Annika Zota,[1] Kim A. Sjøberg,[2] Jonas Schumacher,[3] Tjeerd P. Sijmonsma,[1,4] Anja Pfenninger,[1]
Marie M ... er,[4]
Juan L. I...
Institute for ... Centre,
Department ... rch Center,
Center for M... idelberg,
Germany. [5]Sa...
[6]Centre de Re...
Marseille, France. [7]Division of Metabolism and Cancer, Institute for Diabetes and Obesity, Helmholtz Centre Munich, Munich, Germany.

Table S3. Human study: diet compositions.

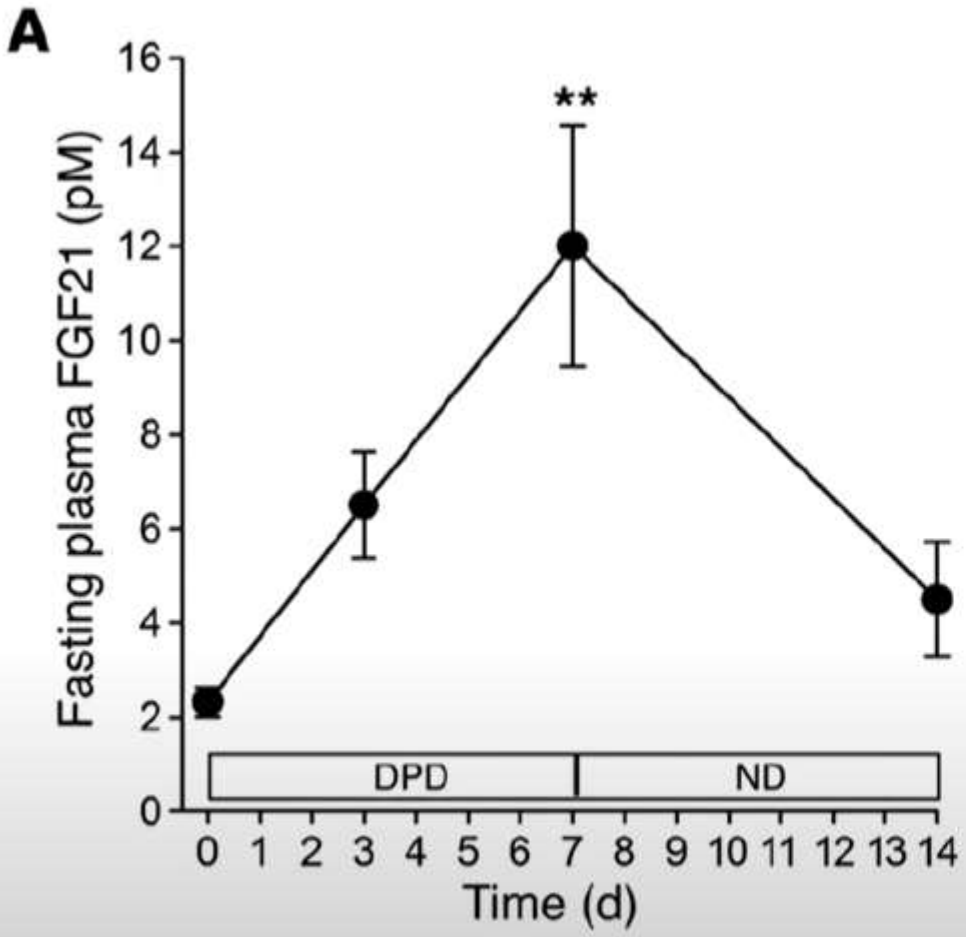
	Habitual diet	Protein restricted diet
Protein %E	20.2 ± 0.5	9.0 ± 0
Protein, g/d	111 ± 11	73 ± 3

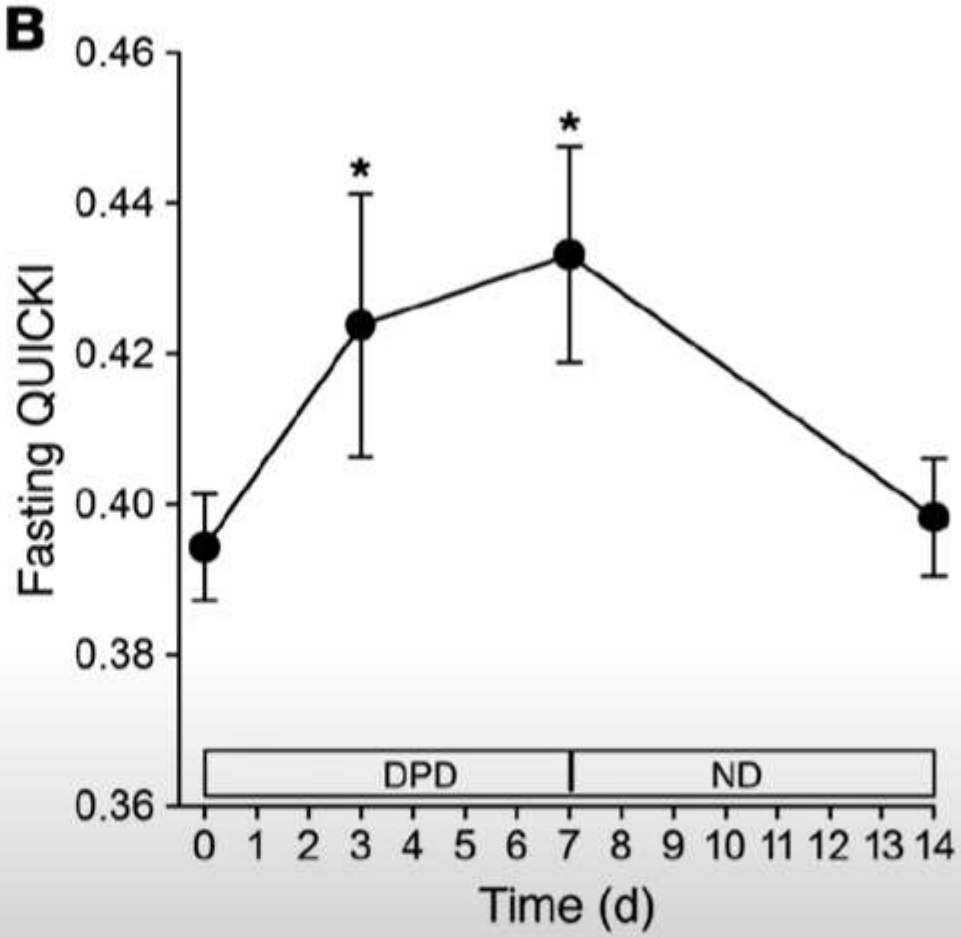
Dietary protein intake is linked to an increased incidence of type 2 diabetes (T2D). Although dietary protein dilution (DPD) can slow the progression of some aging-related disorders, whether this strategy affects the development and risk for obesity-associated metabolic disease such as T2D is unclear. Here, we determined that DPD in mice and humans increases serum

73G get 600% Increase in FGF21 in 1 Week



In One Week, Increased Insulin Sensitivity





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a potential means to combat obesity, while evidence suggesting that a lower protein intake is positively associated with increased health, survival, and insulin sensitivity has continued to mount (Levine et al., 2014; Solon-Biet et al., 2014, 2015). However, an

[6]Endocrinology and Reproductive Physiology Graduate Training Program, University of Wisconsin-Madison, Madison, WI 53706, USA
[7]Interdisciplinary Graduate Program in Nutritional Sciences, University of Wisconsin-Madison, Madison, WI 53706, USA
[8]McArdle Laboratory for Cancer Research, University of Wisconsin-Madison, Madison, WI 53705, USA
[9]Department of Experimental Medicine, Sapienza University of Rome, 00185 Rome, Italy
[10]Department of Medicine, University of Verona, 37129 Verona, Italy
[11]Division of Geriatrics, Department of Medicine, University of Padova, 35122 Padova, Italy

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Review

The

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obtained from the Okinawan diet is derived from 9%protein and 85%carbohydrates [74]. Interestingly, the Okinawan values of dietary protein and the protein to carbohydrate ratio (1:10) are very low and are remarkably similar to those found to optimize the lifespan in recent animal studies investigating ageing.

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Lifespan and metabolic health are influenced by dietary nutrients. Recent studies show that a reduced protei
intake or low-protein/high-carbohydrate diet plays a critical role in longevity/metabolic health. Additionally
specific amino acids (AAs), including methionine or branched-chain AAs (BCAAs), are associated with the regu
lation of lifespan/ageing and metabolism through multiple mechanisms. Therefore, methionine or BCAAs restric
tion may lead to the benefits on longevity/metabolic health. Moreover, epidemiological studies show that a hig
intake of animal protein, particularly red meat, which contains high levels of methionine and BCAAs, may b

Medical Hypotheses 83 (2014) 365–371

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journal homepage: www.elsevier.com/locate/mehy

GCN2 and FGF21 are likely mediators of the protection from cancer, autoimmunity, obesity, and diabetes afforded by vegan diets ☆

Mark F. McCarty *

Catalytic Longevity, 7831 Rush Rose Drive, Apt. 316, Carlsbad, CA 92009, United States

ARTICLE INFO

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ABSTRACT

Third World quasi-vegan cultures have been characterized by low risks for "Western" cancers, autoimmune disorders, obesity, and diabetes. The relatively low essential amino acid contents of many vegan diets may play a role in this regard. It is proposed that such diets modestly activate the kinase GCN2 – a physiological detector of essential amino acid paucity – within the liver, resulting in

Minireview

Mark F. McCarty*

The moderate essential amino acid restriction

summarized in Figure 1. A favorable impact of whole-food plant-based diets on risk for metabolic syndrome, diabetes, and obesity – which in part may reflect increased FGF21 activity [24] – likely also contributes to the favorable impact of such diets on vascular health.

Received October 25, 2015; accepted January 6, 2016; previously

LDL receptor; SREBP-2; vegan.

As noted, Esselstyn reports that, in patients with significant coronary disease, progression of this disease can be largely halted or reversed, and risk for myocardial infarction almost eliminated, by a whole-food low-fat vegan diet coupled with sufficient medication to insure that total serum cholesterol remains below 150 mg/dL [10, 11]. This benefit cannot be attributed

150 mg/dL [10, 11]. This benefit cannot be attributed solely to cholesterol reduction, as potent statin therapy capable of achieving comparable reductions of LDL cholesterol has a useful but far less definitive impact on MI

Roy

Delivery System

SYSTEMS PLAN

FIGURE 1

Restoration of myocardial perfusion[2]

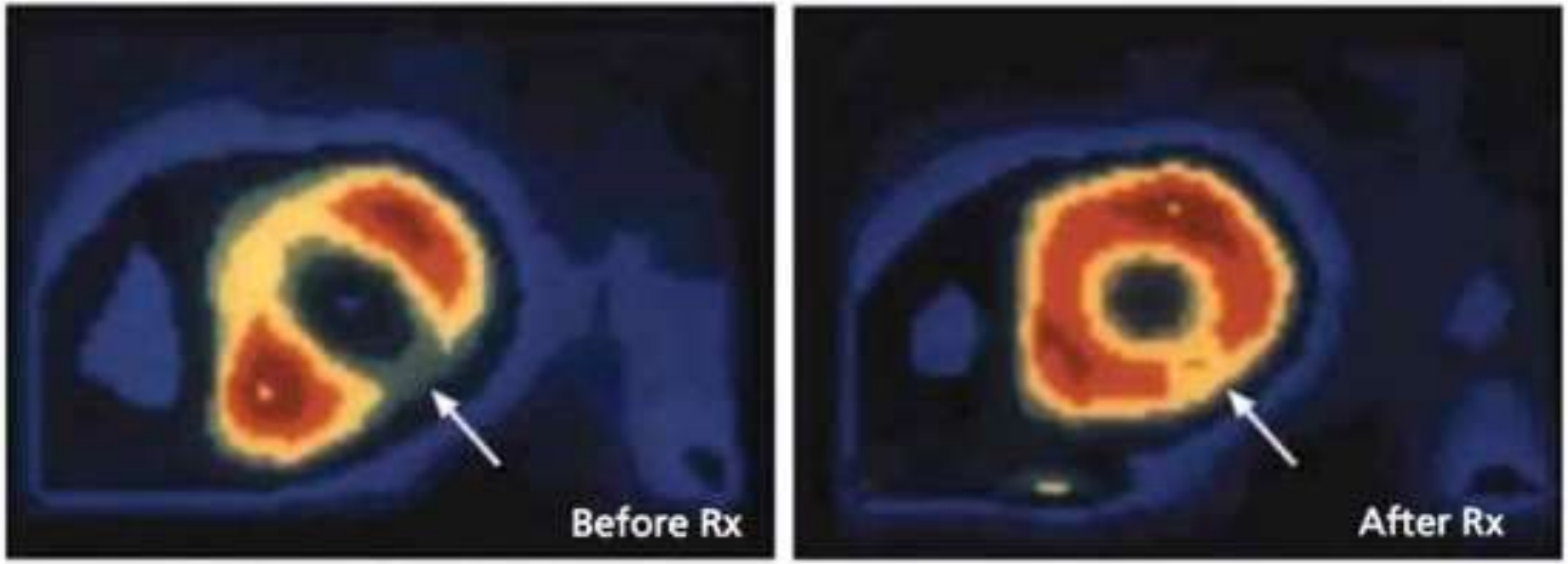
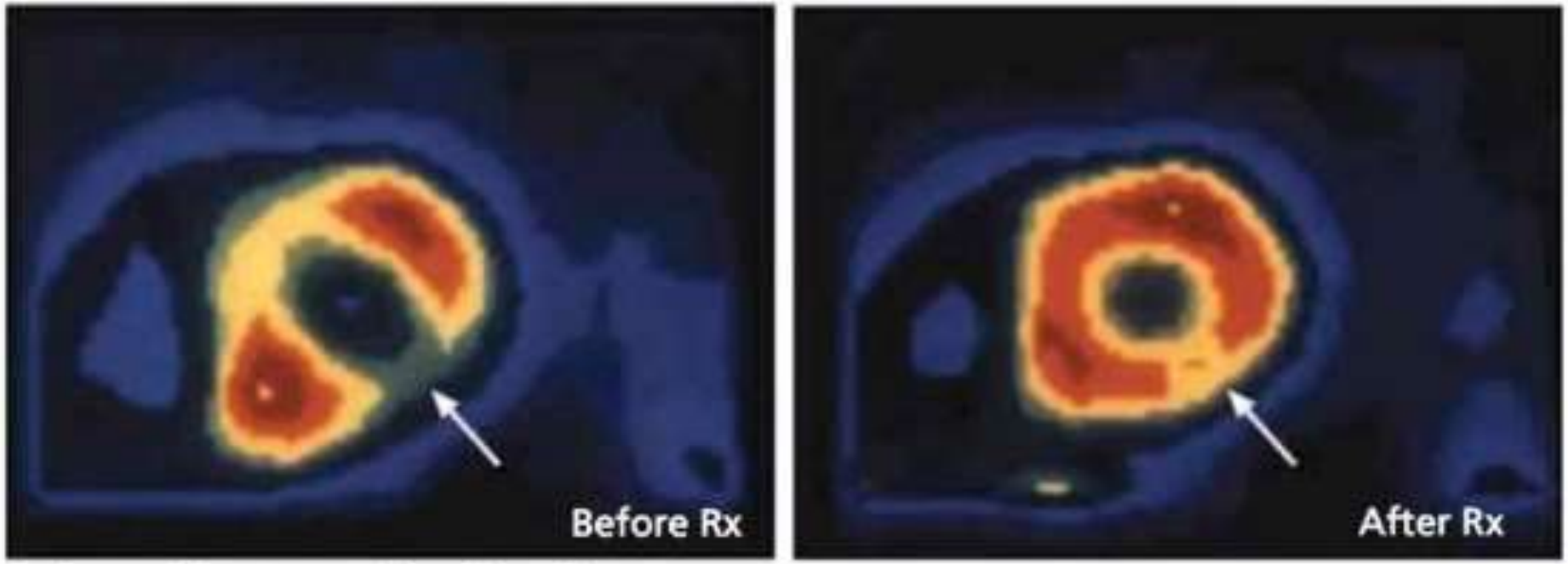


FIGURE 1

Restoration of myocardial perfusion[2]



Positron emission tomography performed on a patient with coronary artery disease shows an area of myocardium with insufficient blood flow Following only 3 weeks of plant-based nutritional intervention, normal blood flow was restored

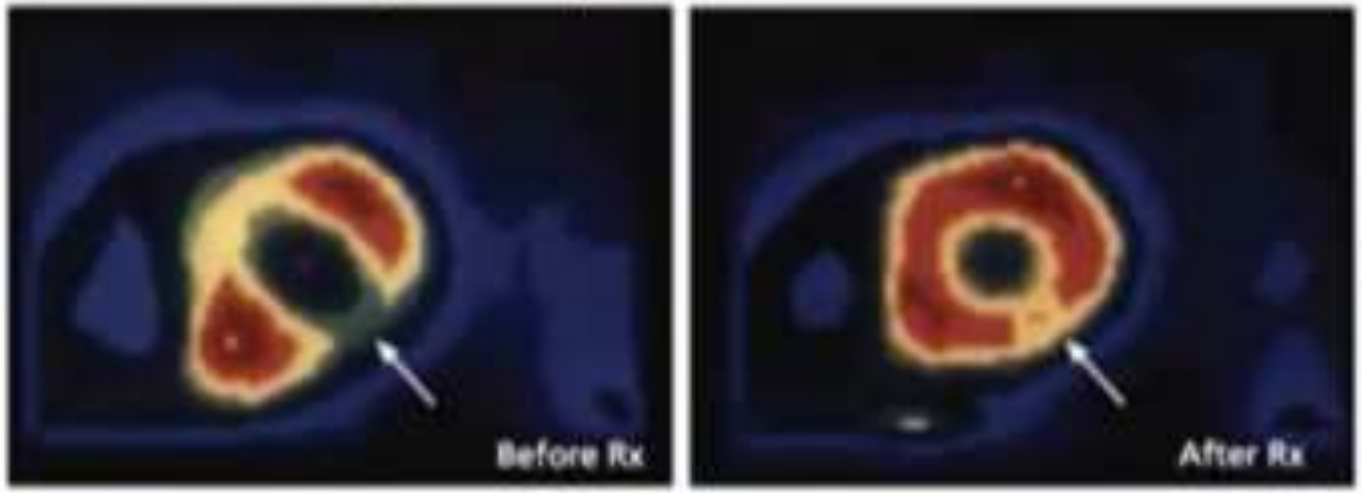
SYSTEMS PLAN

Caldwell B. Esselstyn Jr.

ORIGINAL RESEARCH

FIGURE 1

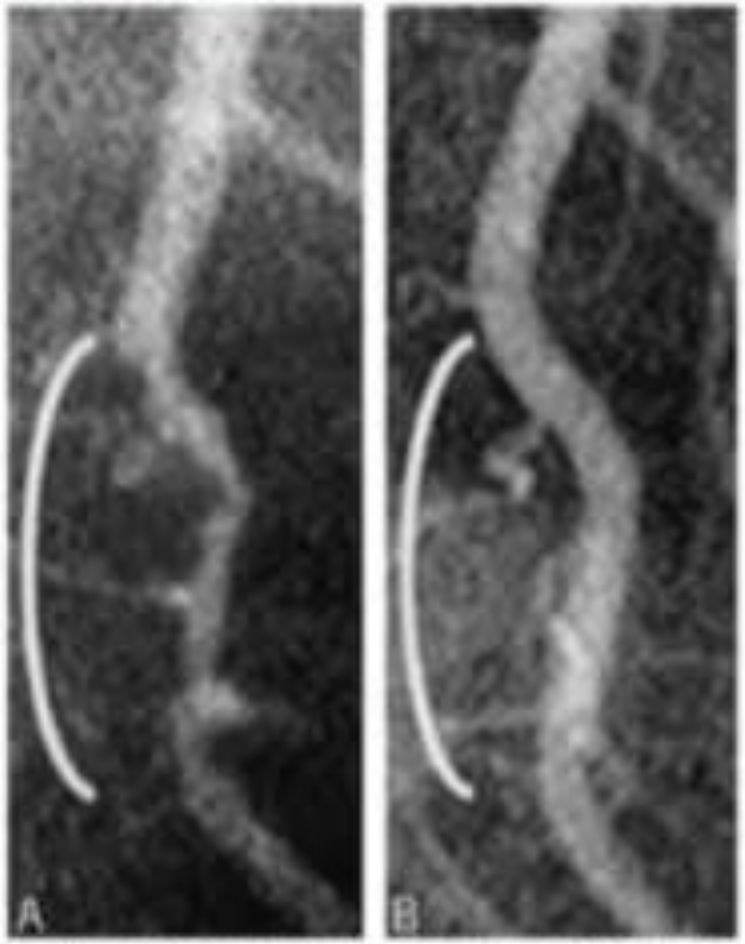
Restoration of myocardial perfusion[2]



Positron emission tomography performed on a patient with coronary artery disease shows an area of myocardium with insufficient blood flow. Following only 3 weeks of plant-based nutritional intervention, normal blood flow was restored

FIGURE 2

Reversal of coronary artery disease[1]



Coronary angiography reveals a diseased distal left anterior descending artery (A). Following 32 months of a plant-based nutritional intervention without cholesterol-lowering medication, the artery regained its normal configuration (B).

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Purpose ▶ Plant-based nutrition achieved

confirm the capacity of whole-food plant-based nutrition to restore health in "there is nothing further we can do" situations.

patient volunteers who received counseling

advanced coronary artery disease (CAD) in

Intensive Lifestyle Changes for Reversal of Coronary Heart Disease

Dean Ornish, MD; L MD;

In brief, participants were instructed to

Overall, 82% of experimental-group patients had an average change towards regression.

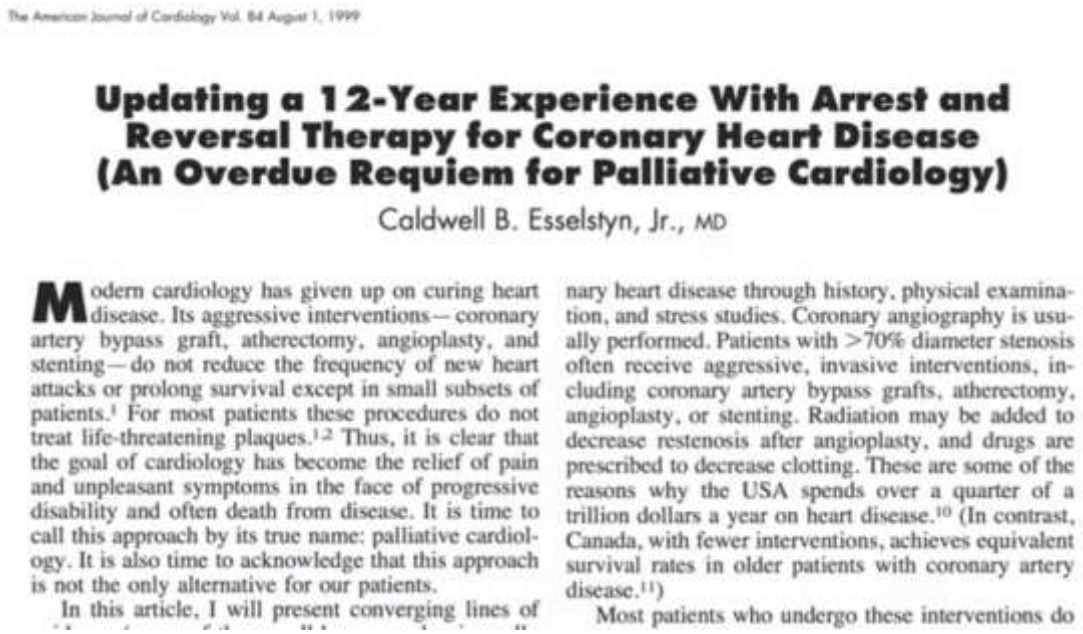
carbohydrates, exercise for a minimum of 3 h/wk (e.g., walking), attend group support meetings, and practice stress management techniques

Objectives.—To
changes for a total of
lipid-lowering drugs)
Design.—Random
randomized invitation
Patients.—Forty-e
were randomized to
group, and 35 comple
Setting.—Two ter
Intervention.—Intensive lifestyle changes (10% fat whole foods vegetarian diet, aerobic exercise, stress management training, smoking cessation, group psycho-

make and sustain com-
yle changes and, if so,
gression of coronary
uld be stopped or re-
using lipid-lowering
ned by computer-as-
e coronary arteriogra-
derived from earlier
d noninvasive mea-
sures.[13]

After 1 year, we found that experi-

12 Years Later



The American Journal of Cardiology Vol. 84 August 1, 1999

Updating a 12-Year Experience With Arrest and Reversal Therapy for Coronary Heart Disease (An Overdue Requiem for Palliative Cardiology)

Caldwell B. Esselstyn, Jr., MD

Modern cardiology has given up on curing heart disease. Its aggressive interventions—coronary artery bypass graft, atherectomy, angioplasty, and stenting—do not reduce the frequency of new heart attacks or prolong survival except in small subsets of patients.[1] For most patients these procedures do not treat life-threatening plaques.[1,2] Thus, it is clear that the goal of cardiology has become the relief of pain and unpleasant symptoms in the face of progressive disability and often death from disease. It is time to call this approach by its true name: palliative cardiology. It is also time to acknowledge that this approach is not the only alternative for our patients.

In this article, I will present converging lines of

nary heart disease through history, physical examination, and stress studies. Coronary angiography is usually performed. Patients with >70% diameter stenosis often receive aggressive, invasive interventions, including coronary artery bypass grafts, atherectomy, angioplasty, or stenting. Radiation may be added to decrease restenosis after angioplasty, and drugs are prescribed to decrease clotting. These are some of the reasons why the USA spends over a quarter of a trillion dollars a year on heart disease.[10] (In contrast, Canada, with fewer interventions, achieves equivalent survival rates in older patients with coronary artery disease.[11])

Most patients who undergo these interventions do

Adherent patients have experienced:

- no coronary events
- no interventions

SYSTEMS PLAN

Mark F. McCarty*

Practical prospects for boosting hepatic production of the "pro-longevity" hormone FGF21

DOI 10.1515/hmbci-2015-0057
Received October 25, 2015; accepted November 20, 2015

Keywords: ATF4; bilirubin; FGF21; FXR; GLP-1; glucagon; PPARα; vegan.

in protein or methionine. Whether vegans do indeed have higher levels of FGF21 has not been assessed; however, in

maximal longevity comparable to that evoked by calorie restriction – but without a reduction in food intake. Transcriptional factors which promote hepatic FGF21 expression include PPARα, ATF4, STAT5, and FXR; hence, fibrate drugs, elevated lipolysis, moderate-protein vegan diets, growth hormone, and bile acids may have potential to

In recent years, fibroblast growth hormone-21 (FGF21) has emerged as a key agent for promotion of metabolic and vascular health, leanness, and longevity [1–5]. Produced primarily by hepatocytes and adipocytes, FGF21 activates hybrid receptors comprised of an isoform of the

THE FASEB JOURNAL • RESEARCH • www.fasebj.org

Methionine restriction prevents onset of type 2 diabetes in NZO mice

Teresa Castaño-Martinez,*,† Fabian Schumacher,‡,§ Silke Schumacher,* Bastian Kochlik,¶,‖ Daniela Weber,¶,‖ Tilman Grune,¶,‖ Ronald Biemann,# Adrian McCann,** Klaus Abraham,†† Cornelia Weikert,†† Burkhard Kleuser,§,‖ Annette Schürmann,*,†,‡‡ and Thomas Laeger*,†,1

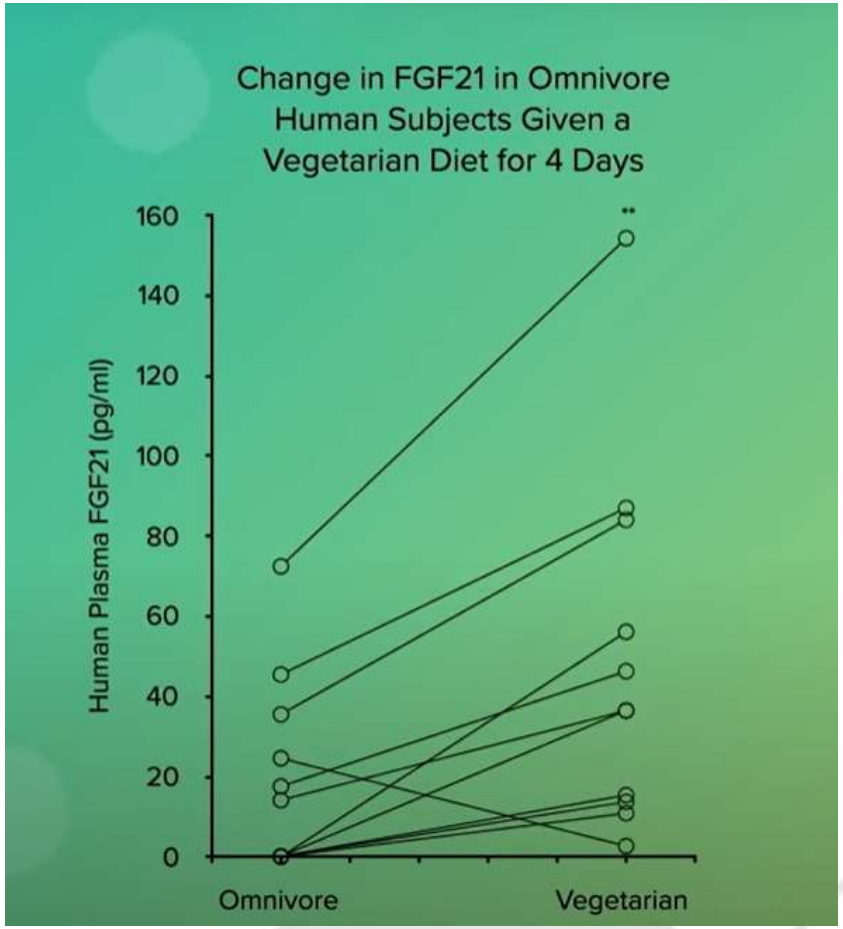
glucose homeostasis and insulin sensitivity were analyzed. Among humans, low methionine intake and circulating FGF21 levels were investigated by comparing a vegan and a vegetarian diet to an omnivore diet and evaluating the effect of a short-term vegetarian diet on FGF21 induction. In comparison with the Con group, MR led to elevated plasma FGF21 levels and

implicated as a potential underlying mechanism. The aims of our study were to test whether dietary MR in the context of a high-fat regimen protects against type 2 diabetes in mice and to investigate whether vegan and vegetarian diets, which have naturally low methionine levels, modulate circulating FGF21 in humans. New Zealand obese (NZO) mice, a model for polygenic obesity and type 2 diabetes, were placed on isocaloric high-fat diets (protein, 16 kcal%; carbohydrate, 52 kcal%;

Food intake and fat mass did not change. Plasma FGF21 levels were markedly higher in vegan humans compared with omnivores, and circulating FGF21 levels increased significantly in omnivores after 4 d on a vegetarian diet. These data

Vegetarian Diet for 4 Days

- FGF21 increased by 232%



For Longevity do not Overconsume Protein

- Decrease protein and animal products
- 60-80 grams may be the sweet spot
- More protein may be necessary to increase muscle mass
- Strength training is essential to build muscle
- Adequate protein in elderly is important

Fats

The Most Destructive Ingredient in Your Diet Linked to a Shorter Life

7 SYSTEMS PLAN

Silent 'Killer in your Kitchen'

Worse Than Sugar

Experts blame the epidemic of obesity and chronic disease on **sugar**, it's relatively minor when you compare it to.....

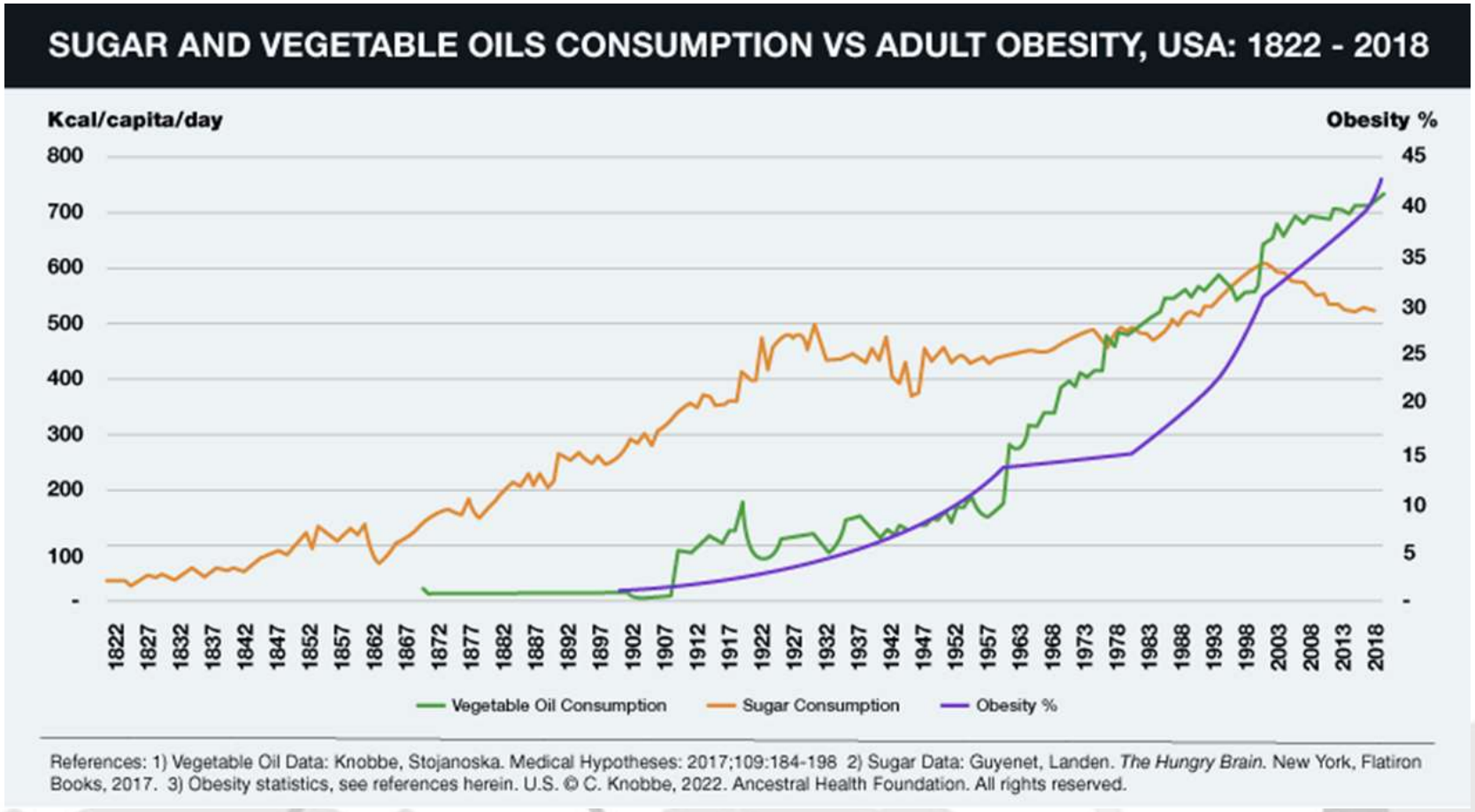
Seed Oils

Consumption of **seed oils** has increased from 1% of total calories to more than 25% of total calories

Processed foods

- Typically contain about **21% sugar**.
- **50%** or more of the overall calories contained in most processed foods come from **seed oils**.

What has Caused Obesity?



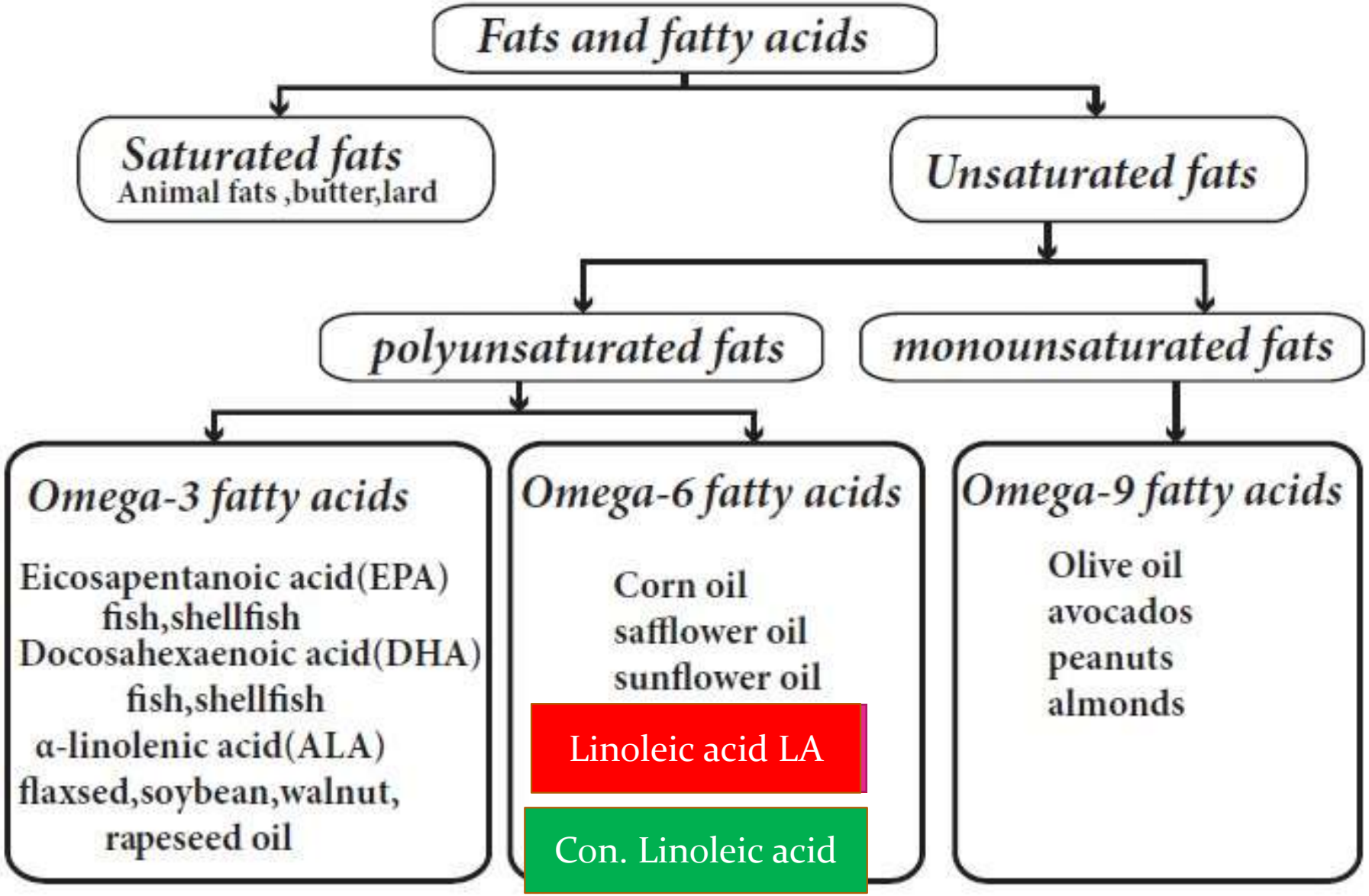
- Sugar has been **declining since 1997**, yet obesity and Type 2 diabetes have steadily increased.
- The continued rise coincides with the surge of **seed oil consumption.**

SYSTEMS PLAN

Crisco

- Crystalized cottonseed oil
- Cheap not healthy
- Hydrogenated so lasts a long time

Which is Worse?


Fats and fatty acids
Saturated fats
Animal fats ,butter,lard
Unsaturated fats
polyunsaturated fats
monounsaturated fats
Omega-3 fatty acids
Eicosapentanoic acid(EPA)
fish,shellfish
Docosahexaenoic acid(DHA)
fish,shellfish
α-linolenic acid(ALA)
flaxsed,soybean,walnut,
rapeseed oil
Omega-6 fatty acids
Corn oil
safflower oil
sunflower oil
Linoleic acid LA
Con. Linoleic acid
Omega-9 fatty acids
Olive oil
avocados
peanuts
almonds

“Bad” Omega 6

vegetable oil

*Increase clotting

*Constrict arteries

*Pro-inflammation

*Increase cancer

*Suppress immune system

Good Omega 3

fish, supplements, walnuts

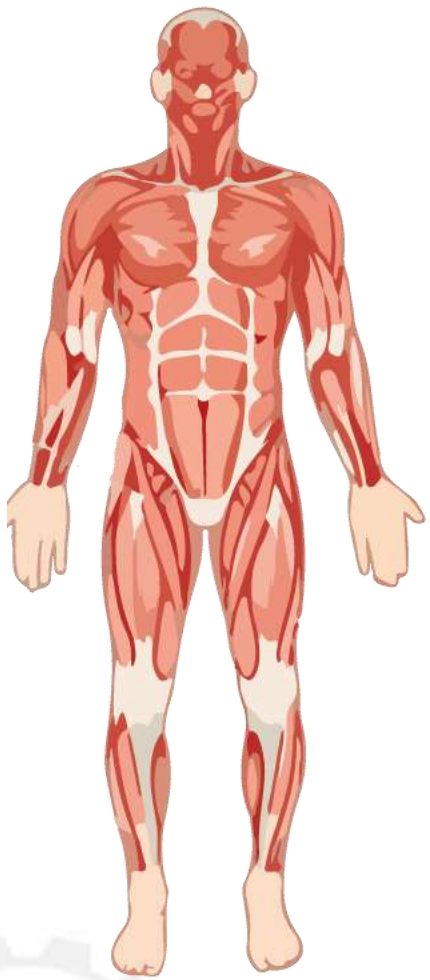
- *Decrease clotting
- *Dilate arteries
- *Anti-inflammatory
- *Decrease cancer
- *Enhance immune system

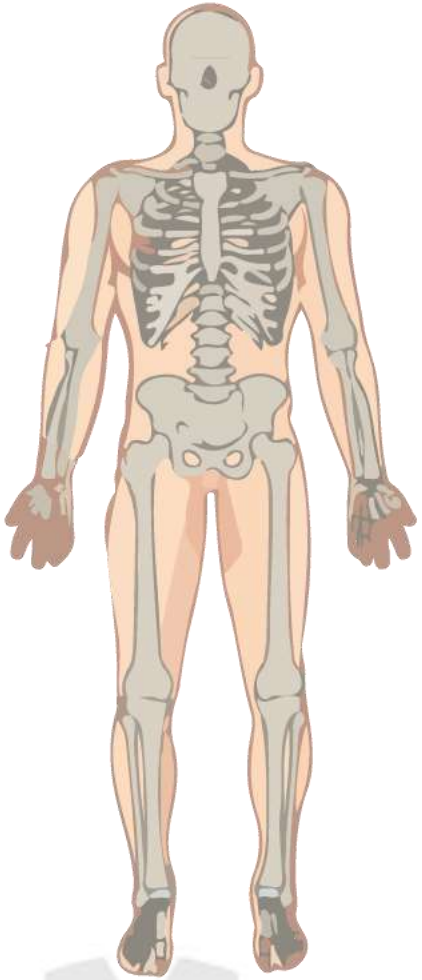
Ideal ratio 2:1

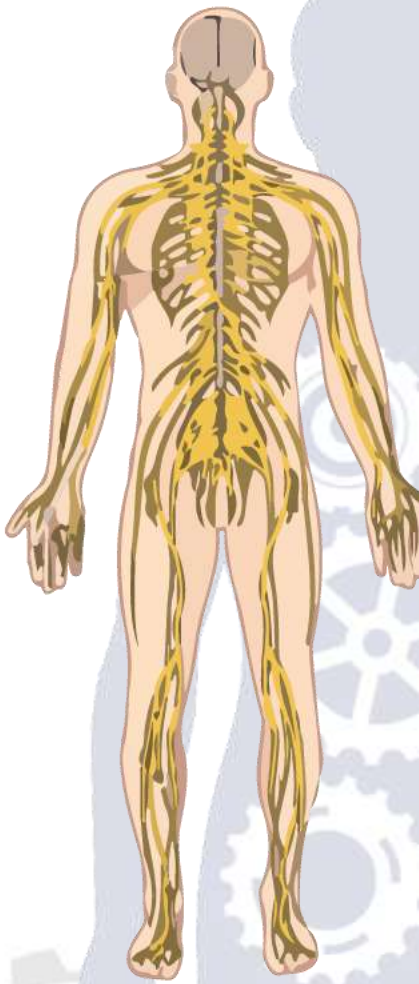
Current US ratio 20:1

Your Body Tissues

- Because your tissues are made up mostly of **saturated and monounsaturated fats**, your body requires more of them than PUFAs

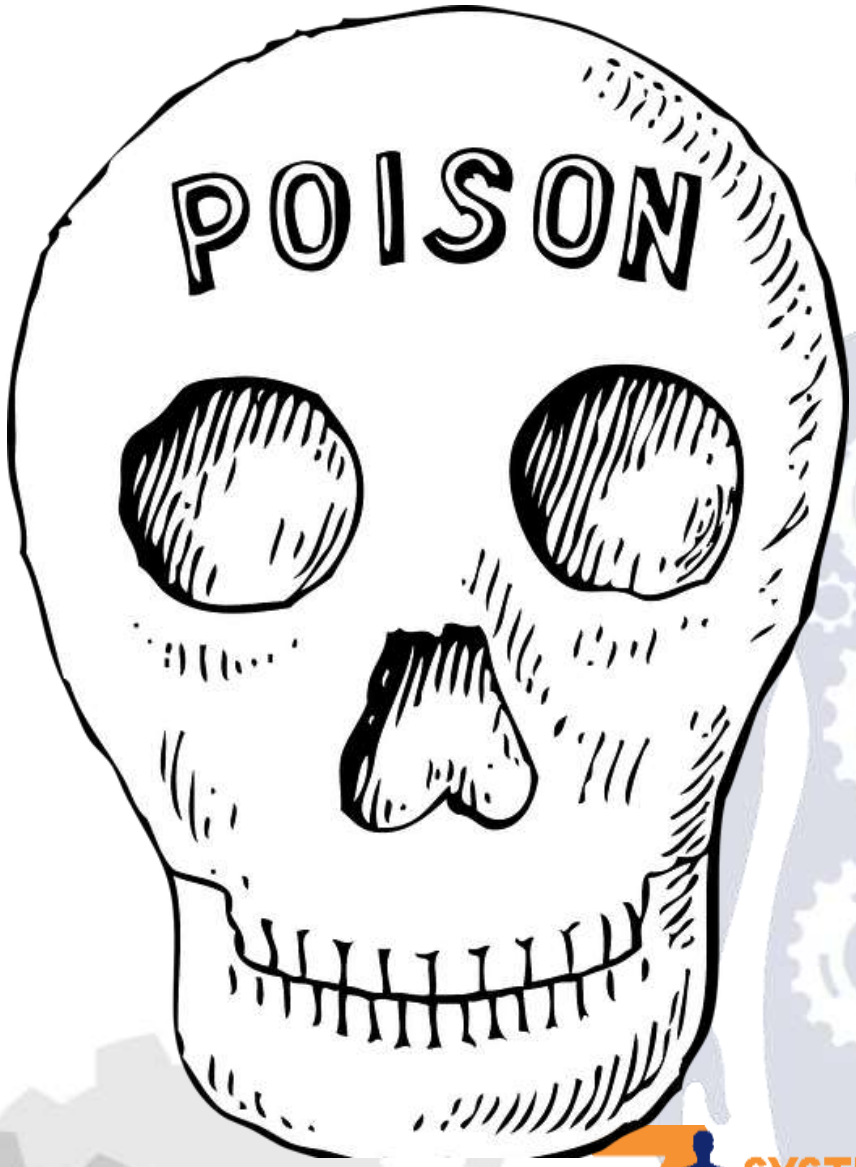




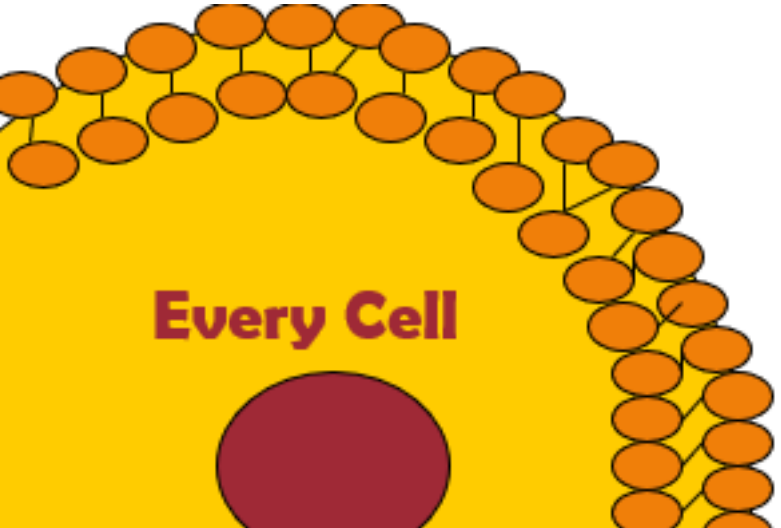


Omega-6 (LA)

- The most pernicious toxin in the modern diet, and the fat you need to minimize consumption of, is the **omega-6 fat linoleic acid**
- The half life of linoleic acid is **380 day**



The Biggest Key to Living Longer???

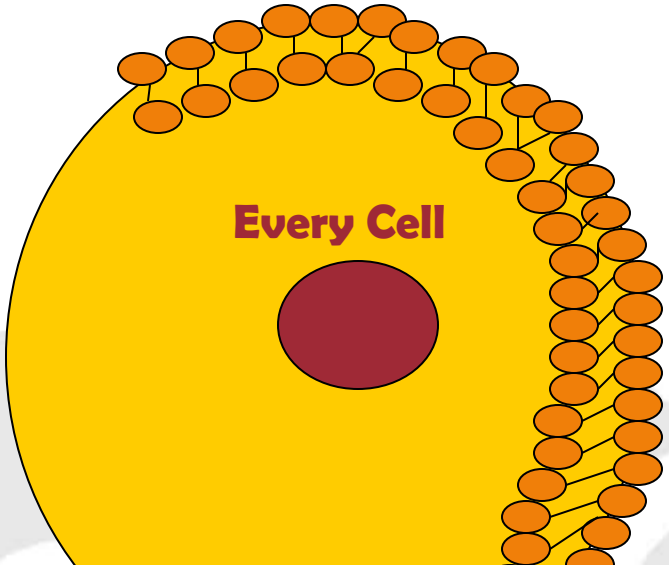


Cell Membranes

What are Cell Membranes made of?

Fats are the primary building blocks of cell membranes

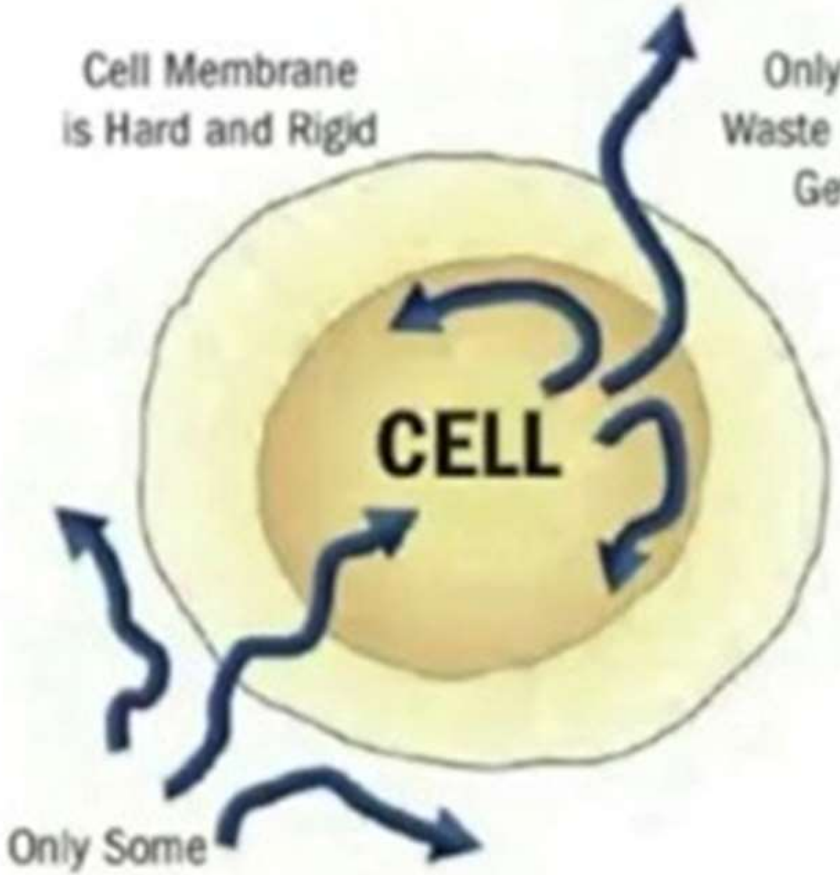
- Phospholipids
- Two fatty acids linked to a phosphate
- What kind of fats?



Cell

SYSTEMS PLAN

UNHEALTHY CELL



UNHEALTHY CELL

Some
Products
Out

Only Some
Nutrients
Get In

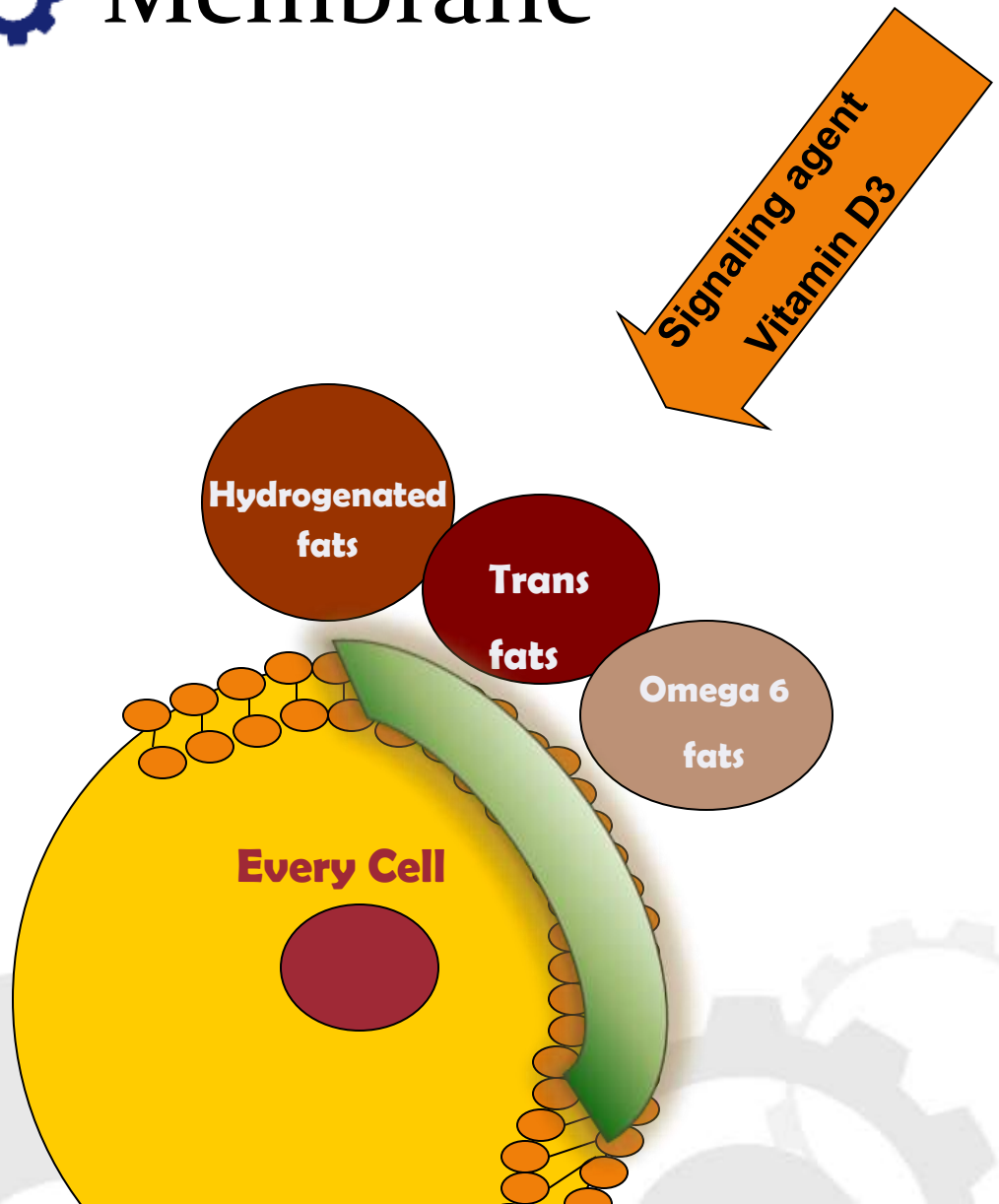
HEALTHY CELL

Cell Membrane

Waste Products
Out

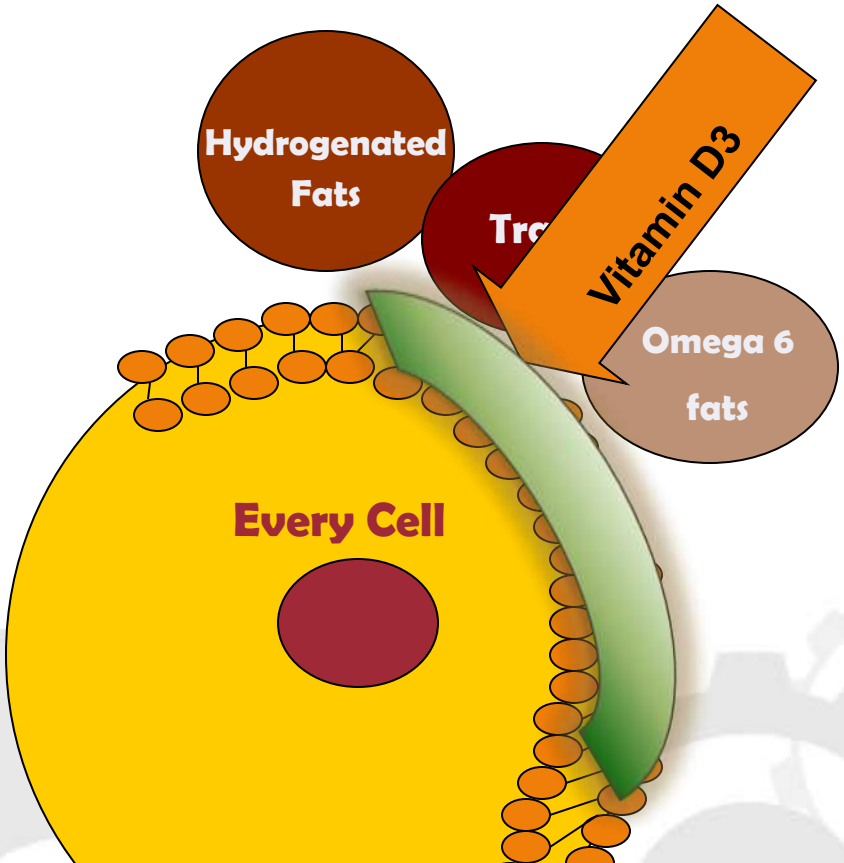
Nutrients Can
Get In

Bad Fats make a **Plastic (Stiff)** Cell Membrane



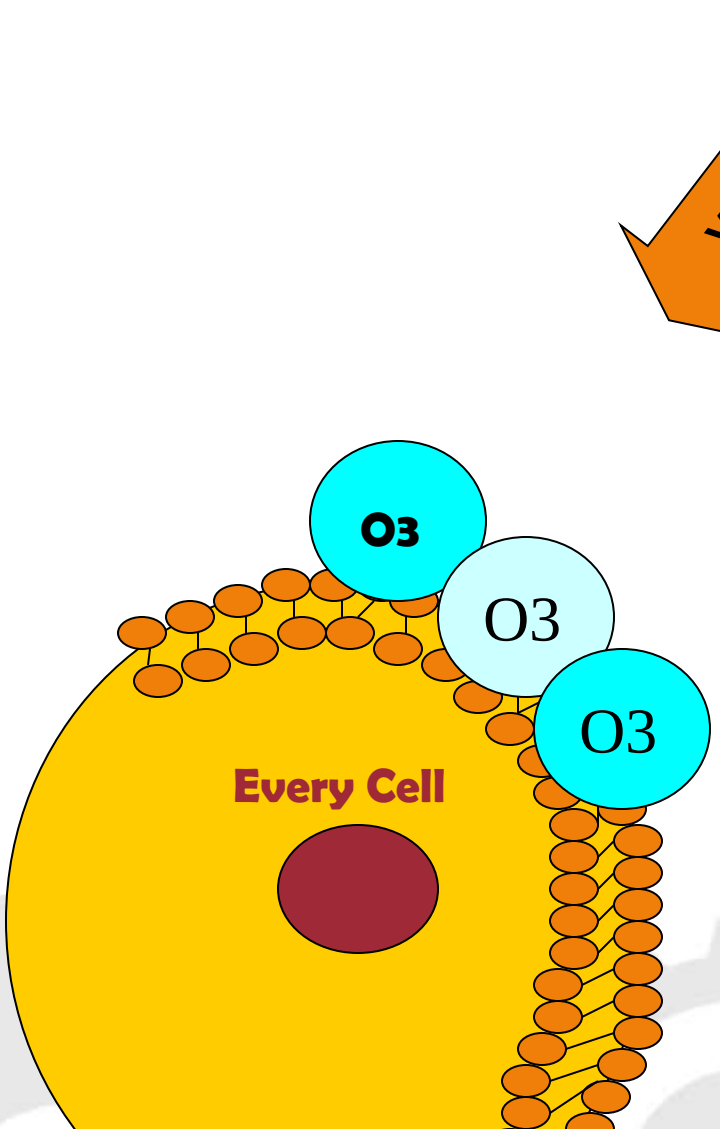
SYSTEMS PLAN

Bad Fats make a **Plastic (Stiff)** Cell Membrane

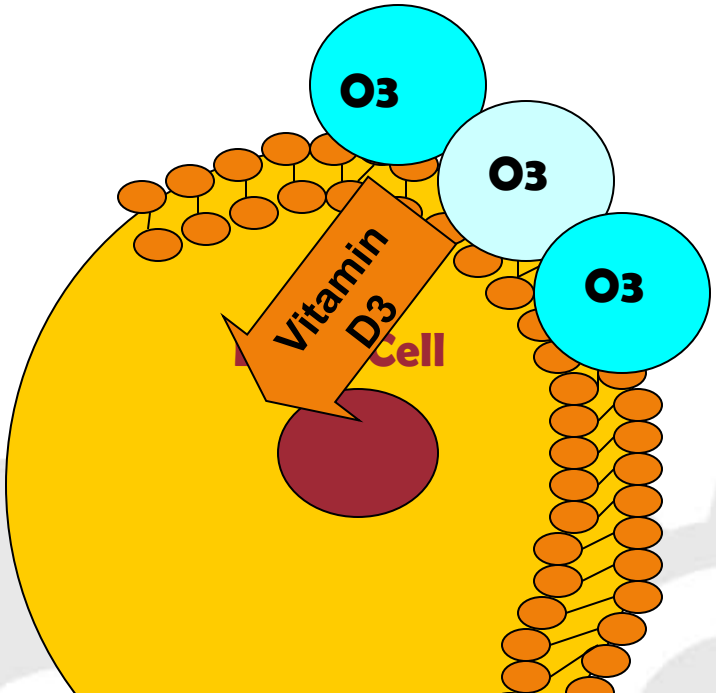


7 SYSTEMS PLAN

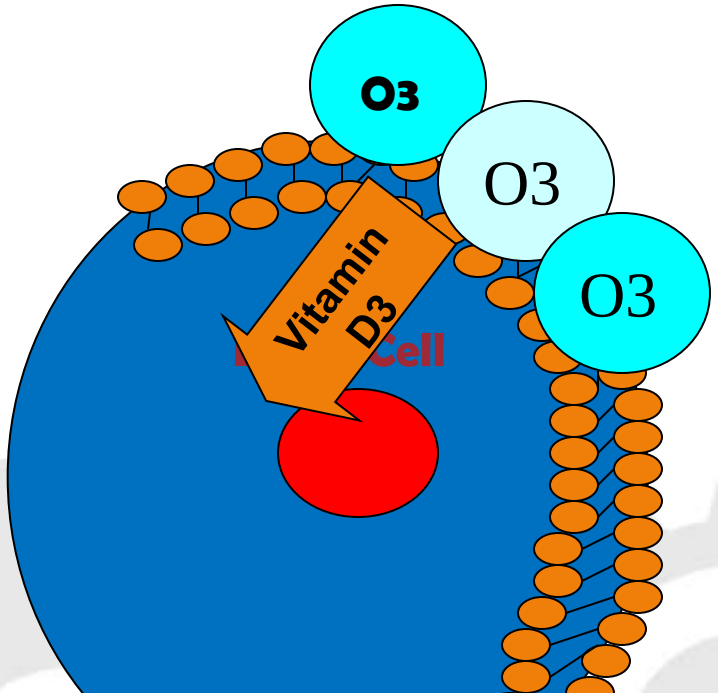
Good Fats make a Good **Fluid** Membrane



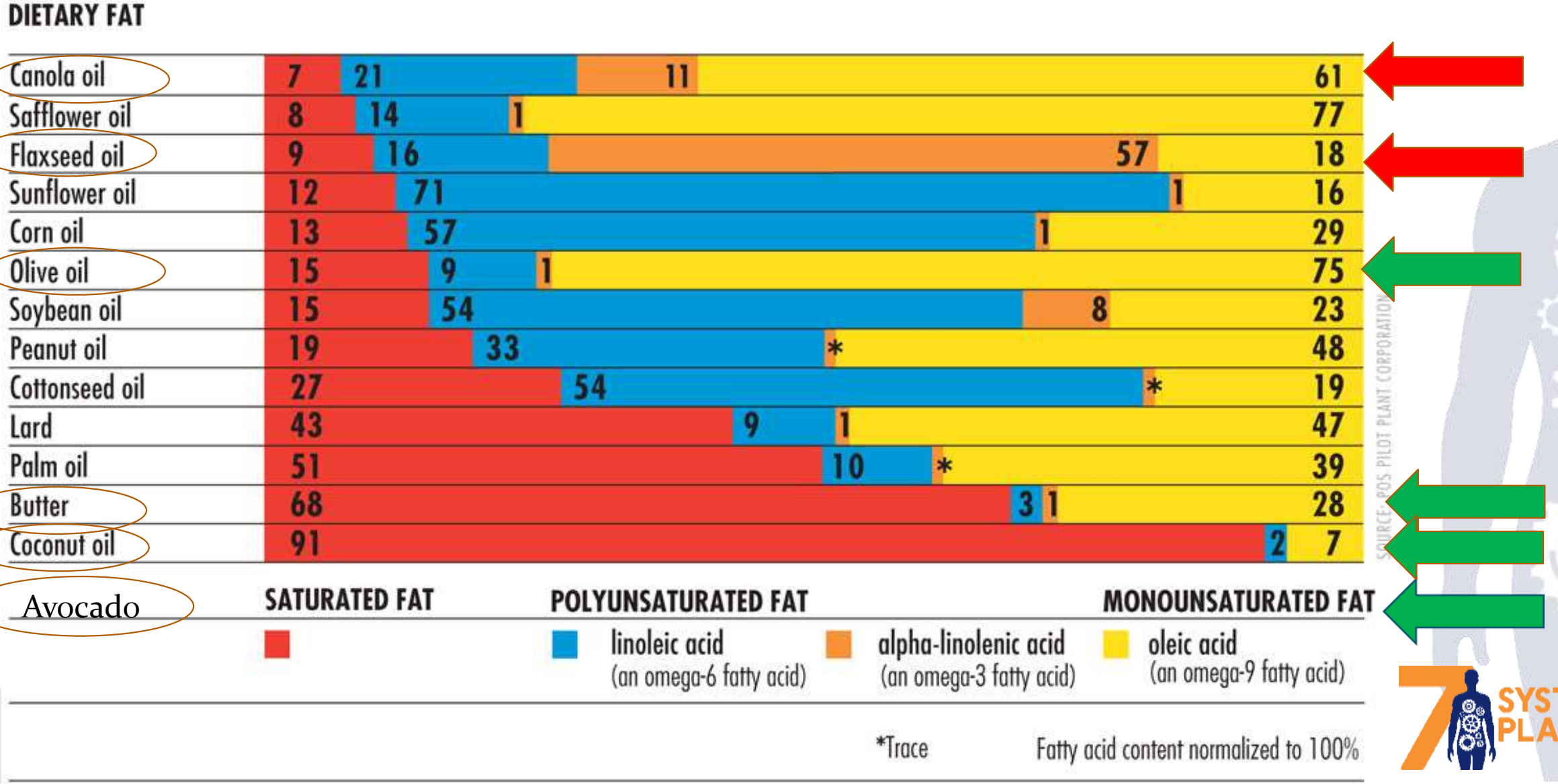
Good Fats make a Good **Fluid** Membrane



Change Your Oil, Improve Your Health!



Comparison of Dietary Fats



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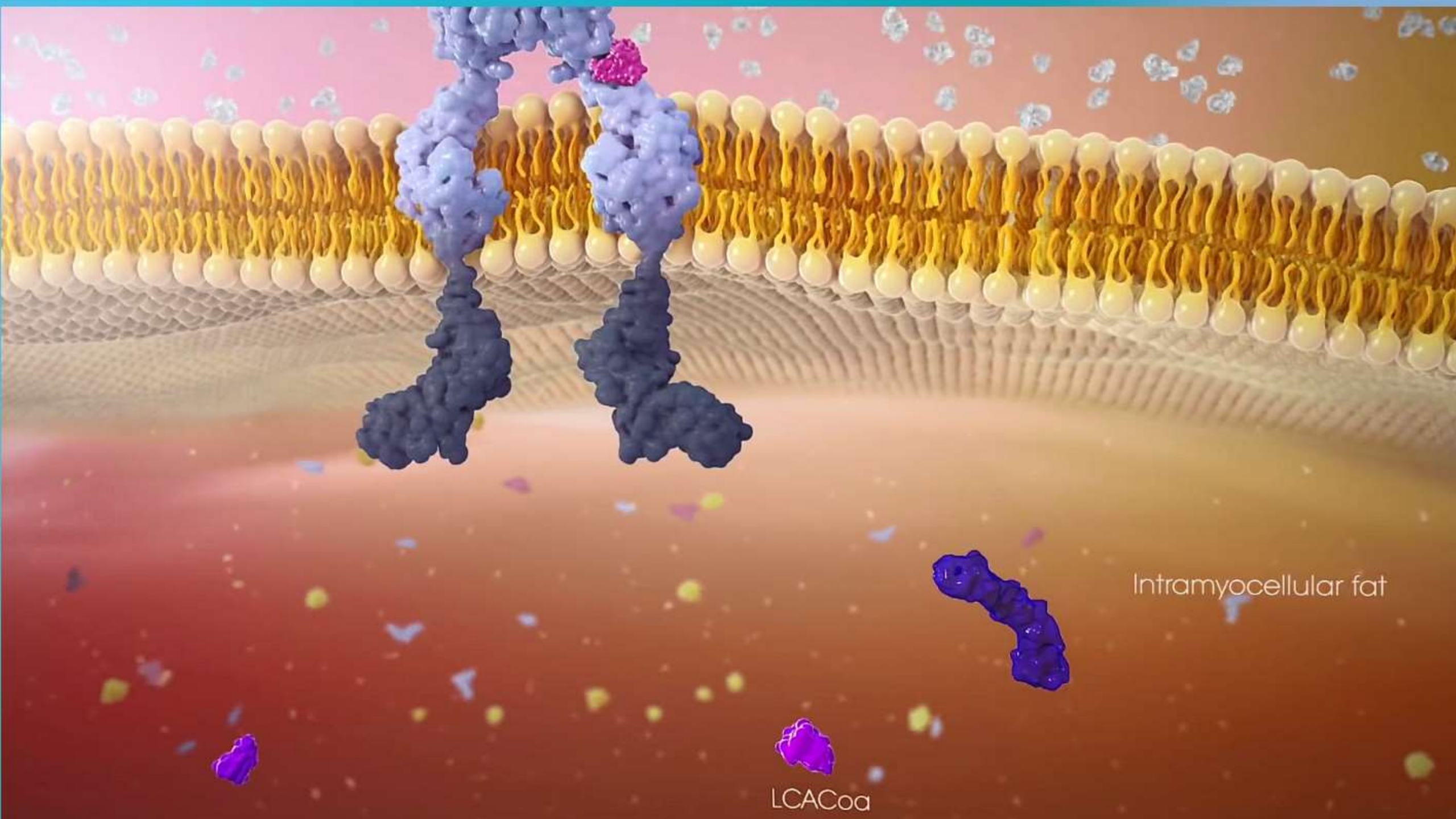

Intramyocellular fat
LCACoa

Test for Omega 3

Keratosis Pilaris (bumps)

Xeroderma (dry skin)

How Much Omega-3 (EPA-DHA) Should You Take?

Dosage Guide	
Application:	**Daily Levels:**
Adult Maintenance	1-2 grams EPA-DHA
Cardiovascular Health	1-2 grams EPA-DHA
Healthy Blood Fat Levels	2-4 grams EPA-DHA
Inflammation	2-7 grams EPA-DHA
Mental Function	2-10 grams EPA-DHA

7 SYSTEMS PLAN

Test Your Omega-3 Level

7 SYSTEMS PLAN

LOW

OMEGA-3 INDEX REPORT

Your Index

Your Index 2,94%

Undesirable < 4% | Intermediate 4% - 8% | Desirable > 8%

2% 4% 6% 8% 10% 12%

HIGH

OMEGA-3 INDEX REPORT

Your Index 10,07%

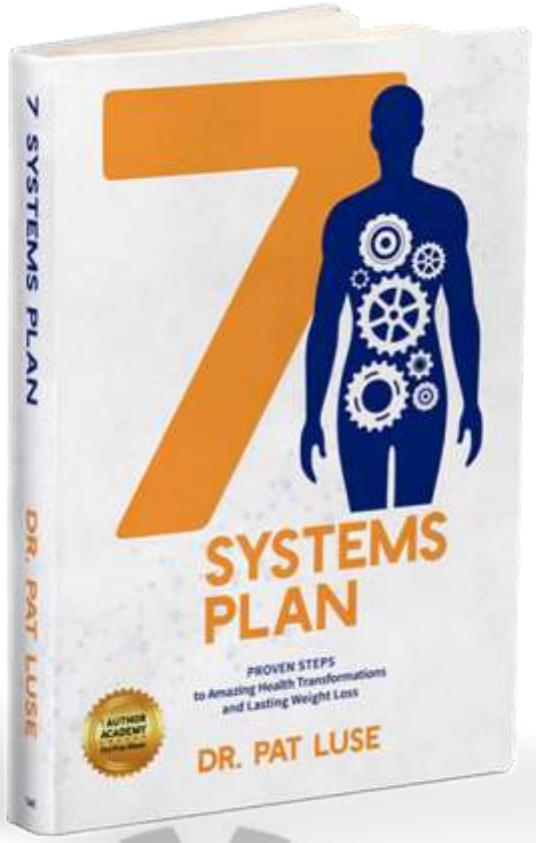
Your Index

Undesirable < 4% | Intermediate 4% - 8% | Desirable > 8%

2% 4% 6% 8% 10% 12%

SYSTEMS PLAN

For Longevity and Great Cell Membranes



- Eliminate the bad oils
- Use the good oils
- Eat lots of vegetables
- Eat nuts
- Eat healthy fish
- Take omega-3

7 SYSTEMS PLAN

SYSTEMS PLAN

Does Coffee Shorten Life?

Coffee

- New research suggests that coffee consumption remains health promoting. Up to 3 cups per day was associated with:
  - 12% less all-cause mortality
  - 17% less cardiovascular mortality
  - 21% less incident stroke.

Simon J, Fung K, Raisi-Estabragh Z, et al. Light to moderate coffee consumption is associated with lower risk of death: A UK Biobank study. *Eur J Prev Cardiol.* 2022;29(6):982–991. doi:10.1093/eurjpc/zwac008

SYSTEMS PLAN

How to Stimulate Autophagy

Stimulate Autophagy

- **Foods- coffee and tea**

7 Benefits of Coffee

1. Stimulating Autophagy

Coffee has been found to stimulate this process, contributing to healthier cells and reduced risk of certain diseases

The polyphenols present in coffee can induce autophagy, thereby supporting the body's ability to generate new and healthier cells

SYSTEMS PLAN

Chlorogenic Acid in Coffee

Chlorogenic acid enhances autophagy by upregulating lysosomal function to protect against SH-SY5Y cell injury induced by H_2O_2

LI-JUAN GAO[1,2*], YUAN DAI[2*], XIAO-QIONG LI[1,2], SHI MENG[1,2], ZHAN-QIONG ZHONG[1,3] and SHI-JUN XU[1,2]

[1]Institute of Meterial Medica Integration and Transformation for Brain Disorders; [2]School of Pharmacy; [3]School of Basic Medical Sciences, Chengdu University of Traditional Chinese Medicine, Chengdu, Sichuan 611137, P.R. China

Received November 4, 2019; Accepted August 11, 2020

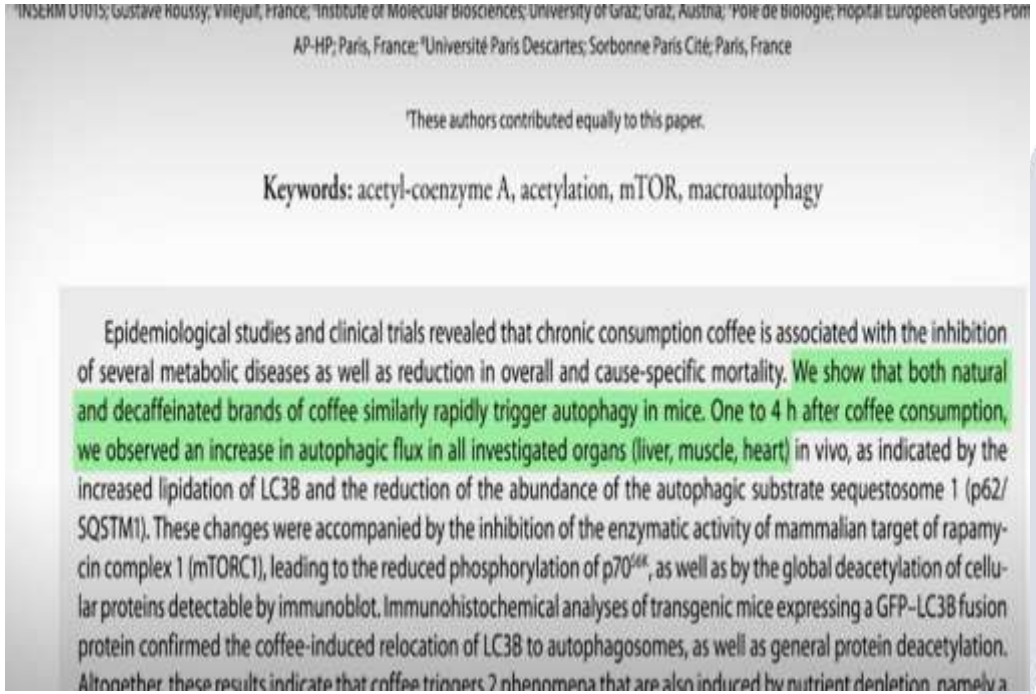
DOI: 10.3892/etm.2021.9843

Abstract. Autophagy serves an important role in amyloid-β (Aβ) metabolism and τ processing and clearance in Alzheimer's disease. The progression of Aβ plaque accumu-

Importantly, these effects of CGA on H_2O_2-treated SH-SY5Y cells were mediated via the mTOR-transcription factor EB signaling pathway. These results indicated that CGA protected

Coffee

- Decaff and regular trigger autophagy



[1]INSERM U1015; Gustave Roussy; Villejuif, France; [2]Institute of Molecular Biosciences; University of Graz; Graz, Austria; [3]Pole de Biologie; Hopital Europeen Georges Pom
AP-HP; Paris, France; [4]Université Paris Descartes; Sorbonne Paris Cité; Paris, France

[†]These authors contributed equally to this paper.

Keywords: acetyl-coenzyme A, acetylation, mTOR, macroautophagy

Epidemiological studies and clinical trials revealed that chronic consumption coffee is associated with the inhibition of several metabolic diseases as well as reduction in overall and cause-specific mortality. We show that both natural and decaffeinated brands of coffee similarly rapidly trigger autophagy in mice. One to 4 h after coffee consumption, we observed an increase in autophagic flux in all investigated organs (liver, muscle, heart) in vivo, as indicated by the increased lipidation of LC3B and the reduction of the abundance of the autophagic substrate sequestosome 1 (p62/SQSTM1). These changes were accompanied by the inhibition of the enzymatic activity of mammalian target of rapamycin complex 1 (mTORC1), leading to the reduced phosphorylation of $p70^{S6K}$, as well as by the global deacetylation of cellular proteins detectable by immunoblot. Immunohistochemical analyses of transgenic mice expressing a GFP–LC3B fusion protein confirmed the coffee-induced relocation of LC3B to autophagosomes, as well as general protein deacetylation. Altogether, these results indicate that coffee triggers 2 phenomena that are also induced by nutrient depletion, namely a

2. Longer Life

As reported by Reuters, **male** coffee drinkers had a **12% lower risk of dying** during the study period compared to non-drinkers

For **women**, the likelihood of dying was reduced by about **7%** among those who drank coffee

Longer Life

Results: We included 21 cohort study articles (10 103 115 study participants and 240 303 deaths). We found a nonlinear association between coffee consumption and all-cause mortality ($P_{nonlinearity} < 0.001$). Compared with no or rare coffee consumption, with a consumption of 3 cups day^{-1}, the risk of all-cause mortality might reduce 13% (RR = 0.87; 95% confidence interval = 0.84–0.89).

Conclusions: The findings of the present study provide quantitative data suggesting that coffee consumption plays a role in reducing the risk of all-cause mortality. Similar inverse associations are found for caffeinated coffee

3. Enhancing Brain Activity

Coffee's ability to boost energy and brain performance is well documented

Studies have shown that it improves alertness, energy levels, and overall performance

4. Aiding in Fat Burning

Coffee is a natural aid for fat burning

Caffeine, its active ingredient, is known to enhance thermogenesis – the body's way of generating heat and energy from digesting food

Research has shown that caffeine can **increase metabolic rate,** supporting weight loss or weight maintenance efforts

Am J Clin Nutr. 1989 Jan;49(1):44-50. doi: 10.1093/ajcn/49.1.44

SYSTEMS PLAN

Caffeine Increases Metabolism

Am J Clin Nutr. 1989 Jan;49(1):44-50. doi: 10.1093/ajcn/49.1.44.

Normal caffeine consumption: influence on thermogenesis and daily energy expenditure in lean and postobese human volunteers

A G Dulloo [1], C A Geissler, T Horton, A Collins, D S Miller

Affiliations + expand

PMID: 2912010 DOI: 10.1093/ajcn/49.1.44

Abstract

Single-dose oral administration of 100 mg caffeine increased the resting metabolic rate of both lean and postobese human volunteers by 3-4% (p less than 0.02) over 150 min and improved the defective diet-induced thermogenesis observed in the postobese subjects. Measurements of energy expenditure (EE) in a room respirometer indicate that repeated caffeine administration (100 mg) at 2-h intervals over a 12-h day period increased the EE of both subject groups by 8-11% (p less than 0.01) during that period but had no influence on the subsequent 12-h night EE. The net effect was a significant increase (p less than 0.02) in daily EE of 150 kcal in the lean volunteers and 79 kcal in the postobese subjects. Caffeine at commonly consumed doses can have a significant influence on energy balance and may promote thermogenesis in the treatment of obesity.

Similar articles

Effects of caffeine on energy metabolism, heart rate, and methylxanthine metabolism in

- Studies have shown that the caffeine in coffee can boost metabolism by 3–11%.
- Green tea also promotes fat burning

7 SYSTEMS PLAN

5. Decrease Heart Disease

European Society of Cardiology indicated that drinking 4-5 cups of coffee, is linked to a lower risk of arrhythmia (caffeinated only)

All coffee types, including decaf, were associated with a reduced risk of CVD and a decrease in all-cause mortality, particularly at 2-3 cups per day

6. Regulating Blood Sugar

Studies suggest that regular coffee consumption may reduce the risk of developing type 2 diabetes

This protective effect could be due to the ability of coffee to influence factors like insulin sensitivity and glucose metabolism

7. Promoting Bowel Movements

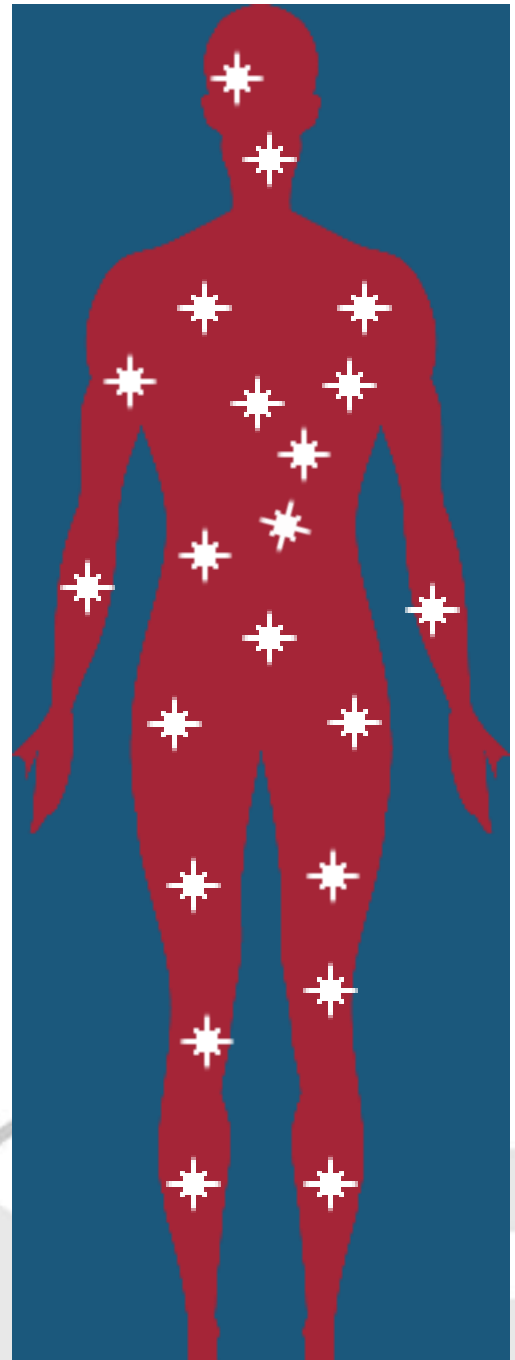
It stimulates colon muscles and aids peristalsis, the process that moves food through the Digestive System

This effect is not solely due to caffeine, as studies have shown similar benefits with decaffeinated coffee

To Get the Maximum Benefits from Your Coffee

- Coffee is a heavily pesticide-contaminated crop, use a good brand
- Purchase coffee in whole bean form and then grind it yourself to prevent rancidity
- Drink it black and use an unbleached coffee filter
- Purchase light or medium roast beans rather than dark
- For those with sleep problems, stop caffeine after 2 PM

Energy System



1 Mitochondria

One test to check your fitness level in 30 seconds?

BMJ. 2018; 361: k1651.
Published online 2018 May 8. doi: 10.1136/bmj.k1651

PMCID: PMC5939721
PMID: 29739772

Associations of grip strength with cardiovascular, respiratory, and cancer outcomes and all cause mortality: prospective cohort study of half a million UK Biobank participants

Carlos A Celis-Morales, research associate,[1] Paul Welsh, senior lecturer,[1] Donald M Lyall, research associate,[2] Lewis Steell, student,[1] Fanny Petermann, student,[1] Jana Anderson, research associate,[2] Stamatina Iliodromiti, clinical lecturer,[1] Anne Sillars, clinical fellow,[1] Nicholas Graham, clinical fellow,[2] Daniel F Mackay, reader,[2] Jill P Pell, professor,[2] Jason M R Gill, professor,[1] Naveed Sattar, professor,[1] and Stuart R Gray, lecturer[1]

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Study BMJ

- This study has shown that grip strength is **strongly and inversely** associated with:
  - all cause mortality
  - mortality from cardiovascular disease
  - respiratory disease
  - chronic obstructive pulmonary disease
  - all cancer, and subtypes of cancer, including colorectal, lung, and breast cancer

New Screening Tool

- Our results show that **adding handgrip strength** to an **existing office-based risk score** improves the prediction ability for all cause mortality and incidence of and mortality from cardiovascular disease and that muscle weakness (using previously defined grip strength cut-offs) is associated with poorer health outcomes.

Weakness

- Muscle grip strength weakness
  - <26 kg for men
  - <16 kg for women
- associated with a higher hazard for all health outcomes

Grip Strength Ratings for Males (in kg)

AGE	Weak	Normal	Strong
10-11	< 12.6	12.6-22.4	> 22.4
12-13	< 19.4	19.4-31.2	> 31.2
14-15	< 28.5	28.5-44.3	> 44.3
16-17	< 32.6	32.6-52.4	> 52.4
18-19	< 35.7	35.7-55.5	> 55.5
20-24	< 36.8	36.8-56.6	> 56.6
25-29	< 37.7	37.7-57.5	> 57.5
30-34	< 36.0	36.0-55.8	> 55.8
35-39	< 35.8	35.8-55.6	> 55.6
40-44	< 35.5	35.5-55.3	> 55.3
45-49	< 34.7	34.7-54.5	> 54.5
50-54	< 32.9	32.9-50.7	> 50.7
55-59	< 30.7	30.7-48.5	> 48.5
60-64	< 30.2	30.2-48.0	> 48.0
65-69	< 28.2	28.2-44.0	> 44.0
70-99	< 21.3	21.3-35.1	> 35.1

Grip Strength Ratings for Females (in kg)

AGE	Weak	Normal	Strong
10-11	< 11.8	11.8-21.6	> 21.6
12-13	< 14.6	14.6-24.4	> 24.4
14-15	< 15.5	15.5-27.3	> 27.3
16-17	< 17.2	17.2-29.0	> 29.0
18-19	< 19.2	19.2-31.0	> 31.0
20-24	< 21.5	21.5-35.3	> 35.3
25-29	< 25.6	25.6-41.4	> 41.4
30-34	< 21.5	21.5-35.3	> 35.3
35-39	< 20.3	20.3-34.1	> 34.1
40-44	< 18.9	18.9-32.7	> 32.7
45-49	< 18.6	18.6-32.4	> 32.4
50-54	< 18.1	18.1-31.9	> 31.9
55-59	< 17.7	17.7-31.5	> 31.5
60-64	< 17.2	17.2-31.0	> 31.0
65-69	< 15.4	15.4-27.2	> 27.2
70-99	< 14.7	14.7-24.5	> 24.5

How to Stimulate Autophagy

Stimulate Autophagy

- **Exercise**
- Foods- coffee, tea, mushrooms,
- Spermidine

Amino Acids (2015) 47:2037–2063
DOI 10.1007/s00726-014-1765-4

REVIEW ARTICLE

Regulation of autophagy by amino acids and MTOR-dependent signal transduction

Alfred J. Meijer · Séverine Lorin · Edward F. Blommaart · Patrice Codogno

Proper in vivo manipulation of autophagy, either pharmacologically or by dietary restriction, under many pathological conditions may be used to the benefit of patients (Hermans et al. 2013). The safest way is dietary restriction.

Dysregulation of autophagy has been implicated in the etiology of several pathologies. The history of the studies on the interrelationship between amino acids, MTOR signaling and autophagy is the subject of this review. The mechanisms responsible for the stimulation of MTOR-mediated signaling, and the inhibition of autophagy, by amino acids have been studied intensively in the past but are still not completely clarified. Recent developments in this field are discussed.

Keywords Glutamine · Leucine · Rapamycin · Lysosomes · Mitochondria

ATG	Autophagy related
BAD	Bcl-2-associated death promoter
BARKOR	Beclin1-associated autophagy-related key regulator
Bcl-2	B cell lymphoma 2
Bcl-xL	B cell lymphoma extra large
Beclin1	Bcl-2-interacting coiled-coil protein 1
BH3	Bcl-2 homology domain
BNIP3	Bcl-2/adenovirus E1B 19 kDa interacting protein 3
CHO	Chinese hamster ovary
DAPK	Death-associated protein kinase
DEPTOR	DEP domain-containing MTOR-interacting protein

FASTING

cient to interfere with autophagy. There is already a substantial amount of leucine present in blood and cells in your body, and the small amount of leucine in the stevia will not have much of an effect. Another comment is that 5 days of fasting is too long for activating autophagy. The greatest acceleration of autophagy takes place after 24–48 h of fasting.

Exercise

Chapter 2
Autophagy: 'Self-Eating' Your Way to Longevity

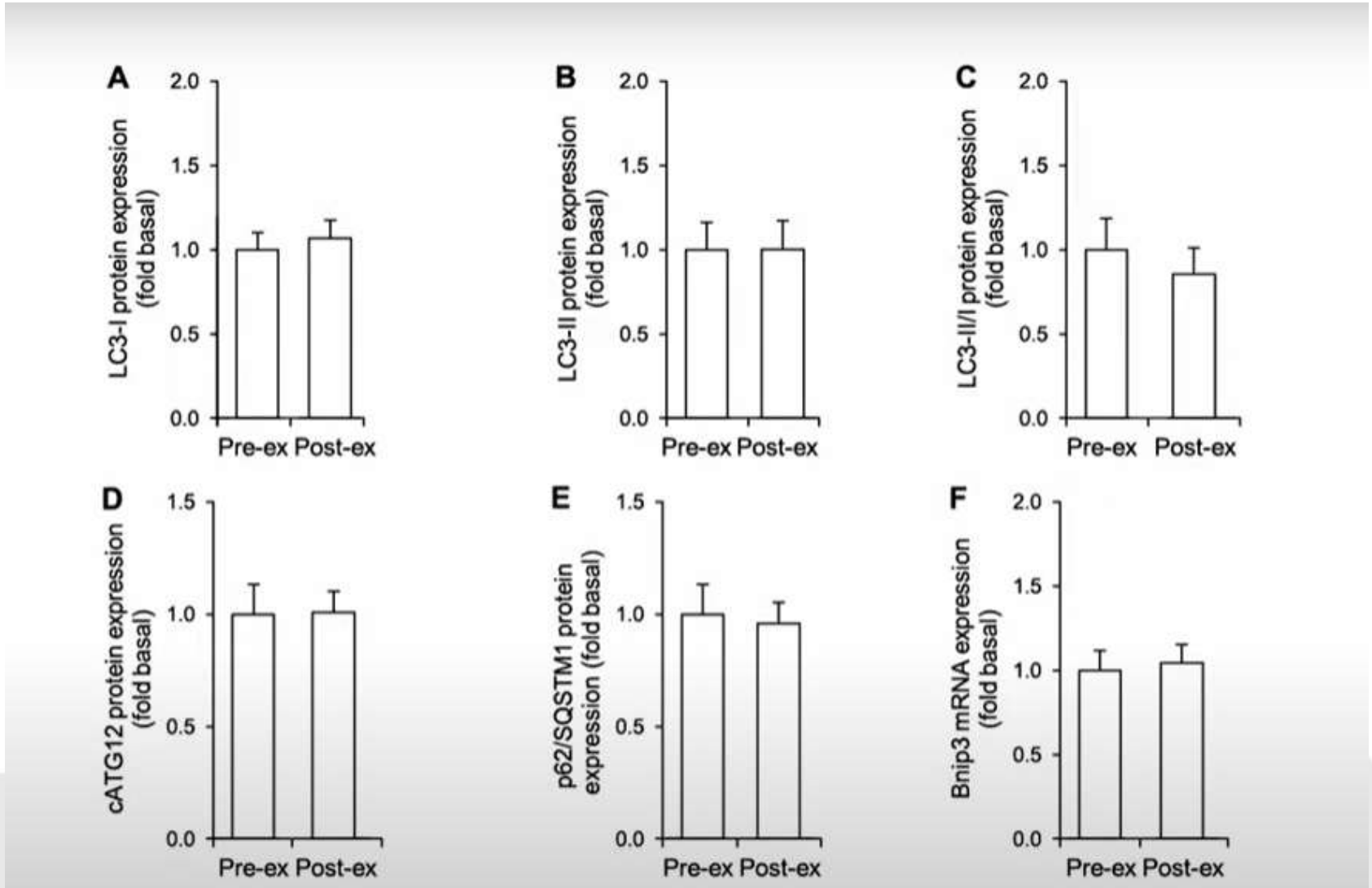
Charlotte J. Pattison and Viktor I. Korolchuk

Beclin-1 (He et al. 2012; Dagon et al. 2015). By subjecting mice to periods of running, it was found that after 30 min of exercise, autophagy levels in skeletal and cardiac cells had increased by 40%, and reached a maximum at 80 min. In addition

sequestration of damaged or surplus cytoplasmic components which are then delivered to the lysosome for degradation. This house-keeping mechanism is essential to maintain cellular homeostasis and survival, particularly during stress. A decline or loss of sensitivity/responsiveness of autophagy is intimately linked with an accelerated rate of ageing as well as many age-related diseases including neurodegeneration, cancer and metabolic disease where damage accumulation exceeds damage removal. This chapter summarises current knowledge regarding the relationship between autophagy and ageing and outlines some strategies that can be implemented to promote the anti-ageing effects of autophagy to improve human health and lifespan.

7 SYSTEMS PLAN

How Long do You have to Exercise?



The effect of environmental hypoxia and exercise on autophagy- and mitophagy-related markers. LC3-I

postexercise cellular degradation activity is mediated by the UPS, while autophagy activity demonstrates a more delayed response (Tam & Shi, 2014; Vainshtein & Hood, 2016); however, both systems have been shown to be activated simultaneously in some conditions (Jamart, Benoit, et al., 2012; Jamart, Francaux, et al., 2012). The exercise-elicited autophagic response appears to be regulated in a duration and intensity-dependent manner (Jamart, Benoit, et al., 2012; Schwalm et al., 2015; Tachtsis, Smiles, Lane, Hawley, & Camera, 2016), although an established "dose" of exercise to initiate

7 | CHRONIC EFFECTS OF EXERCISE ON AUTOPHAGIC ACTIVITY

Currently, the long-term effects of exercise on autophagic activity are ill-characterized; however, they appear mediated by activation of a transcriptional program (Vainshtein & Hood, 2016). While emerging data in both rodent and human models do point to chronic exercise augmenting autophagy activity (Feng et al., 2011; Ghaneghani et al., 2017; Lira et al., 2013; Mejias-Pena et al., 2017, 2016; Wohlgemuth et al., 2011), its interaction with longev-

Aerobic exercise for 60 min or greater at 55%–70% VO_{2max} has been shown to stimulate autophagic activity in skeletal muscle

ce exercise has long mitigate age-related 14; Schnohr et al., onstrates an inverse

et al., 2015; Schwalm et al., 2015). Table 1 depicts the current data of the autophagy response to acute exercise in skeletal muscle. Prolonged endurance exercise (i.e., 150 and 200 km marathon running) increased markers of autophagy and a number of related proteins in ultra-endurance-trained males (Jamart, Benoit, et al., 2012; Jamart, Francaux, et al., 2012). More modest bouts of exercise have also

relationship between regular exercise and mortality (Ruiz, Moran, Arenas, & Lucia, 2011; Teramoto & Bungum, 2010; Vina et al., 2016). Longitudinal data show that physically active men and women have ~30% lower risk of death versus inactive counterparts (Schnohr et al., 2015). Moreover, highly trained individuals

SYSTEMS PLAN

Exercise induces autophagy in peripheral tissues and in the brain

Congcong He,[1] Rhea Sumpter, Jr.[2] and Beth Levine[3,*]

[1]Howard Hughes Medical Institute; Department of Internal Medicine; Center for Autophagy Research; University of Texas Southwestern Medical Center; Dallas, TX USA; [2]Department of Internal Medicine; Center for Autophagy Research; University of Texas Southwestern Medical Center; Dallas, TX USA; [3]Howard Hughes Medical Institute; Departments of Internal Medicine and Microbiology; Center for Autophagy Research; University of Texas Southwestern Medical Center; Dallas, TX USA

We recently identified physical exercise as a newly defined inducer of autophagy in vivo. Exercise induced autophagy in multiple organs involved in metabolic regulation, such as muscle, liver, pancreas and adipose tissue. To study the physiological role of exercise-induced autophagy, we generated mice with a knock-in nonphosphorylatable

has numerous health benefits, such as life-span expansion, and protection against cardiovascular diseases, diabetes, cancer and neurodegenerative diseases.[1] Many of these health benefits overlap with known protective functions of the cellular pathway of macroautophagy (herein referred to as autophagy).[2,3] Thus, we proposed that some of the health benefits of exercise may

Exercise

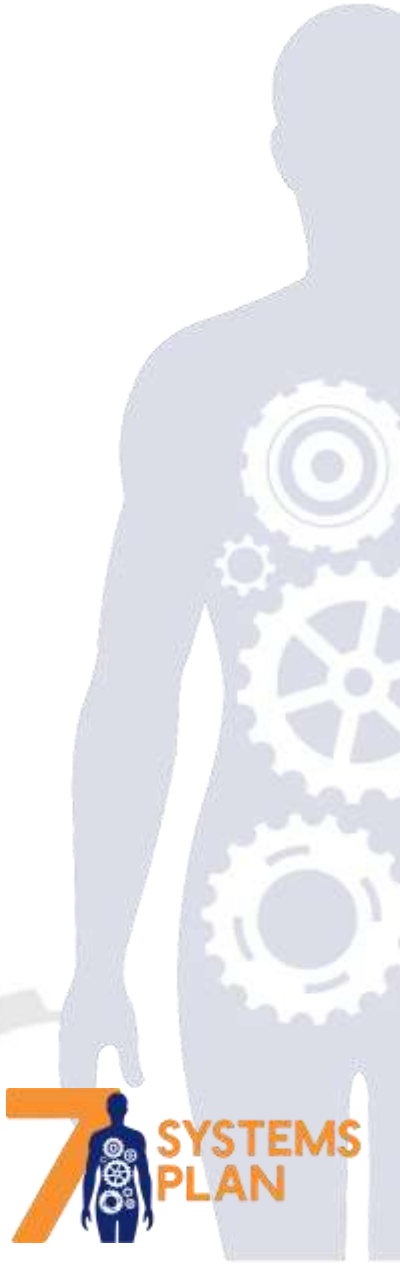
- Autophagy is activated in skeletal muscle in response to exercise.
- 30 minutes of exercise was sufficient to induce GFP-LC3 puncta (autophagosome) formation.

Autophagy-Dependent Beneficial Effects of Exercise – PMC www.ncbi.nlm.nih.gov/pmc/articles/PMC5538402/

fasting

+ exercise

maximum autophagy

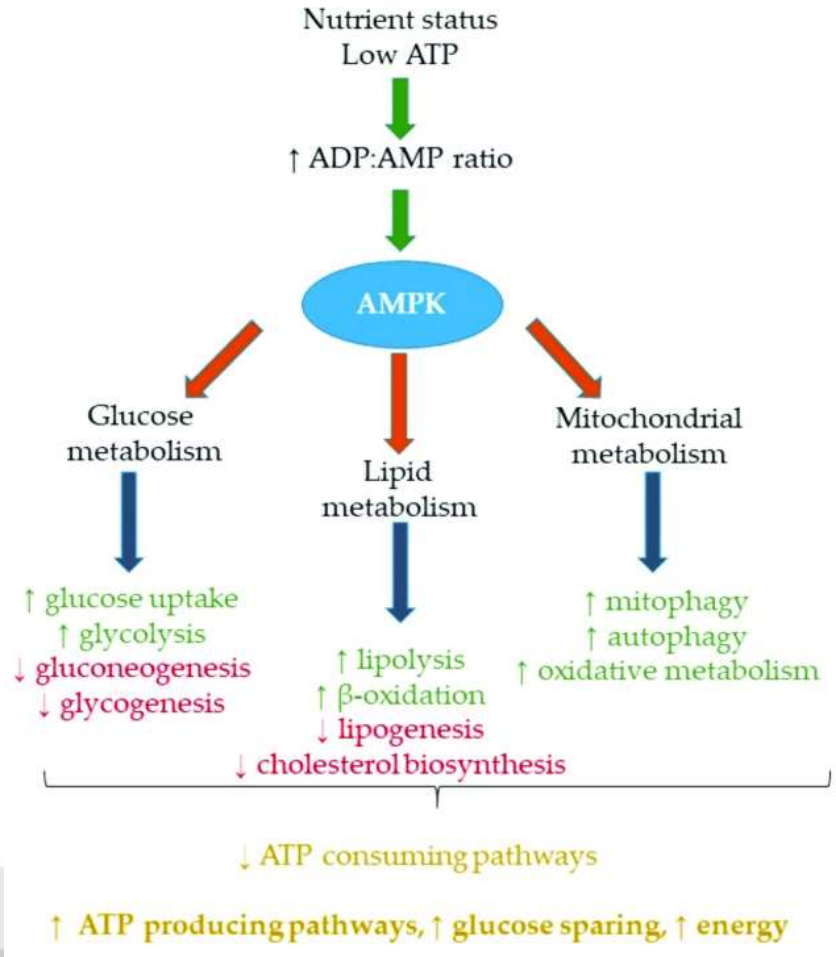


SYSTEMS PLAN

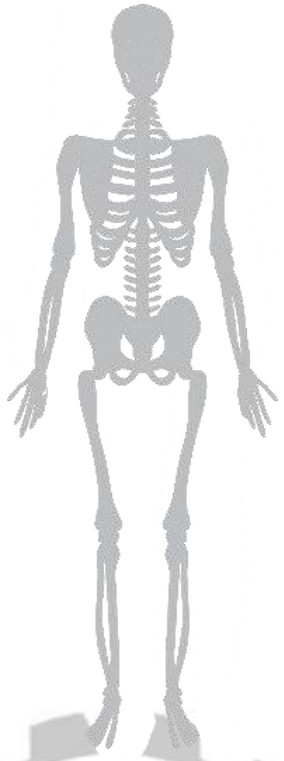
SYSTEMS PLAN

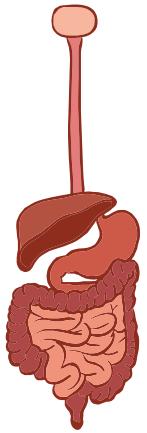
“The Secret to a High Energy, Long Life: The role of AMPK"

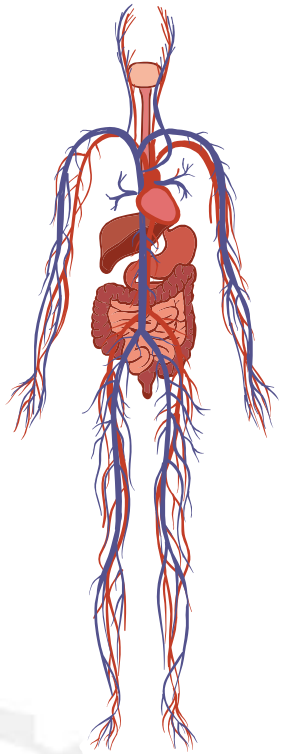
AMPK, the downstream protein of FGF21, may be the key to FGF21's effect.



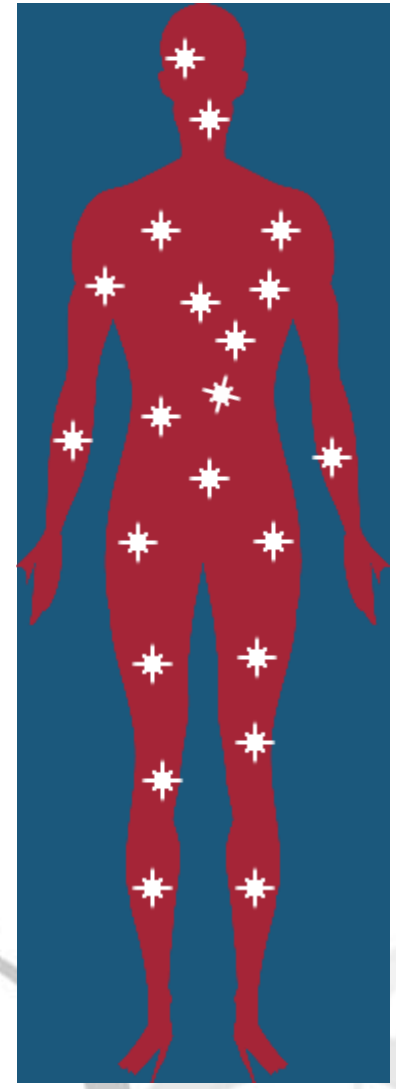
Eat→ Digest→ Deliver→ Energy







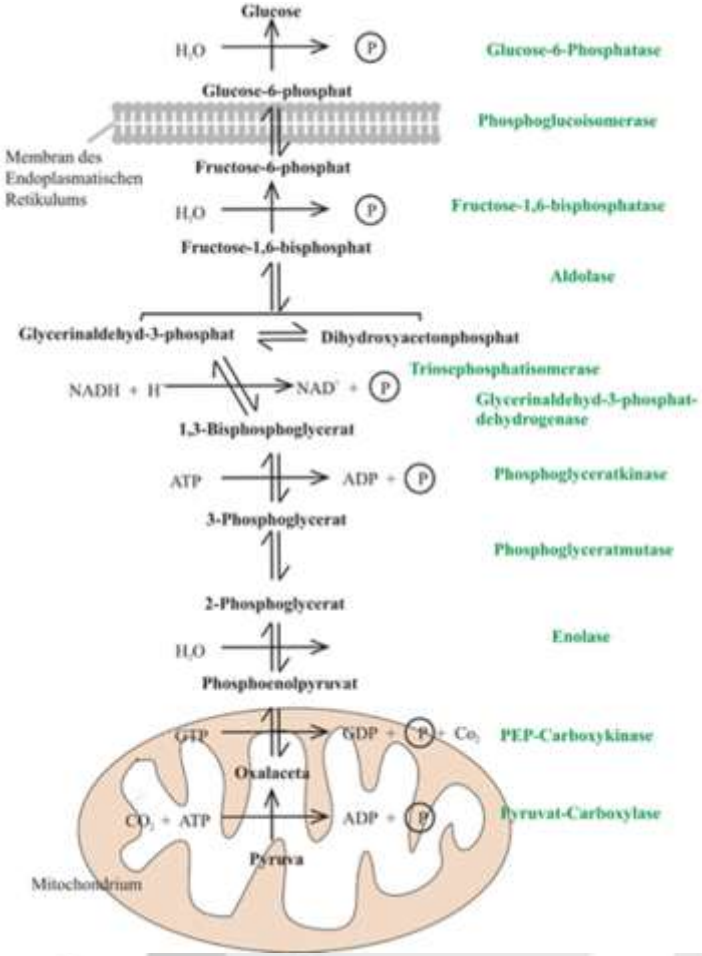
Energy System



1 Mitochondria

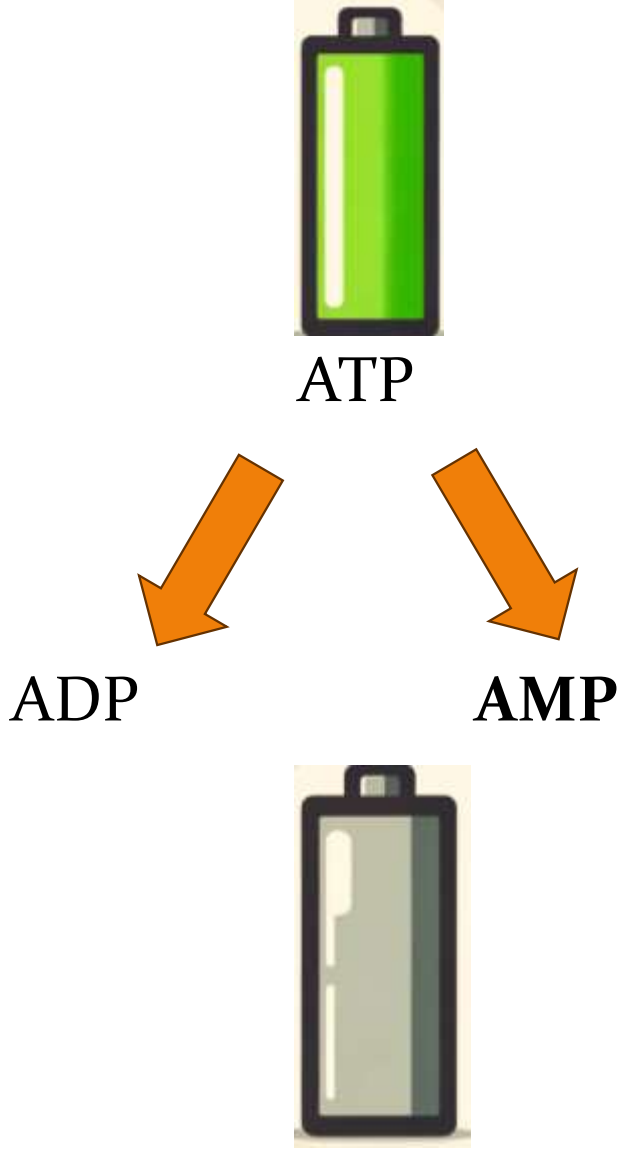
Mitochondria Produce Adenosine Triphosphate(ATP)

- ATP is the fuel the body uses to do everything.
- The body uses food (especially sugar) and oxygen to make ATP.
- ATP is made in the cells through a process called cellular respiration.



ATP

- When the body uses ATP, it turns into something called ADP and AMP.



Reusing Energy

- The body has a way to recharge them by adding back a phosphate group.
- This turns them back into ATP.

What Happens When Fuel is Low?

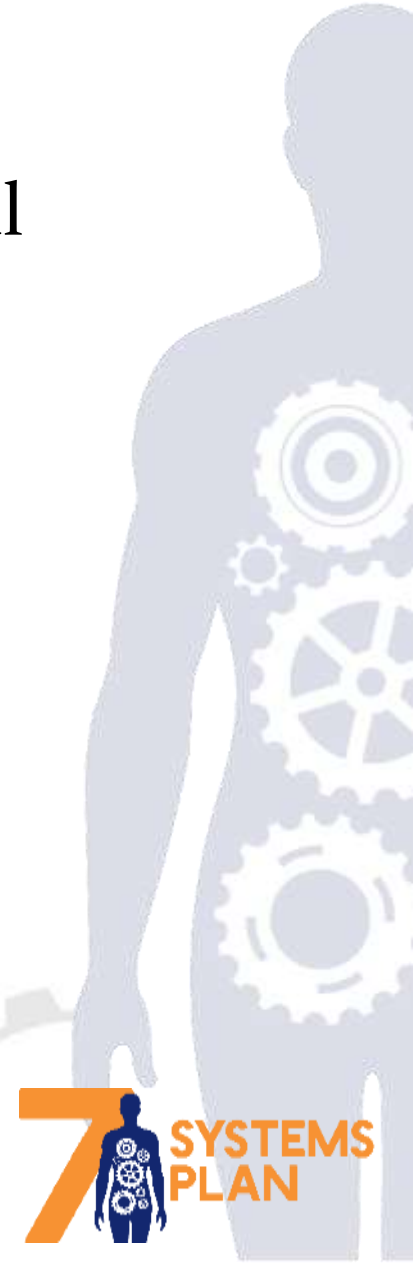
- When sugar is low, the body uses fat and old cells for energy.
- This is like cleaning up old things to make new things.
- When fuel is low, **AMPK is activated** and helps start this process.

What is AMPK?

- AMPK is a helper in our cells.
- It helps the cell decide when to save energy and clean house and when to use energy.

AMPK- the Longevity Enzyme

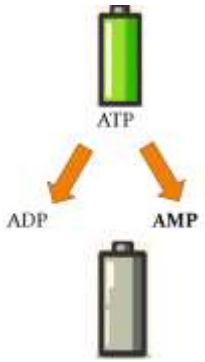
1. Improves energy balance
2. Enhances fat burning
3. Increases insulin sensitivity
4. Promotes longevity
5. Improves cardiovascular health
6. Enhances mitochondrial function
7. Supports weight loss
8. Reduces inflammation
9. Regulates appetite
10. Prevents cancer



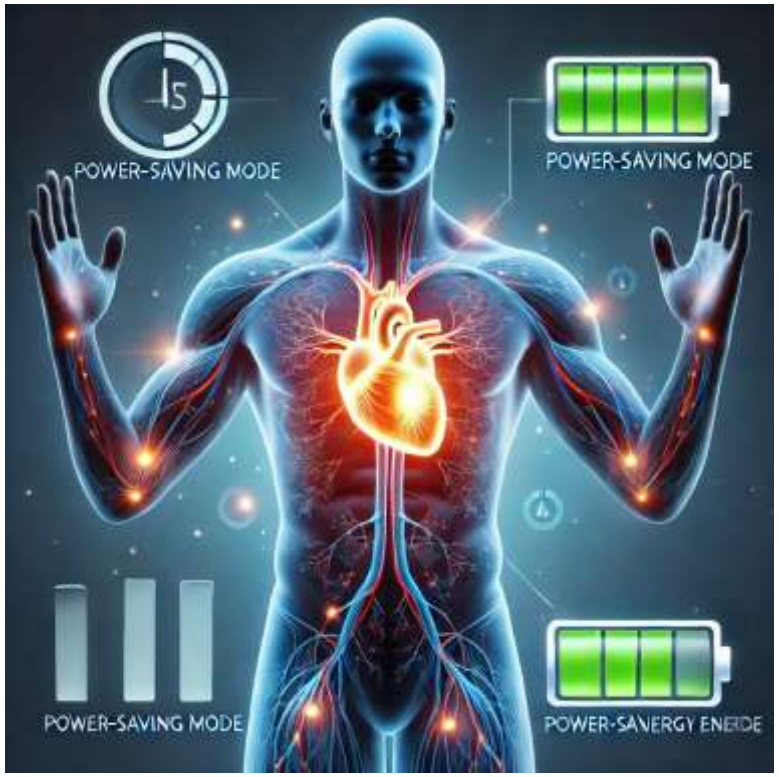
SYSTEMS PLAN

How AMPK gets Turned on

- When the cell is low on energy, AMP (a signal) rises.



- AMP attaches to part of AMPK and starts saving energy.



AMPK

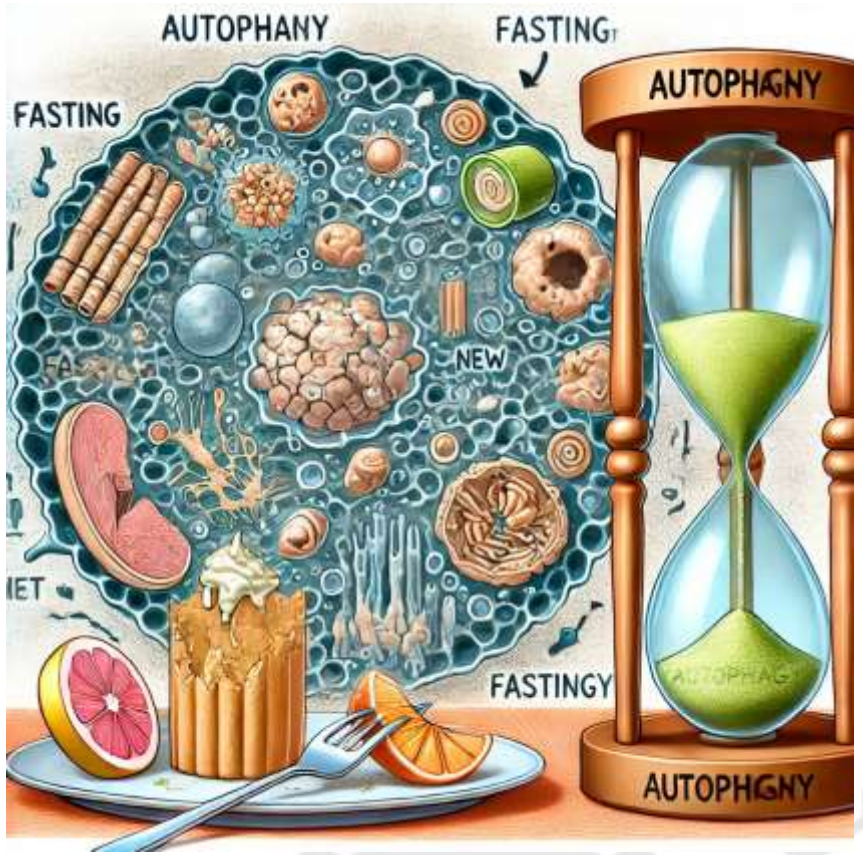
- Turns on energy-making processes like burning fat.

Why AMPK is Important

- AMPK helps keep our cells and bodies healthy.
- It makes sure we have enough energy when we need it.
- It also actives **autophagy** which recycles old and damaged cells.

What is Autophagy?

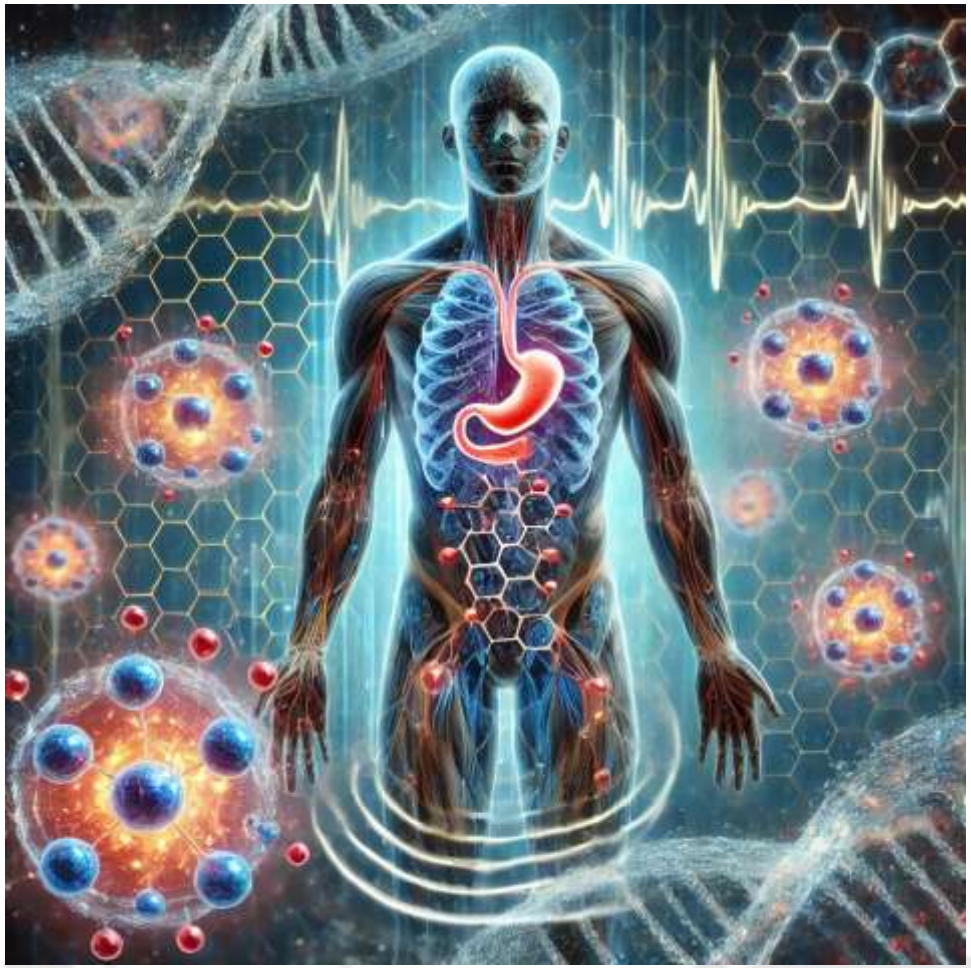
- Autophagy is when the body cleans out old, broken cells.
- Fasting is a great way start this clean-up process.



AMPK

- AMPK is like a switch that tells the body to start the clean-up process.

7 Ways to Activate AMPK



1. Fasting and Calorie Restriction

- Fasting or reducing calorie intake lowers the availability of glucose and other nutrients, which increases AMP levels and activates AMPK.

2. Eat Fiber-Rich Foods

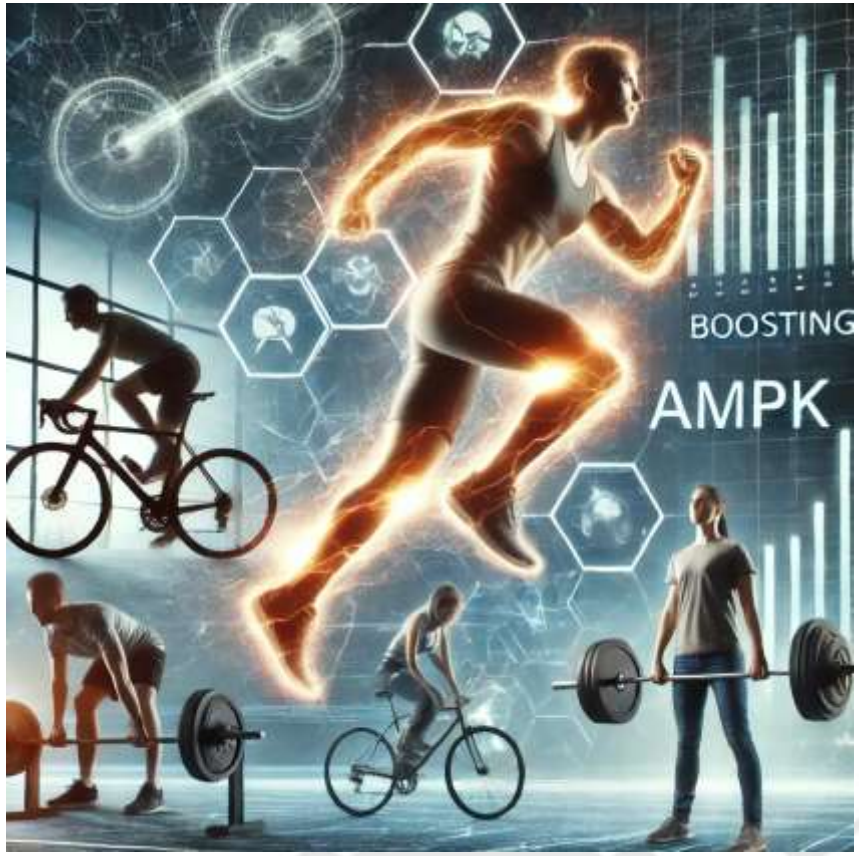
- Foods like fruits, vegetables, and whole grains are rich in fiber.

3. Eat Healthy Fats

- Healthy fats, like those in fish, nuts, and avocados, support AMPK.

4. Exercise Regularly

- Physical activity, especially **high-intensity** exercise, is one of the most effective ways to activate AMPK.
- Exercise increases the demand for energy in the muscles, which leads to a rise in AMP levels, triggering AMPK activation.



5. Eat High-Antioxidant Foods

- Foods like berries, dark chocolate, and green tea are high in antioxidants.

6. Metformin

- Metformin is a medication commonly used to treat type 2 diabetes, and it activates AMPK.

7. What Else Increases AMPK?

Is Vinegar an Effective Treatment for Glycemic Control or Weight Loss?

the US Food and Drug Administration (FDA) has defined the amount of acetic acid for a product to be labeled as vinegar to be 4 g of acetic acid per 100 mL.

the amount of acetic acid for a product to be labeled as vinegar to be 4 g of acetic acid per 100 mL.[5,8]

in pill form, the supplements available to consumers have varied greatly in their "contents and acidity."[9]

low, glycaemic index meal. *Eur J Clin Nutr.* 2010;64(7):727-732.

3. Johnston CS, Steplewska I, Long CA,

Acetic Acid in Vinegar Activates AMPK

AMPK: Regulating Energy Balance at the Cellular and Whole Body Levels

D. Grahame Hardie,
and Michael L. J. Ashford

Division of Cell Signalling & Immunology, College of Life Sciences, and Division of Cardiovascular and Diabetes Medicine, College of Medicine, Dentistry & Nursing, University of Dundee, Dundee, Scotland, United Kingdom

AMP-activated protein kinase appears to have evolved in single-celled eukaryotes as an adenine nucleotide sensor that maintains energy homeostasis at the cellular level. However, during evolution of more complex multicellular organisms, the system has adapted to interact with hormones so that it also plays a key role in balancing energy intake and expenditure at the whole body level.

Although discovered via its ability to phosphorylate and inactivate two enzymes involved in lipid synthesis, i.e., acetyl-CoA carboxylase and HMG-CoA reductase (6, 9, 10), the AMP-activated protein kinase (AMPK) is now recognized to have dozens of downstream targets (23–25, 53) and may turn out to have hundreds. Its principal role is as an energy sensor monitoring the cellular ratios of AMP to ATP

the host cell; this remains one of the key functions of AMPK today.

Genes encoding the α- and γ-subunits of the AMPK ortholog in the yeast *Saccharomyces cerevisiae* (*SNF1* and *SNF4*) were cloned in the 1980s (11, 12), although their relationship with AMPK was not recognized until 1994 (51, 76). If yeast are grown in batch culture in high glucose, they initially grow

Boost AMPK for Energy and Life

1. Fasting and calorie restriction
2. Fiber-rich foods
3. Foods rich in omega-3s
4. Exercise
5. High-antioxidant foods
6. ~~Metformin~~
7. Apple cyder vinegar

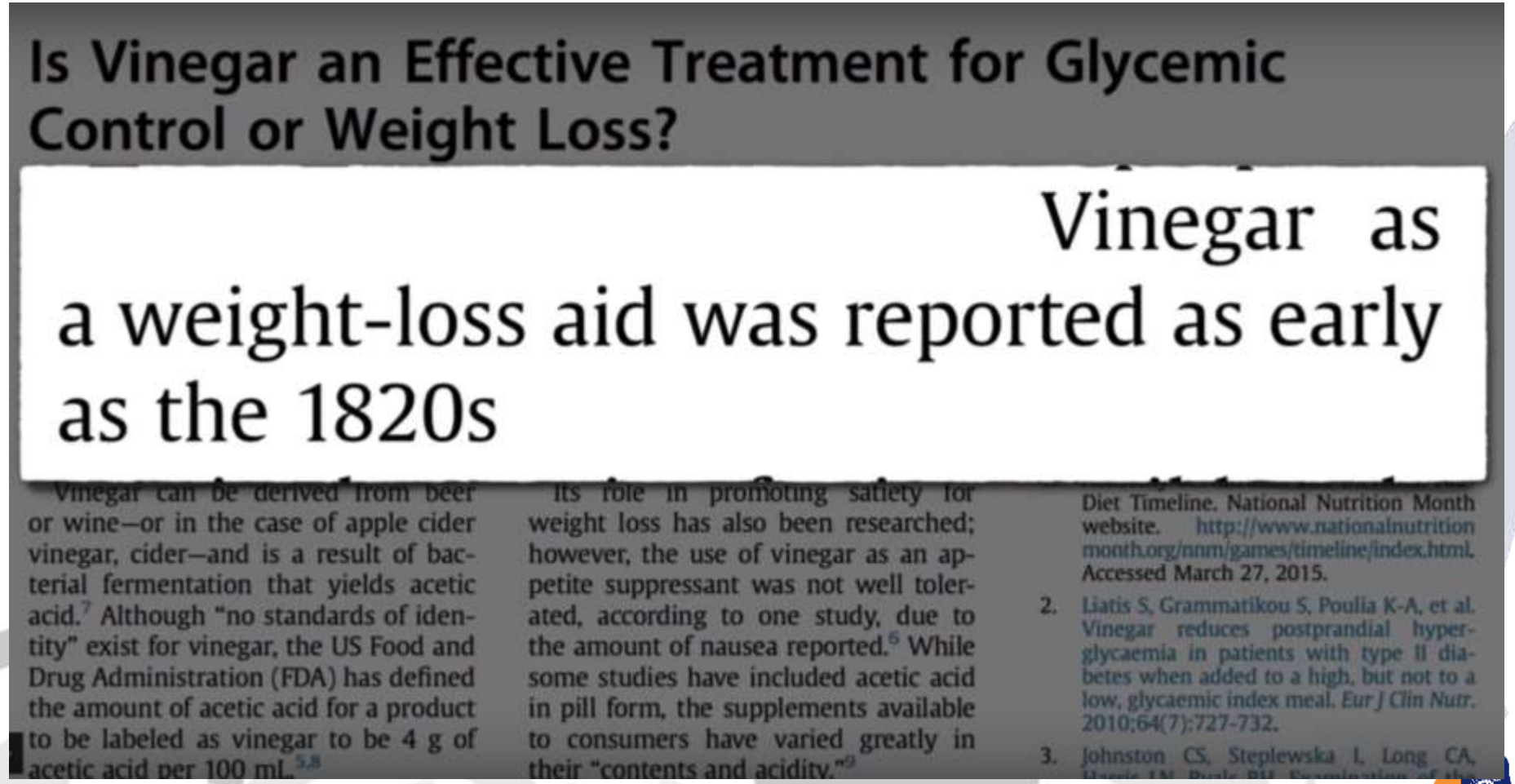
The 7 Systems Plan
7SystemsPlan.com

7 SYSTEMS PLAN

ACV


BRAGG
ORGANIC
RAW ~ UNFILTERED
APPLE CIDER
VINEGAR
With The
'Mother'
UNPASTEURIZED
Naturally Gluten Free
16 FL OZ (1PT) 473 mL
Serving Health Worldwide Since 1912

Reported as Weight-loss Aid Since 1820



Is Vinegar an Effective Treatment for Glycemic Control or Weight Loss?

Vinegar as a weight-loss aid was reported as early as the 1820s

Vinegar can be derived from beer or wine—or in the case of apple cider vinegar, cider—and is a result of bacterial fermentation that yields acetic acid.[7] Although "no standards of identity" exist for vinegar, the US Food and Drug Administration (FDA) has defined the amount of acetic acid for a product to be labeled as vinegar to be 4 g of acetic acid per 100 mL.[5,8]

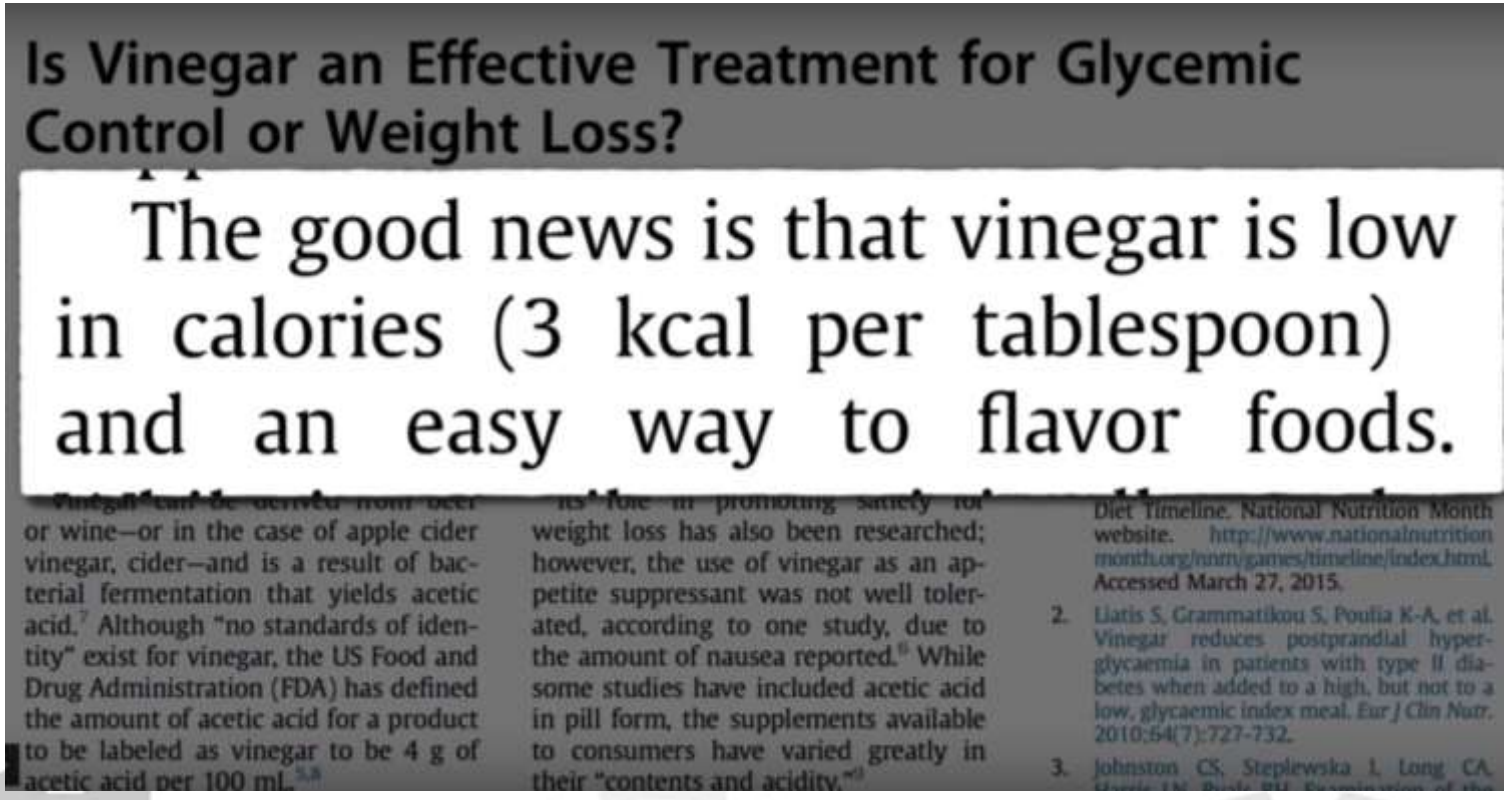
Its role in promoting satiety for weight loss has also been researched; however, the use of vinegar as an appetite suppressant was not well tolerated, according to one study, due to the amount of nausea reported.[6] While some studies have included acetic acid in pill form, the supplements available to consumers have varied greatly in their "contents and acidity."[9]

Diet Timeline. National Nutrition Month website. http://www.nationalnutritionmonth.org/nnm/games/timeline/index.html. Accessed March 27, 2015.

2. Liatis S, Grammatikou S, Poulia K-A, et al. Vinegar reduces postprandial hyperglycaemia in patients with type II diabetes when added to a high, but not to a low, glycaemic index meal. *Eur J Clin Nutr*. 2010;64(7):727-732.

3. Johnston CS, Steplewska I, Long CA,

Only 3 Calories Per Tablespoon



Is Vinegar an Effective Treatment for Glycemic Control or Weight Loss?

The good news is that vinegar is low in calories (3 kcal per tablespoon) and an easy way to flavor foods.

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Diet Timeline. National Nutrition Month website. http://www.nationalnutritionmonth.org/nnm/games/timeline/index.html. Accessed March 27, 2015.

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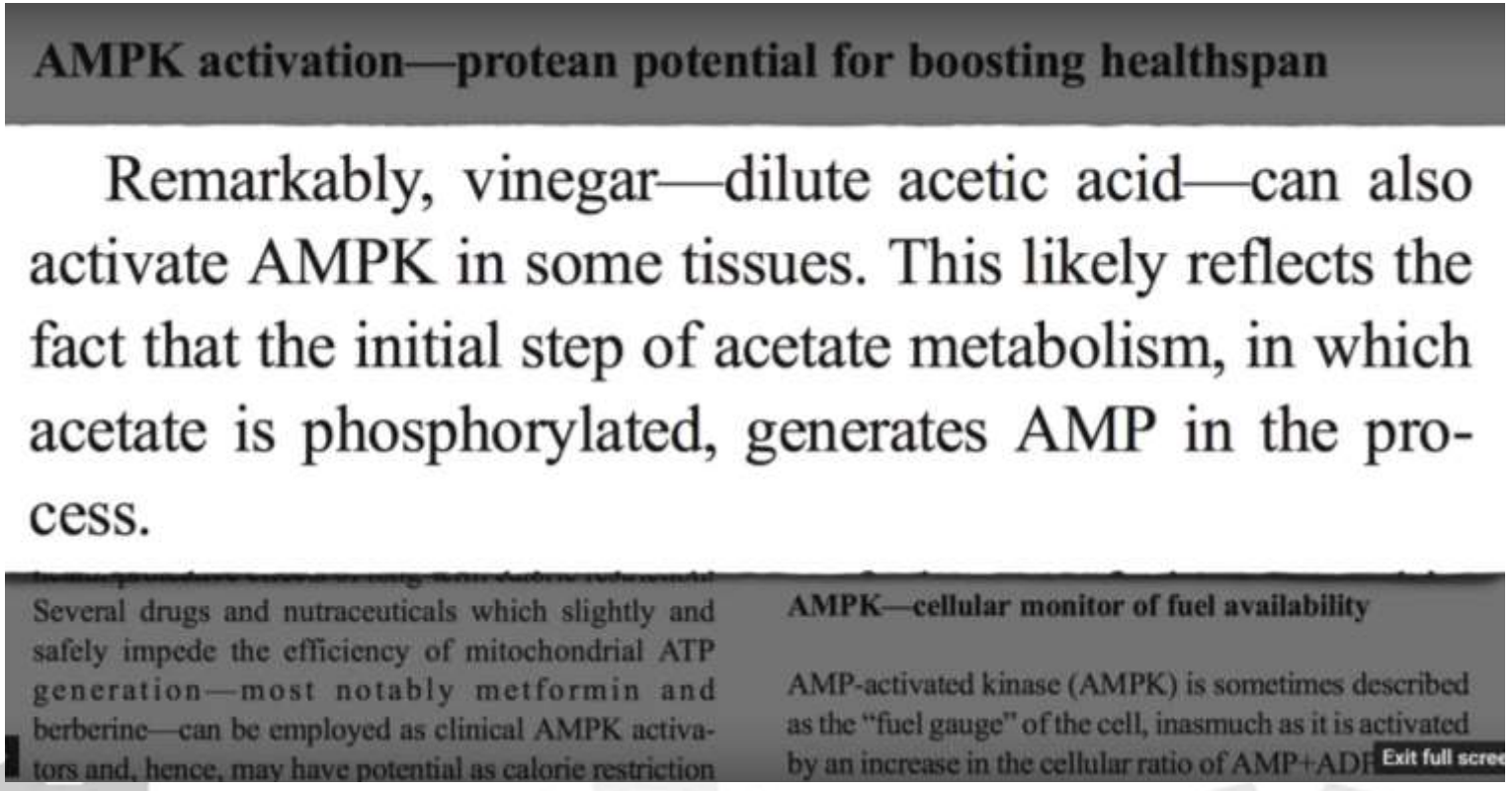
3. Johnston CS, Steplewska I, Long CA,

Vinegar Can Activate AMPK in Human Cells in a Petri Dish



AMPK activation—protean potential for boosting healthspan

Remarkably, vinegar—dilute acetic acid—can also activate AMPK in some tissues. This likely reflects the fact that the initial step of acetate metabolism, in which acetate is phosphorylated, generates AMP in the process.

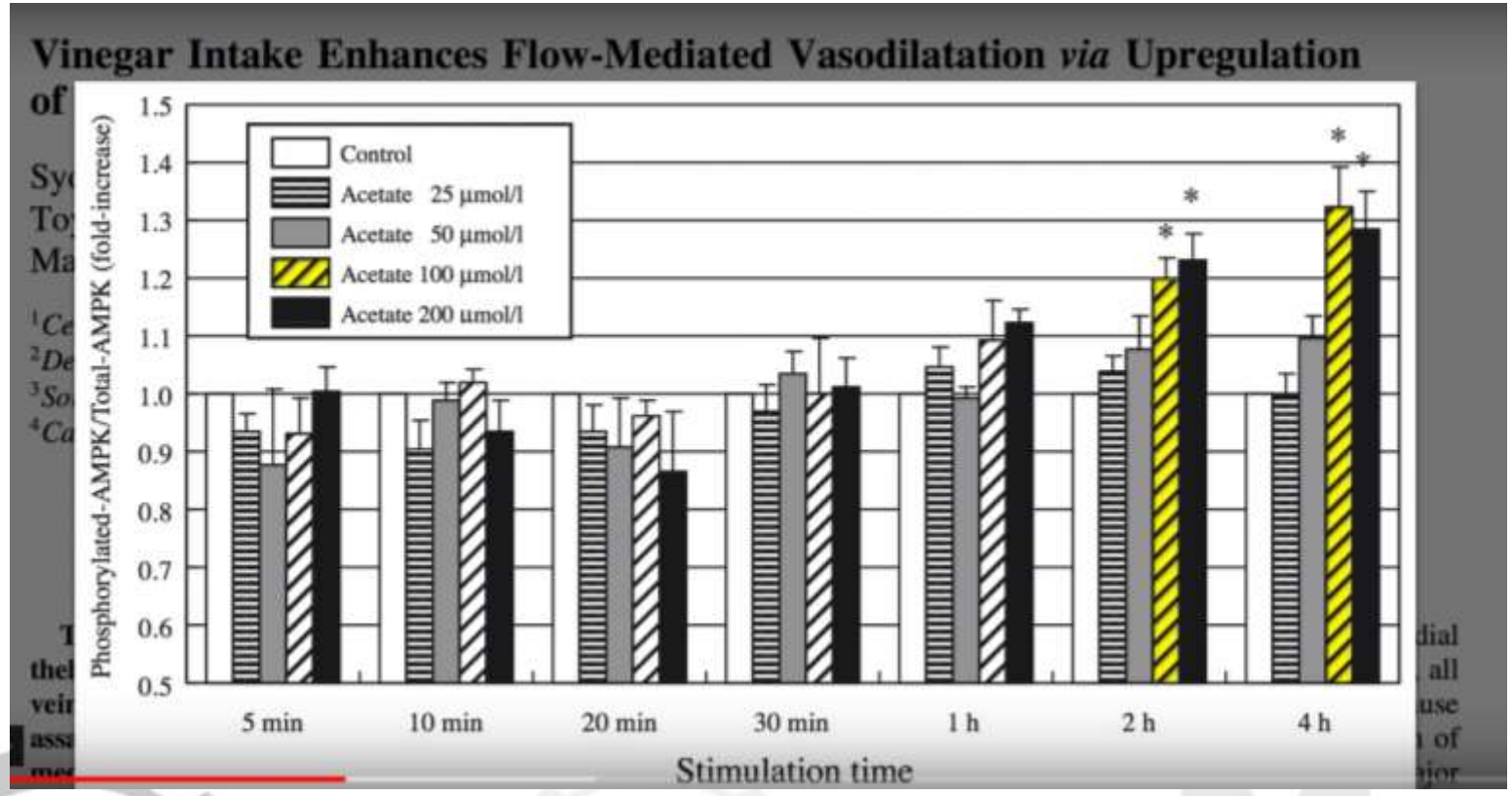
Several drugs and nutraceuticals which slightly and safely impede the efficiency of mitochondrial ATP generation—most notably metformin and berberine—can be employed as clinical AMPK activators and, hence, may have potential as calorie restriction

AMPK—cellular monitor of fuel availability

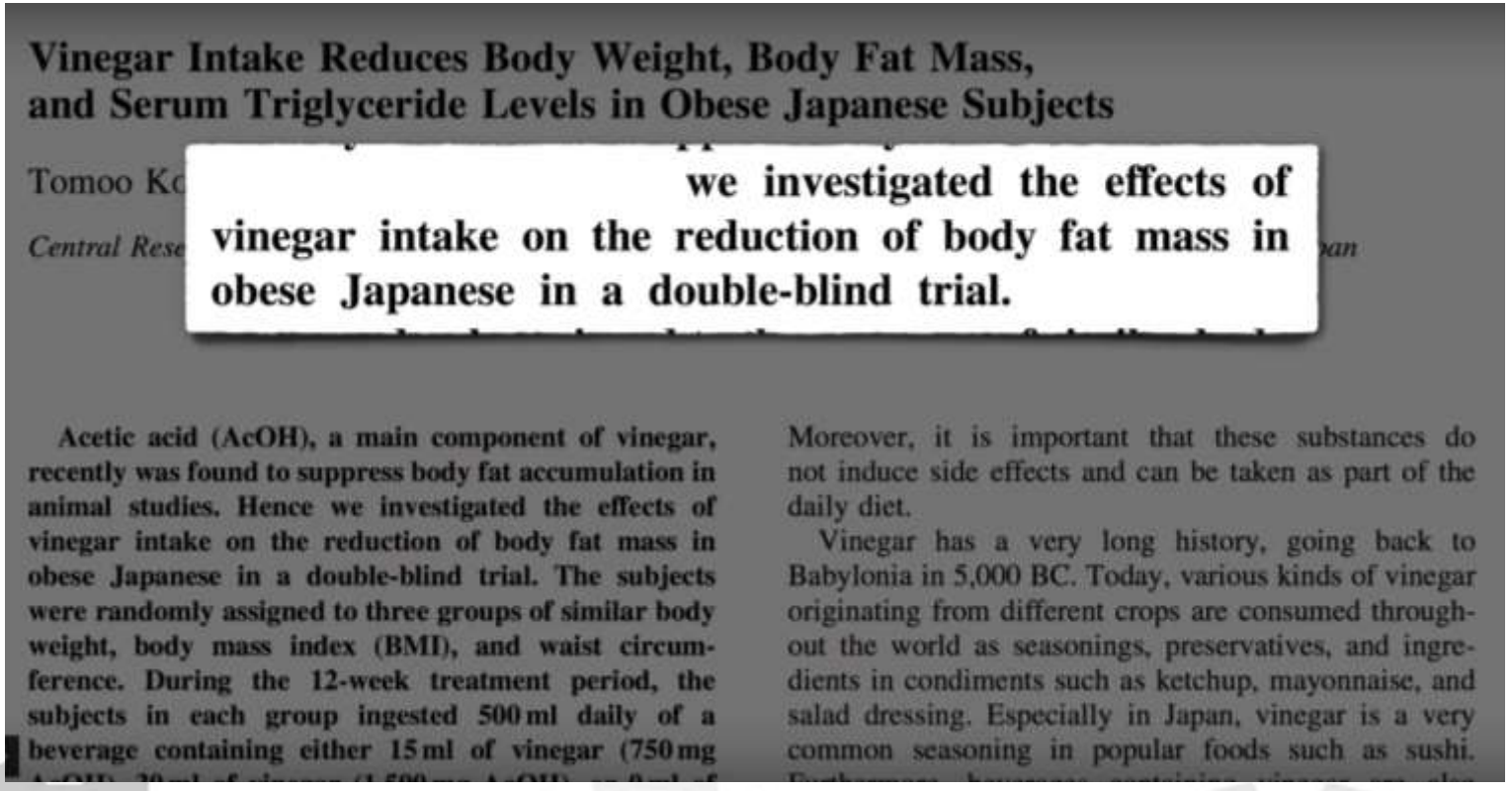
AMP-activated kinase (AMPK) is sometimes described as the "fuel gauge" of the cell, inasmuch as it is activated by an increase in the cellular ratio of AMP+ADP

Exit full scree

A Certain dose is Required to Boost AMPK



How About Inside the Body?



Vinegar Intake Reduces Body Weight, Body Fat Mass, and Serum Triglyceride Levels in Obese Japanese Subjects

Tomoo Ko

Central Rese *pan*

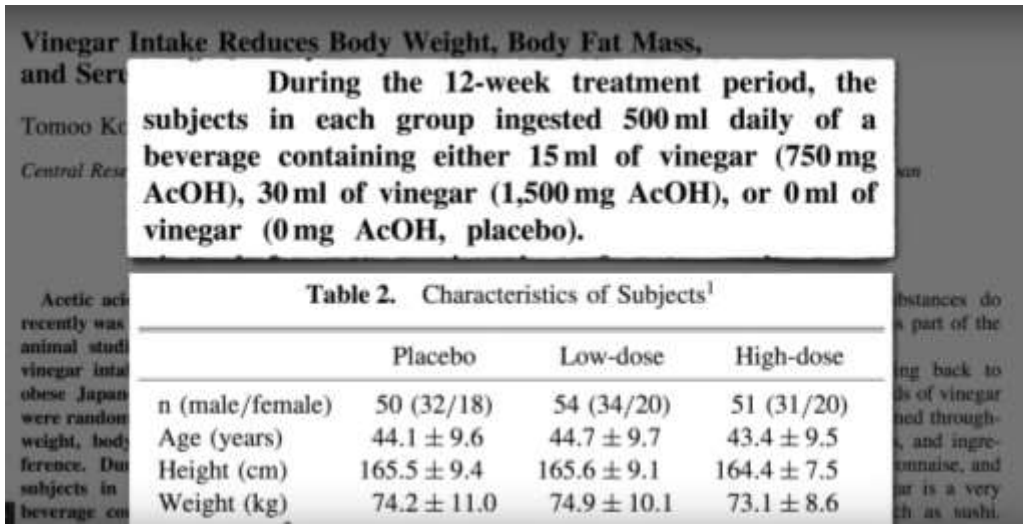
we investigated the effects of vinegar intake on the reduction of body fat mass in obese Japanese in a double-blind trial.

Acetic acid (AcOH), a main component of vinegar, recently was found to suppress body fat accumulation in animal studies. Hence we investigated the effects of vinegar intake on the reduction of body fat mass in obese Japanese in a double-blind trial. The subjects were randomly assigned to three groups of similar body weight, body mass index (BMI), and waist circumference. During the 12-week treatment period, the subjects in each group ingested 500 ml daily of a beverage containing either 15 ml of vinegar (750 mg

Moreover, it is important that these substances do not induce side effects and can be taken as part of the daily diet.

Vinegar has a very long history, going back to Babylonia in 5,000 BC. Today, various kinds of vinegar originating from different crops are consumed throughout the world as seasonings, preservatives, and ingredients in condiments such as ketchup, mayonnaise, and salad dressing. Especially in Japan, vinegar is a very common seasoning in popular foods such as sushi.

3 Groups for 12 Weeks



Vinegar Intake Reduces Body Weight, Body Fat Mass,
and Seru

Tomoo Ko

Central Resa

During the 12-week treatment period, the subjects in each group ingested 500 ml daily of a beverage containing either 15 ml of vinegar (750 mg AcOH), 30 ml of vinegar (1,500 mg AcOH), or 0 ml of vinegar (0 mg AcOH, placebo).

Table 2. Characteristics of Subjects[1]

	Placebo	Low-dose	High-dose
n (male/female)	50 (32/18)	54 (34/20)	51 (31/20)
Age (years)	44.1 ± 9.6	44.7 ± 9.7	43.4 ± 9.5
Height (cm)	165.5 ± 9.4	165.6 ± 9.1	164.4 ± 7.5
Weight (kg)	74.2 ± 11.0	74.9 ± 10.1	73.1 ± 8.6

1. No vinegar
2. Low dose 1T per day
3. High dose 2 T per day

SYSTEMS PLAN

Ate the Same Calories

Vinegar Intake Reduces Body Weight, Body Fat Mass, and Serum Triglyceride Levels in Obese Japanese Subjects

Table 3. Daily Intake of Energy

	Treatment period			
	week 0	week 4	week 8	week 12
Energy (kJ/d)[2]				
Placebo	7393 ± 1536	7435 ± 1318	7343 ± 1368	7351 ± 1226
Low-dose	7774 ± 1356	7531 ± 1247	7627 ± 1230	7577 ± 1209
High-dose	7895 ± 1414	7753 ± 1284	7661 ± 1247	7740 ± 1234

vinegar intake on the reduction of body fat mass in obese Japanese in a double-blind trial. The subjects were randomly assigned to three groups of similar body weight, body mass index (BMI), and waist circumference. During the 12-week treatment period, the subjects in each group ingested 500 ml daily of a beverage containing either 15 ml of vinegar (750 mg

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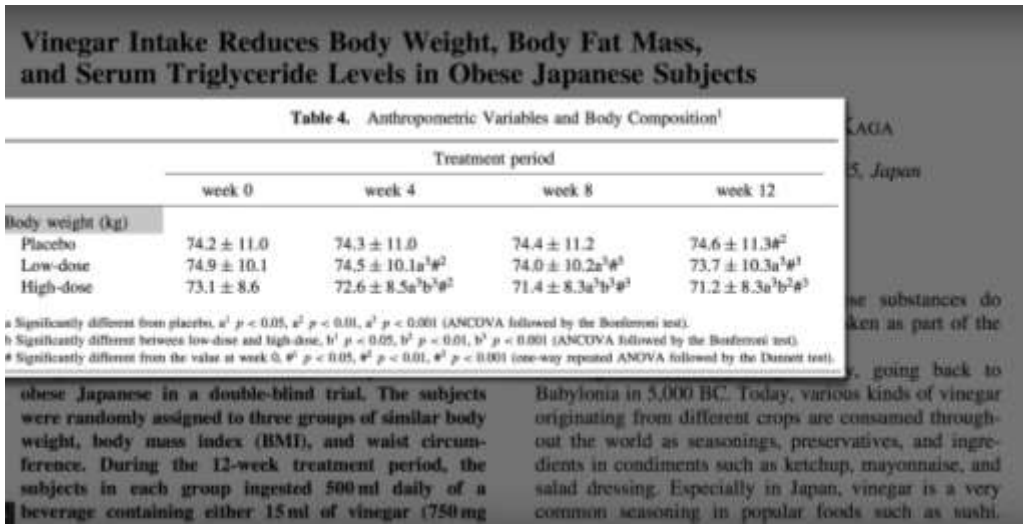
Results?



Vinegar Intake Reduces Body Weight, Body Fat Mass, and Serum Triglyceride Levels in Obese Japanese Subjects

Table 4. Anthropometric Variables and Body Composition[1]

	Treatment period			
	week 0	week 4	week 8	week 12
Body weight (kg)				
Placebo	74.2 ± 11.0	74.3 ± 11.0	74.4 ± 11.2	74.6 ± 11.3#[2]
Low-dose	74.9 ± 10.1	74.5 ± 10.1a[1]#[2]	74.0 ± 10.2a[2]#[3]	73.7 ± 10.3a[2]#[3]
High-dose	73.1 ± 8.6	72.6 ± 8.5a[2]b[2]#[2]	71.4 ± 8.3a[2]b[2]#[2]	71.2 ± 8.3a[2]b[2]#[3]

a Significantly different from placebo, a[1] $p < 0.05$, a[2] $p < 0.01$, a[3] $p < 0.001$ (ANCOVA followed by the Bonferroni test).
b Significantly different between low-dose and high-dose, b[1] $p < 0.05$, b[2] $p < 0.01$, b[3] $p < 0.001$ (ANCOVA followed by the Bonferroni test).
Significantly different from the value at week 0, #[1] $p < 0.05$, #[2] $p < 0.01$, #[3] $p < 0.001$ (one-way repeated ANOVA followed by the Dunnett test).

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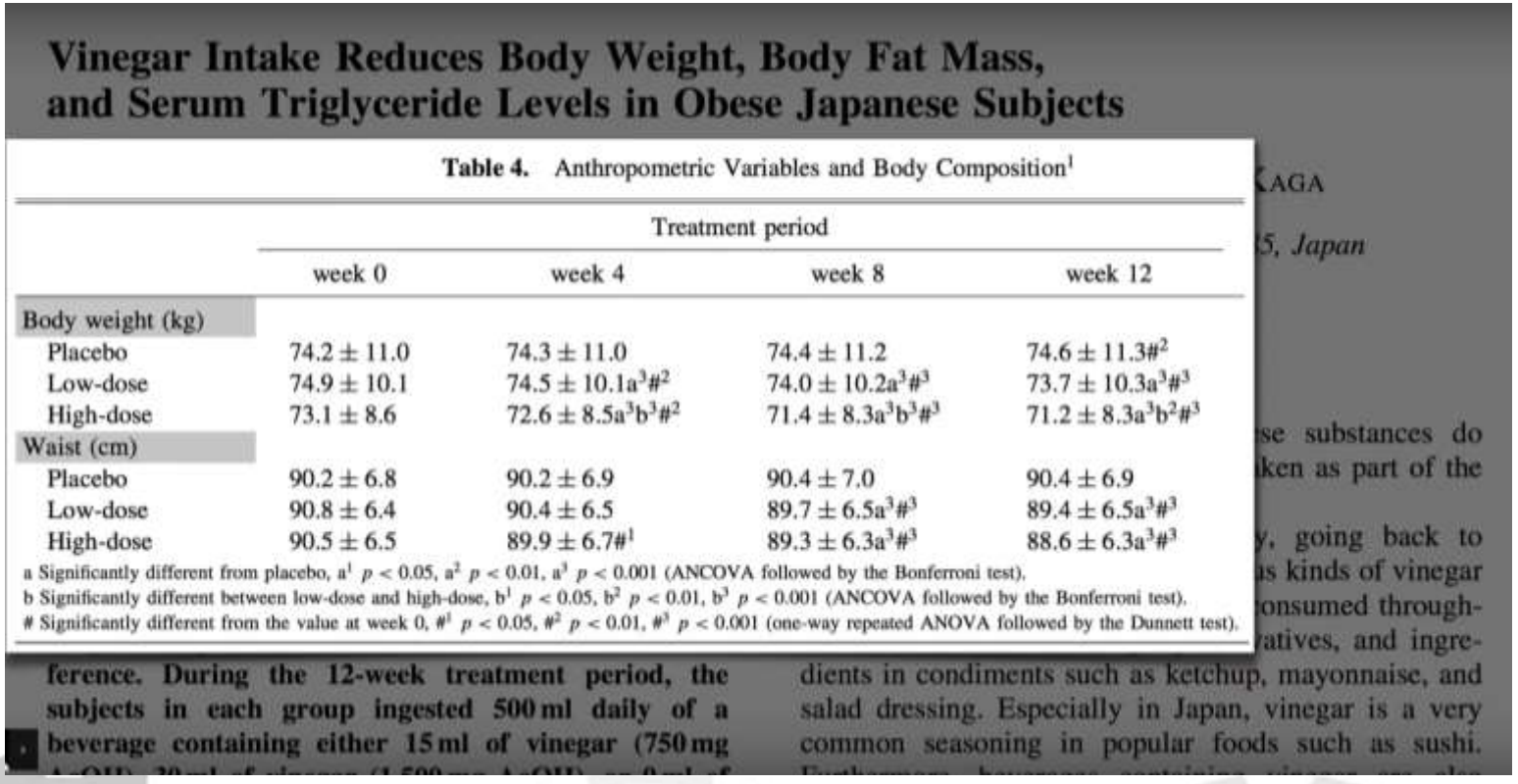
Babylonia in 5,000 BC. Today, various kinds of vinegar originating from different crops are consumed throughout the world as seasonings, preservatives, and ingredients in condiments such as ketchup, mayonnaise, and salad dressing. Especially in Japan, vinegar is a very common seasoning in popular foods such as sushi.

1. Control gained weight
2. 1T lost weight
3. 2T dose dropped 5 pounds in 12 weeks

7 SYSTEMS PLAN

Also Slimmer
Lost 1 Inch off Waist



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High-dose	73.1 ± 8.6	72.6 ± 8.5a^{3}b^{3}#^{2}	71.4 ± 8.3a^{3}b^{3}#^{3}	71.2 ± 8.3a^{3}b^{2}#^{3}
Waist (cm)				
Placebo	90.2 ± 6.8	90.2 ± 6.9	90.4 ± 7.0	90.4 ± 6.9
Low-dose	90.8 ± 6.4	90.4 ± 6.5	89.7 ± 6.5a^{3}#^{3}	89.4 ± 6.5a^{3}#^{3}
High-dose	90.5 ± 6.5	89.9 ± 6.7#^{1}	89.3 ± 6.3a^{3}#^{3}	88.6 ± 6.3a^{3}#^{3}

a Significantly different from placebo, a^{1} $p < 0.05$, a^{2} $p < 0.01$, a^{3} $p < 0.001$ (ANCOVA followed by the Bonferroni test).
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Significantly different from the value at week 0, #^{1} $p < 0.05$, #^{2} $p < 0.01$, #^{3} $p < 0.001$ (one-way repeated ANOVA followed by the Dunnett test).

ference. During the 12-week treatment period, the subjects in each group ingested 500 ml daily of a beverage containing either 15 ml of vinegar (750 mg

dients in condiments such as ketchup, mayonnaise, and salad dressing. Especially in Japan, vinegar is a very common seasoning in popular foods such as sushi.

SYSTEMS PLAN

Low Dose and High Dose Lost 1 Square Inch of Visceral Fat

Vinegar Intake Reduces Body Weight, Body Fat Mass, and Serum Triglyceride Levels in Obese Japanese Subjects

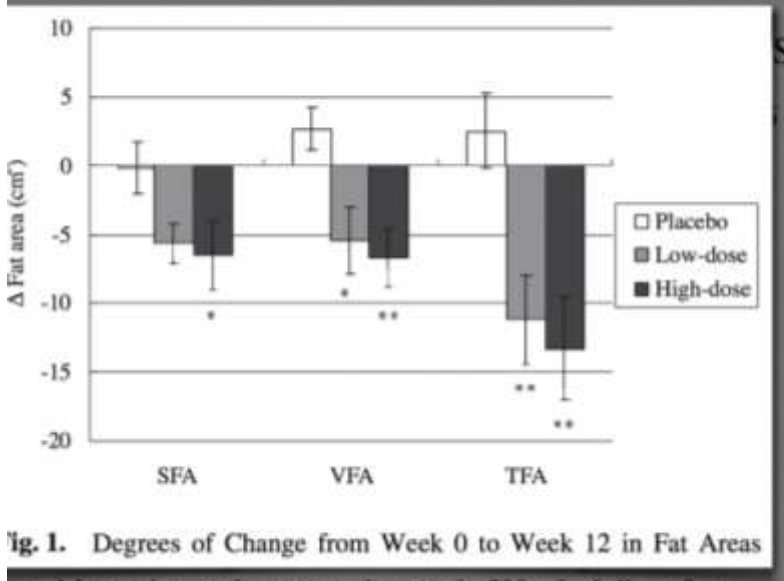
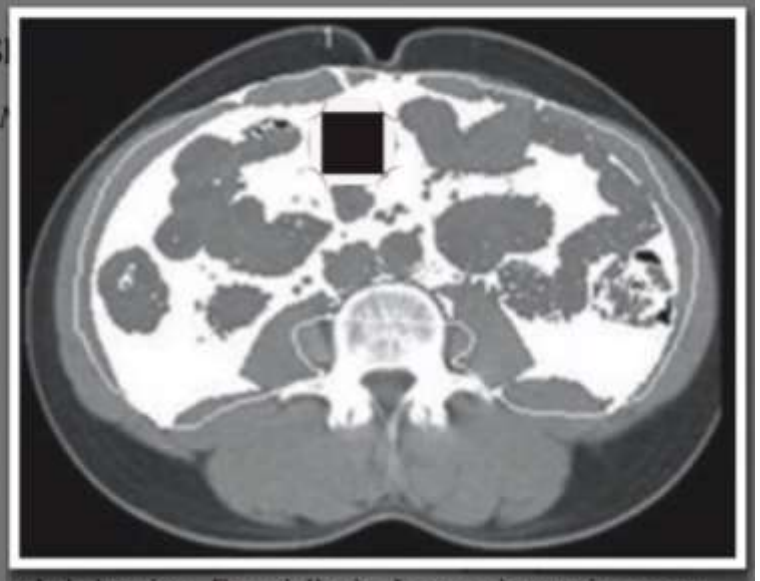


Fig. 1. Degrees of Change from Week 0 to Week 12 in Fat Areas



subjects in each group ingested 500 ml daily of a beverage containing either 15 ml of vinegar (750 mg

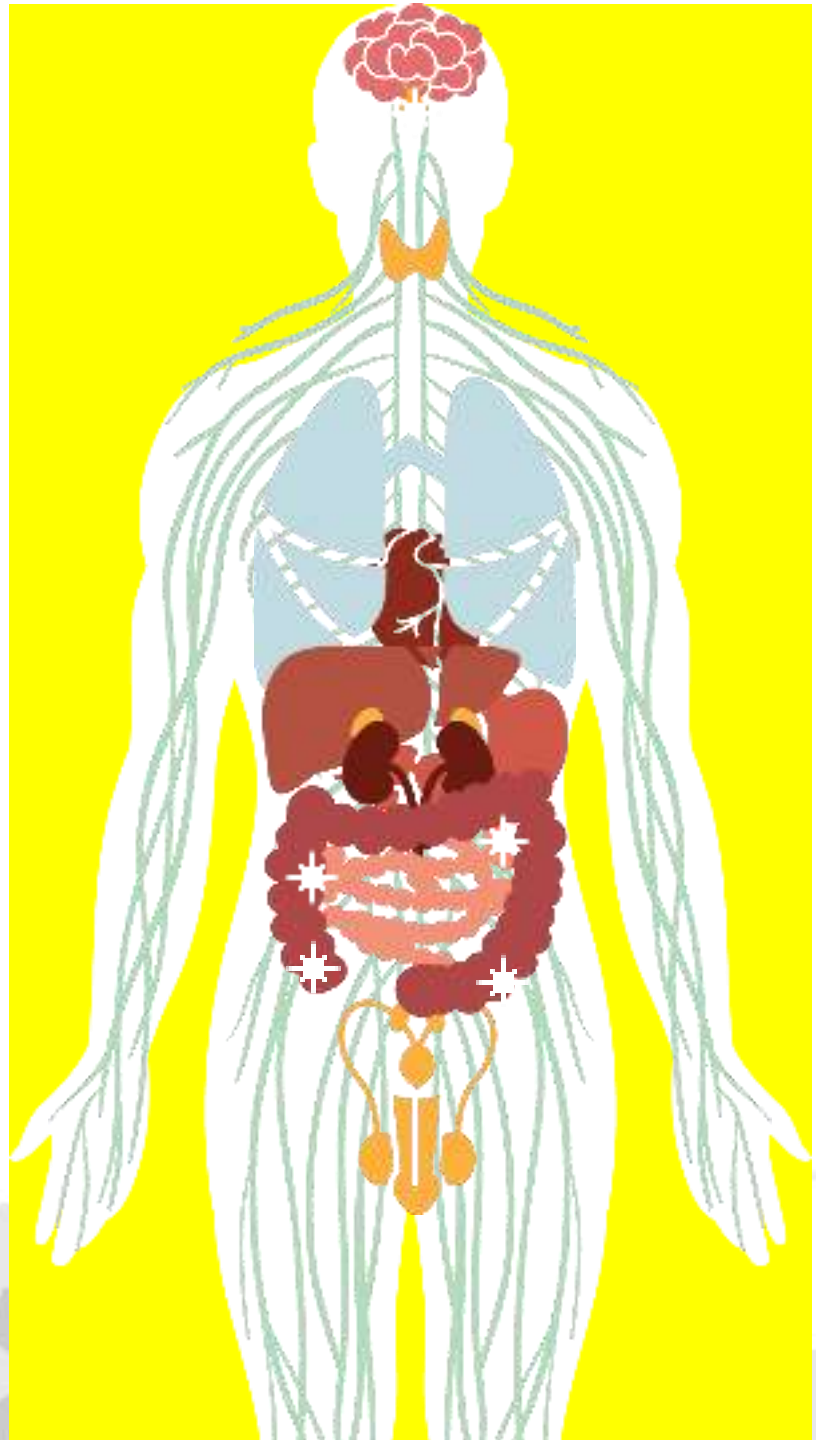
salad dressing. Especially in Japan, vinegar is a very common seasoning in popular foods such as sushi.

Use Apple Cider Vinegar

- Use 2 T of apple cider vinegar per day
- Or put on your salad
- Dilute in 6 oz of water

7 SYSTEMS PLAN

Communication System



1. Hormones- 50
2. Nerves- 100 B neurons
3. Neurotransmitters- 100

7 SYSTEMS PLAN

FGF21 a Systemic Enhancer of Longevity

5 Ways to Boost FGF21

Fibroblast Growth Factor 21 (FGF21)

- A hormone that regulates important metabolic pathways
- FGF21 can:
  - regulate carbohydrate and fat metabolism
  - maintain energy during fasting
  - **increase weight loss**
  - **improve cellular aging**

Cellular Signalling 40 (2017) 10–21

Contents lists available at ScienceDirect

Cellular Signalling

journal homepage: www.elsevier.com/locate/cellsig

Review

Integrated stress response stimulates FGF21 expression: Systemic enhancer of longevity

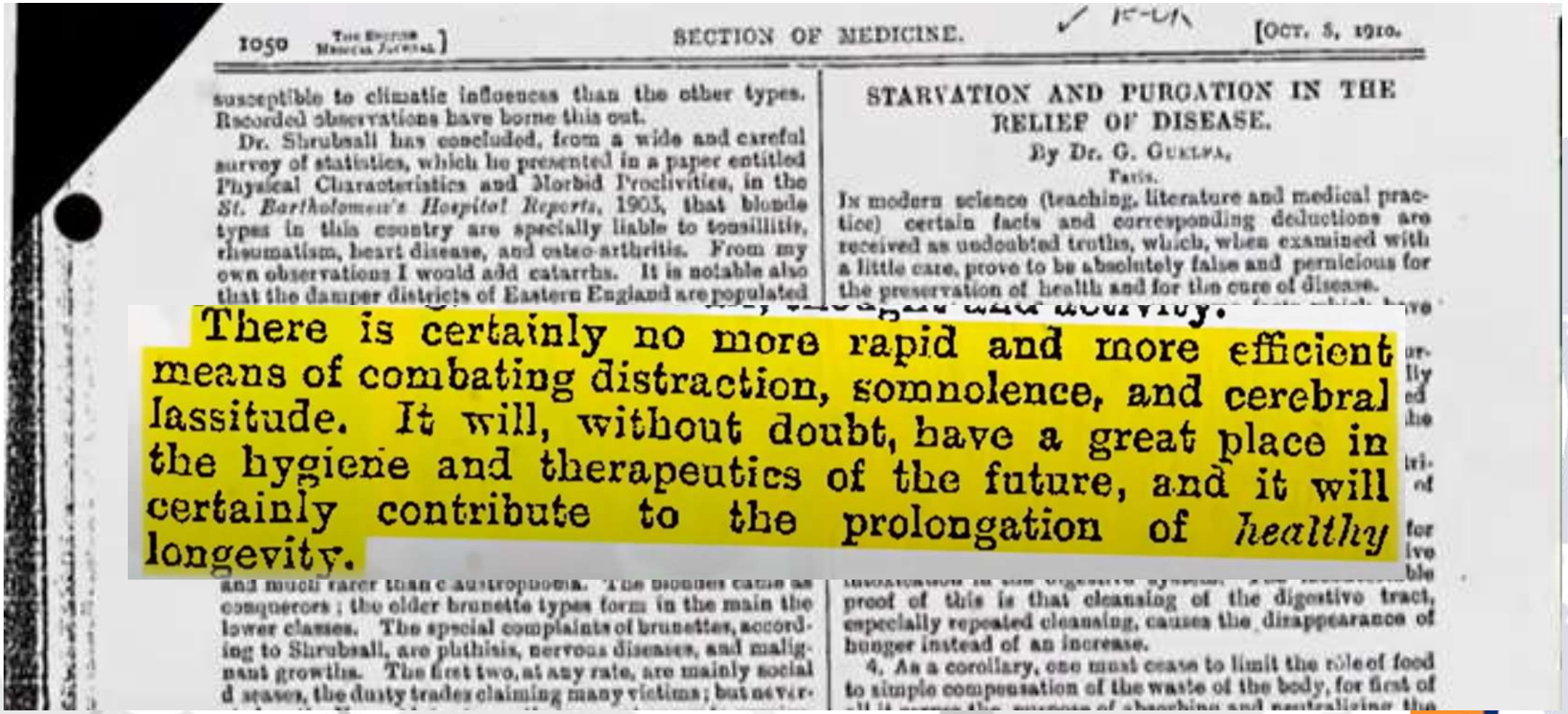
Antero Salminen[a,*], Kai Kaarniranta[b,c], Anu Kauppinen[d]

[a] Department of Neurology, Institute of Clinical Medicine, University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland
[b] Department of Ophthalmology, Institute of Clinical Medicine, University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland
[c] Department of Ophthalmology, Kuopio University Hospital, P.O. Box 100, FI-70029, KYS, Finland
[d] School of Pharmacy, Faculty of Health Sciences, University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland

ARTICLE INFO

ABSTRACT

1. Fasting



1050 [THE BRITISH MEDICAL JOURNAL] SECTION OF MEDICINE. [OCT. 5, 1910.

susceptible to climatic influences than the other types. Recorded observations have borne this out.

Dr. Shrubsall has concluded, from a wide and careful survey of statistics, which he presented in a paper entitled Physical Characteristics and Morbid Proclivities, in the *St. Bartholomew's Hospital Reports*, 1903, that blonde types in this country are specially liable to tonsillitis, rheumatism, heart disease, and osteo-arthritis. From my own observations I would add catarrhs. It is notable also that the damper districts of Eastern England are populated

STARVATION AND PURGATION IN THE RELIEF OF DISEASE.

By Dr. G. GUELPA,

Paris.

IN modern science (teaching, literature and medical practice) certain facts and corresponding deductions are received as undoubted truths, which, when examined with a little care, prove to be absolutely false and pernicious for the preservation of health and for the cure of disease.

There is certainly no more rapid and more efficient means of combating distraction, somnolence, and cerebral lassitude. It will, without doubt, have a great place in the hygiene and therapeutics of the future, and it will certainly contribute to the prolongation of *healthy* longevity.

and much rarer than c austropoeia. The blonder cattle as conquerors; the older brunette types form in the main the lower classes. The special complaints of brunettes, according to Shrubsall, are phthisis, nervous diseases, and malignant growths. The first two, at any rate, are mainly social d seases, the dusty trades claiming many victims; but never-

proof of this is that cleansing of the digestive tract, especially repeated cleansing, causes the disappearance of hunger instead of an increase.

4. As a corollary, one must cease to limit the role of food to simple compensation of the waste of the body, for first of

Cell Metabolism
Previews

FGF21: A Missing Link in the Biology of Fasting

Marc L. Reitman[1,*]
[1] Department of Metabolic Disorders, Merck Research Laboratories, Rahway, NJ 07065, USA
*Correspondence: marc_reitman@merck.com
DOI 10.1016/j.cmet.2007.05.010

A sufficient energy supply is essential for life; consequently, multiple mechanisms have evolved to ensure both energy availability and conservation during fasting and starvation. Two reports in this issue of *Cell Metabolism* (**Badman et al., 2007; Inagaki et al., 2007**) demonstrate that FGF21, a circulating protein produced in the liver in response to the PPARα transcription factor, is a "missing link" in the biology of fasting, inducing adipose tissue lipolysis, liver ketogenesis, and metabolic adaptation to the fasting state.

Biology of Fasting

The adaptation from the fed to fasted

occurs, sending alanine to the liver as another substrate for gluconeogenesis

further metabolism). Metabolic substrate G protein-coupled receptors

2. Cold Exposure Increases FGF21

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

ENDOCRINE SOCIETY

Volume 98, Issue 1
1 January 2013

Article Contents

JOURNAL ARTICLE

Mild Cold Exposure Modulates Fibroblast Growth Factor 21 (FGF21) Diurnal Rhythm in Humans: Relationship between FGF21 Levels, Lipolysis, and Cold-Induced Thermogenesis FREE

Paul Lee ✉, Robert J. Brychta, Joyce Linderman, Sheila Smith, Kong Y. Chen, Francesco S. Celi

The Journal of Clinical Endocrinology & Metabolism, Volume 98, Issue 1, 1 January 2013, Pages E98–E102, https://doi.org/10.1210/jc.2012-3107

7 SYSTEMS PLAN

7 Benefits of Cold Exposure (cold shower)

- 1. Bolster your immunity to common colds
- 2. Combat symptoms of depression
- 3. Improve circulation
- 4. Increase metabolism
- 5. Reduce inflammation and prevent muscle soreness
- 6. Relieve localized pain
- **7. Increase FGF21**

FGF21 and the late adaptive response to starvation in humans

Pouneh K. F
Ciprian Cata
[1]Department of Me
Division of Genetic
[2]Athinoula A. Mart
Division of Cardiov
t of Medicine,
Massachusetts, USA.

and physiologic function of FGF21 in the starved state. While the induction of FGF21 in this human study required the fairly dramatic stimulus of prolonged and complete calorie abstinence, other studies have found evidence for FGF21 release in response to more narrow nutritional interventions, such as with acute carbohydrate administration (44) or prolonged protein restriction

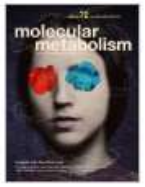
In mice, FGF21 is rapidly induced by fasting, mediates critical aspects of the adaptive starvation response, and displays a number of positive metabolic properties when administered pharmacologically. In humans, however, fasting does not consistently increase FGF21, suggesting a possible evolutionary divergence in FGF21 function. Moreover, many key aspects of FGF21 function in mice have been identified in the context of transgenic overexpression or administration of supraphysiologic doses, rather than in a physiologic setting. Here, we explored the dynamics and function of FGF21 in human volunteers

3. High Carbohydrate Diet

ELSEVIER

Molecular Metabolism

Volume 72, June 2023, 101718



Original Article

Fibroblast growth factor-21 is required for weight loss induced by the glucagon-like peptide-1 receptor agonist liraglutide in male mice fed high carbohydrate diets

Thao D.V. Le [1], Payam Fathi [1], Amanda B. Watters [1 9], Blair J. Ellis [1], Gai-Linn K. Besing [1], Nadejda Bozadjieva-Kramer [2 3], Misty B. Perez [4], Andrew I. Sullivan [4], Jesse P. Rose [4], Laurie L. Baggio [5], Jacqueline Koehler [5], Jennifer L. Brown [6], Michelle B. Bales [1 10], Kaitlyn G. Nwaba [1], Jonathan E. Campbell [6], Daniel J. Drucker [5], Matthew J. Potthoff [4], Randy J. Seeley [2], Julio E. Ayala [1 7 8]

Show more

SYSTEMS PLAN

Brief Communication

MOLECULAR METABOLISM

Circulating FGF21 in humans is potently induced by short term overfeeding of carbohydrates

Ann
Jer

ingested them at home. The CHO diet consisted of carbohydrate-rich food items as bread, pasta, cereals, corn, jam, and juice, with high to moderate glycemic index. The diet was mainly comprised of polysaccharides, with 19% refined sugar and the ratio between glucose and fructose was 1:1 (Supplemental Table S3 and S4). In the FAT diet,

ABS

Obj hown to increase circulating FGF21 levels. However, when energy contribution from dietary protein is lowered, other macronutrients, such as carbohydrates, must be increased to meet eucaloric balance. This raises the possibility that intake of a diet rich in carbohydrates may induce an increase in plasma FGF21 levels per se. Here we studied the role of dietary carbohydrates on the levels of circulating FGF21 and concomitant

Brief Communication

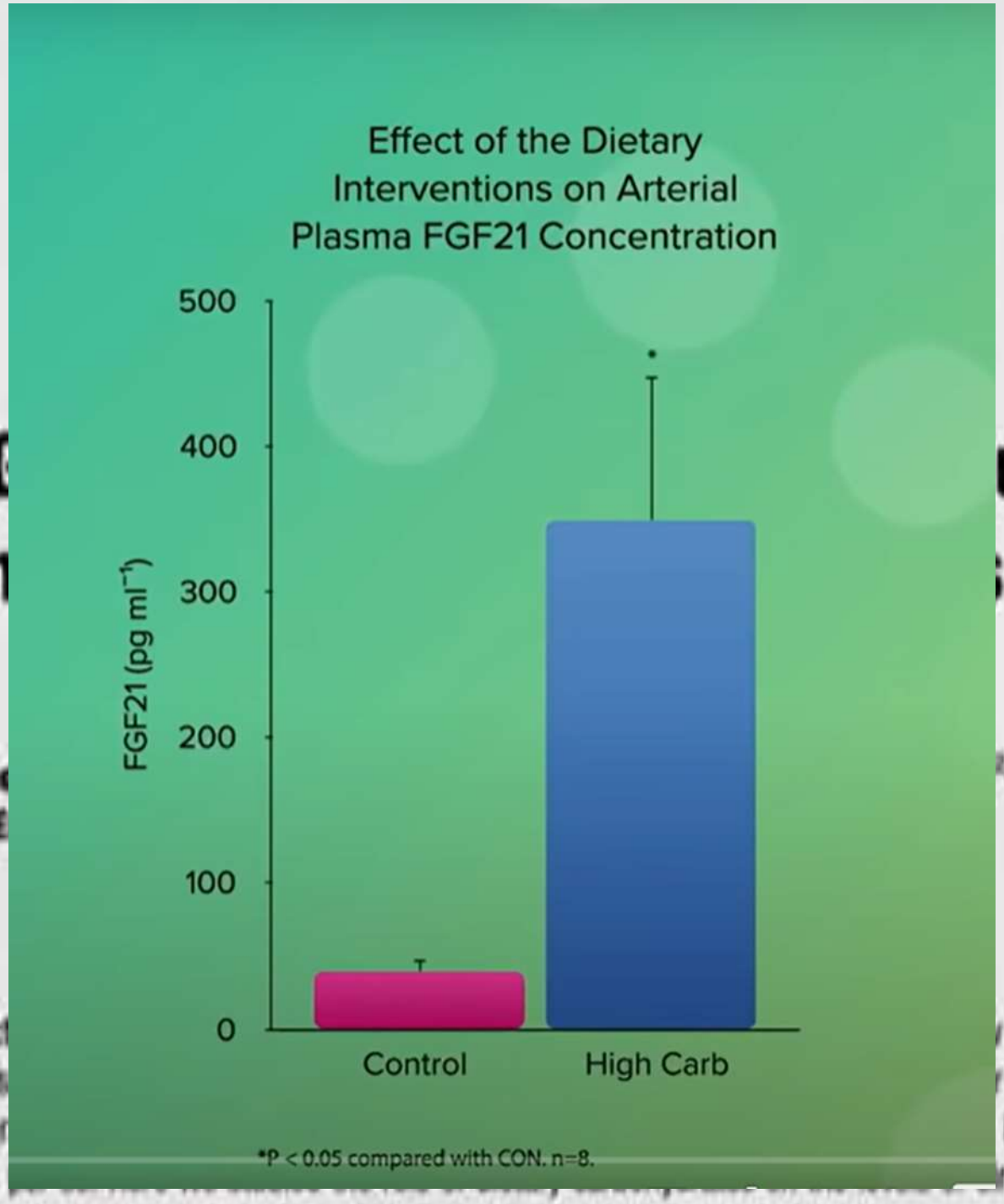
MOLECULAR METABOLISM

Circulating FG… …uced by short term…

Anne-Marie Lundsgaard [1], An… [2,3], Jørgen F.P. Wojtaszewski [1], E…

ABSTRACT

Objective: Fibroblast-growth fact… …protein diets have been shown to increase circulating FGF21 levels… …macronutrients, such as carbohydrates, must be increased to … …in carbohydrates may induce an increase in plasma FGF21 levels … …culating FGF21 and concomitant



4. Butyrate

ORIGINAL ARTICLE

Sodium Butyrate Stimulates Expression of Fibroblast Growth Factor 21 in Liver by Inhibition of Histone Deacetylase 3

Huating Li,[1,2] Zhanguo Gao,[3] Jin Zhang,[3] Xin Ye,[3] Aimin Xu,[4,5] Jianping Ye,[3] and Weiping Jia[1]

Our study suggests that butyrate is a new inducer of FGF21. FGF21 is a cytokine/hormone that stimulates use

we investigated the role of FGF21 in the metabolic activity of sodium butyrate, a dietary histone deacetylase (HDAC) inhibitor. FGF21 expression was examined in serum and liver after injection of sodium butyrate into dietary obese C57BL/6J mice. The role of FGF21 was determined using antibody neutralization or knockout mice. FGF21 transcription was investigated in liver and HepG2 hepatocytes. Trichostatin A (TSA) was used in the control as an HDAC inhibitor. Butyrate was compared with bezafibrate and fenofibrate in the induction of FGF21 expression. Butyrate induced FGF21 in the serum, enhanced fatty acid oxidation in mice, and stimulated ketone body production in liver. The butyrate activity was significantly reduced by the FGF21 antibody or gene knockout. Butyrate induced FGF21 gene expression in liver and hepatocytes by inhibiting HDAC3, which suppresses peroxisome proliferator–activated receptor-α function. Butyrate enhanced bezafibrate activity in the induction of

also leads to glucose reduction in genetic and dietary obese mice (3,6). The physiological role of FGF21 remains to be investigated in humans. Several recent studies show that serum FGF21 levels are elevated in patients of metabolic syndrome (7–10). We reported that serum FGF21 was positively associated with the degree of nonalcoholic fatty liver disease in humans (11). FGF21 resistance may contribute to the association of FGF21 and nonalcoholic fatty liver disease (12,13).

Although FGF21 has beneficial activities in the regulation of lipid metabolism, application of FGF21 is limited by the route of FGF21 administration. Induction of FGF21 expression will be a feasible approach to enhance FGF21 activity in vivo. FGF21 expression is controlled at the transcriptional level by peroxisome proliferator–activated

SYSTEMS PLAN

Review

Anjeza Erickson and Régis Moreau*

The regulation of *FGF21* gene expression by metabolic factors and nutrients

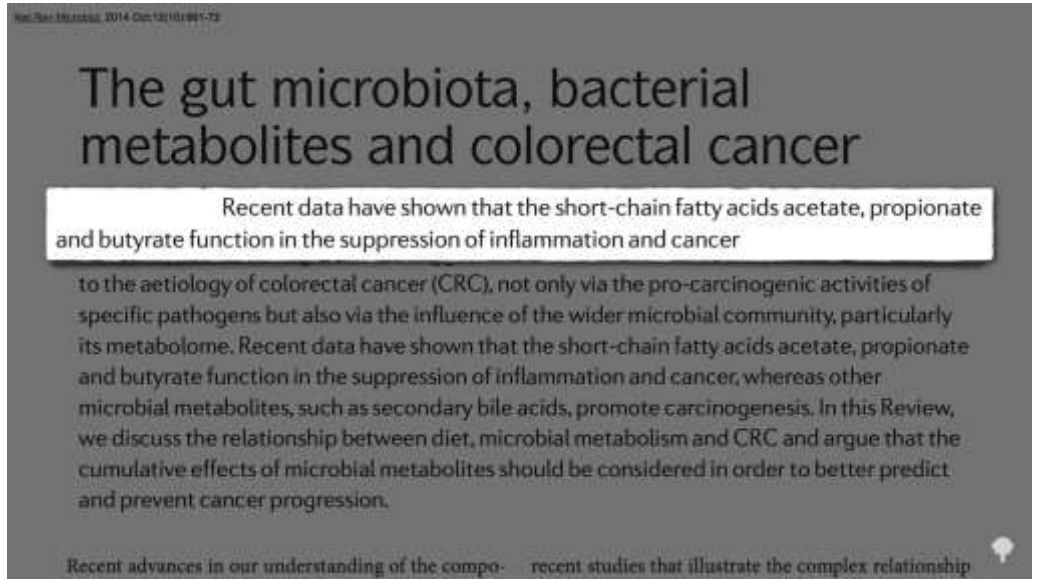
Butyric acid is a short-chain fatty acid produced in large quantities by bacterial fermentation of dietary fiber in the large intestine. Many of butyrate's mechanisms of action

and environmental factors. Among dietary factors, high dextrose, low protein, methionine restriction, short-chain fatty acids (butyric acid and lipoic acid), and all-*trans*-retinoic acid were repeatedly shown to induce *FGF21* expression and circulating levels. These effects are usually more pronounced in liver or isolated hepatocytes than in

Introduction

The importance of diet and nutrition in the etiology of a number of diseases affecting morbidity and mortality is well recognized. However, the exact nature of how diet

Short-chain Fatty Acids Produced by Bacteria



The gut microbiota, bacterial metabolites and colorectal cancer

Recent data have shown that the short-chain fatty acids acetate, propionate and butyrate function in the suppression of inflammation and cancer

to the aetiology of colorectal cancer (CRC), not only via the pro-carcinogenic activities of specific pathogens but also via the influence of the wider microbial community, particularly its metabolome. Recent data have shown that the short-chain fatty acids acetate, propionate and butyrate function in the suppression of inflammation and cancer, whereas other microbial metabolites, such as secondary bile acids, promote carcinogenesis. In this Review, we discuss the relationship between diet, microbial metabolism and CRC and argue that the cumulative effects of microbial metabolites should be considered in order to better predict and prevent cancer progression.

Recent advances in our understanding of the compo- recent studies that illustrate the complex relationship

- Suppress inflammation
- Suppress cancer
- Boost FGF21

SYSTEMS PLAN

5. Low Protein Diets

Cell Metabolism
Review

Cell PRESS

Fasting: Molecular Mechanisms and (

Valter D. Lo
[1]Longevity In
CA 90089-25
[2]National Ins
[3]Department
*Correspond
http://dx.doi

is overcome. Notably, the various fasting approaches are likely to have limited efficacy, particularly on aging and conditions other than obesity, unless combined with high-nourishment diets such as the moderate calorie intake and mostly plant-based Mediterranean or Okinawa low-protein diets (0.8 g protein/kg of body weight), consistently associated with health and longevity.

ornia, Los Angeles,
SA

Fasting has been practiced for millennia, but, only recently, studies have shed light on its role in adaptive cellular responses that reduce oxidative damage and inflammation, optimize energy metabolism, and bolster

The Journal of Clinical Investigation RESEARCH ARTICLE

FGF21 is an endocrine signal of protein restriction

Thomas Laeger,[1] Tara M. Henagan,[1] Diana C. Albarado,[1] Leanne M. Redman,[1] George A. Bray,[1] Robert C. Noland,[1] Heike Münzberg,[1] Susan M. Hutson,[2] Thomas W. Gettys,[1] Michael W. Schwartz,[3] and Christopher D. Morrison[1]

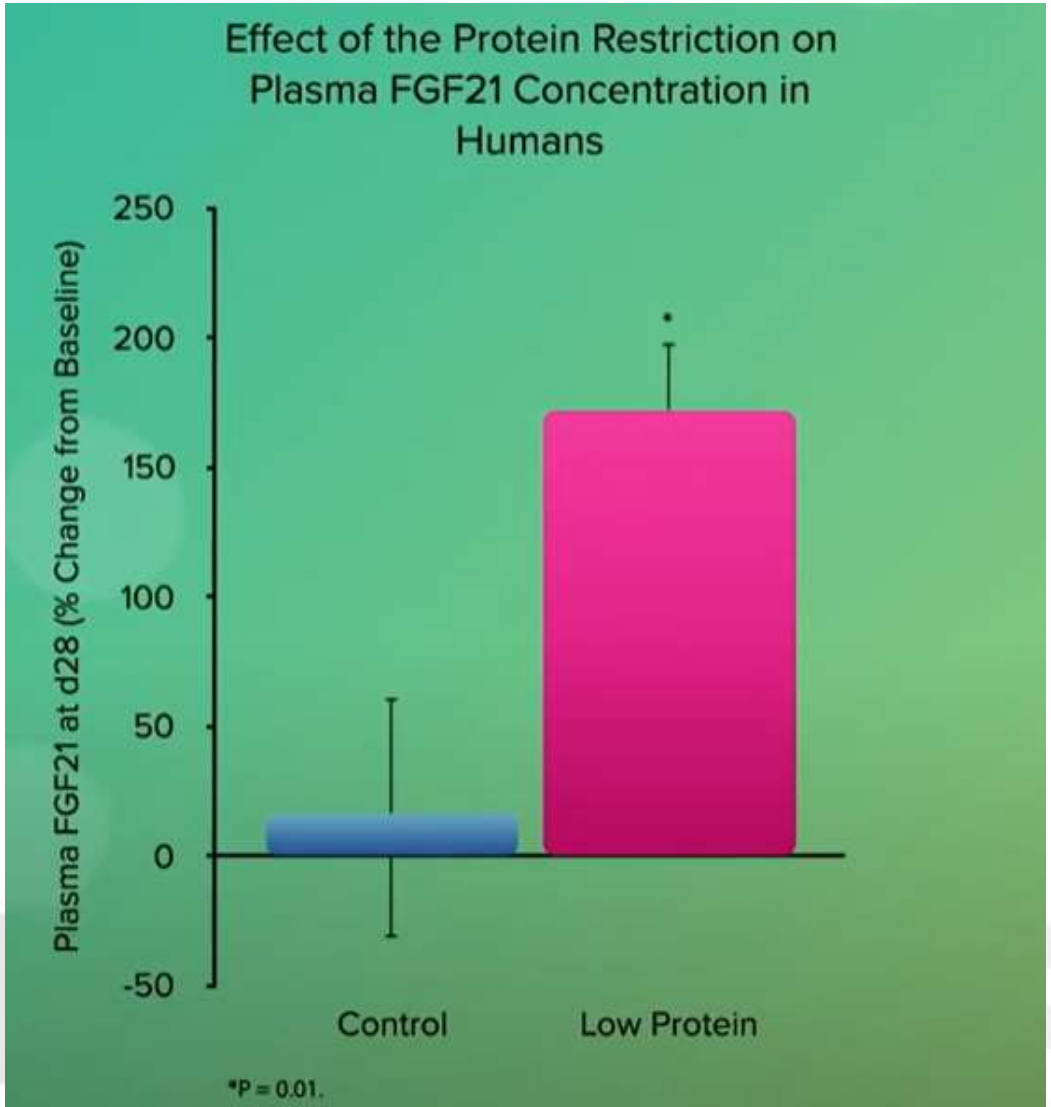
[1]Pennington Biomedical Research Center (PBRC), Baton Rouge, Louisiana, USA. [2]Virginia Polytechnic Institute and State University, Blacksburg, Virginia, USA. [3]Diabetes and Obesity Center of Excellence, Department of Medicine, University of Washington, Seattle, Washington, USA.

Enhanced fibroblast growth factor 21 (FGF21) production and circulation has been linked to the metabolic adaptation to starvation. Here, we demonstrated that hepatic FGF21 expression is induced by dietary protein restriction, but not energy

Fgf21 expression was increased within 24 hours of reduced protein intake. In humans, circulating FGF21 levels increased dramatically following 28 days on a LP diet. LP-induced increases in FGF21 were associated with increased phosphorylati

of eukaryotic initiation factor 2α (eIF2α) in the liver, and both baseline and LP-induced serum FGF21 levels were reduced in mice lacking the eIF2α kinase general control nonderepressible 2 (GCN2). Finally, while protein restriction altered food intake, energy expenditure, and body weight gain in WT mice, FGF21-deficient animals did not exhibit these changes in response to a LP diet. These and other data demonstrate that reduced protein intake underlies the increase in circulating FGF21 in response to starvation and a ketogenic diet and that FGF21 is required for behavioral and metabolic responses to protein restriction. FGF21 therefore represents an endocrine signal of protein restriction, which acts to coordinate metabolism and growth during periods of reduced protein intake.

Decrease Protein

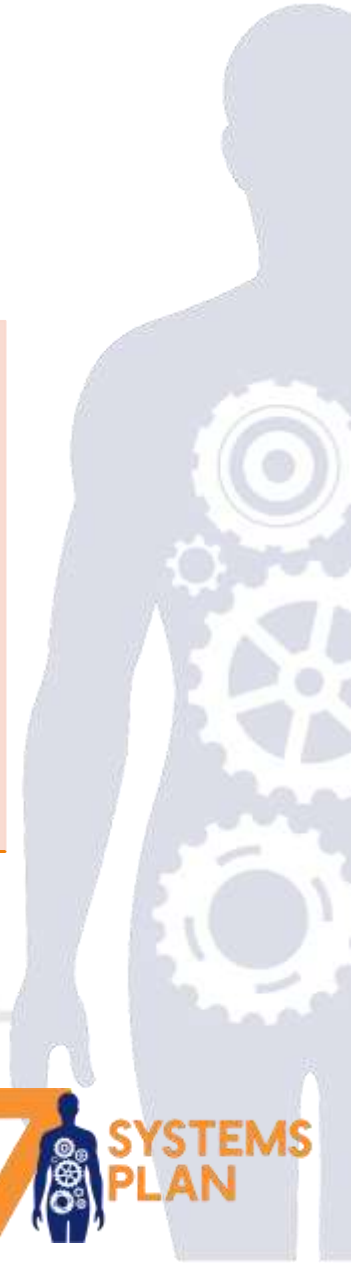


- 150% FGF21 increase with less protein in 4 weeks
- This in just a decrease in eating excess protein

SYSTEMS PLAN

To Boost FGF21

1. Use fasting and FMDs
2. Try cold showers
3. Increase good carbs
4. Support your microbiome
5. Decrease protein intake

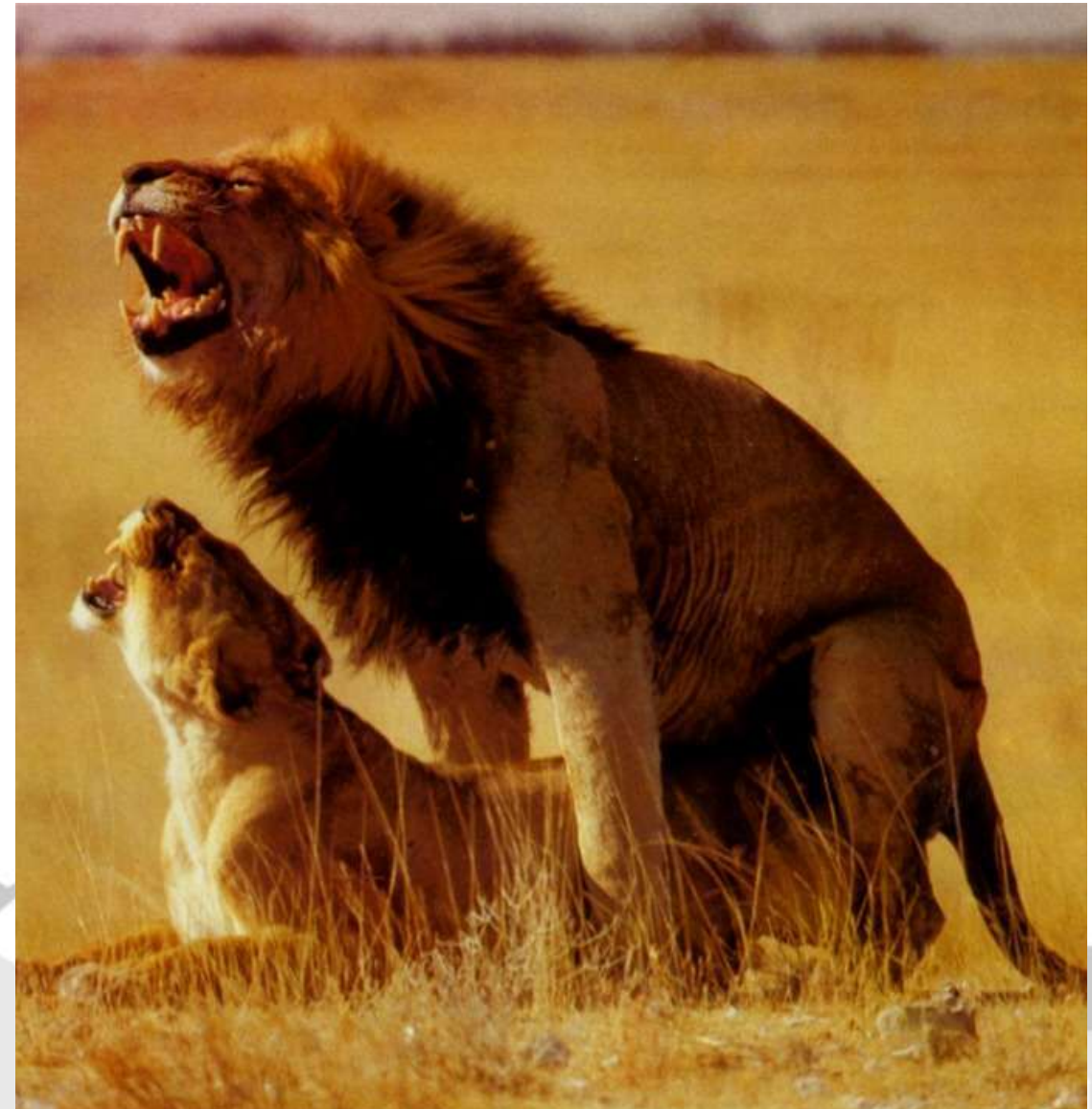


7 SYSTEMS PLAN

Sex And Longevity

by Pat Luse

Good Testosterone



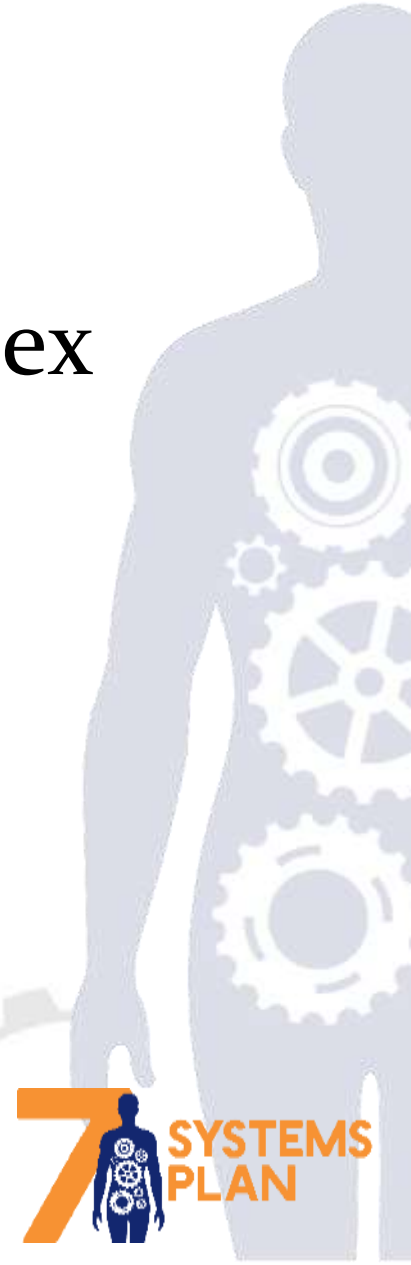
Low Testosterone

Your Sex Life

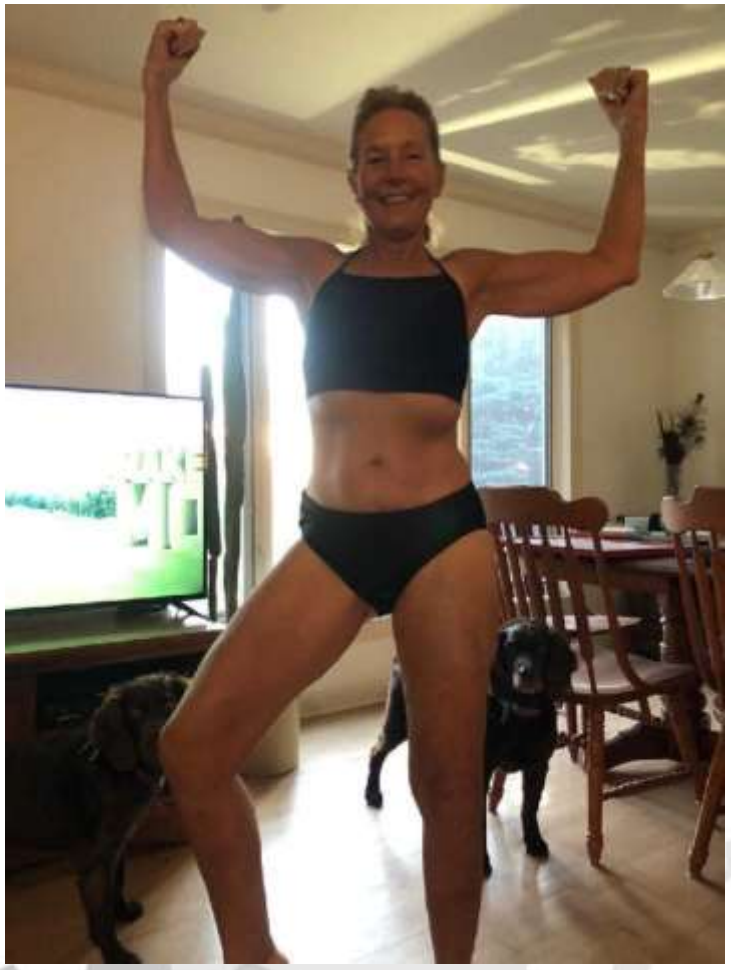
If your Systems are working optimally, your sex life at age 65 should be..

better than your sex life at 25

Dr. Pat Luse



Manon (63 years old)



A Tip for Men- Don't Try to Fix Things

The Top 11 Health Benefits Of Sex

1. Improved immunity
2. Heart health
3. Lower blood pressure
4. It's a form of exercise
5. Pain relief
6. May help reduce risk of prostate cancer
7. Improve sleep
8. Stress relief
9. Boost your libido
10. Improved bladder control in women
11. Increase intimacy and improve your relationship

Does Sex Lead to a Longer Life?

Queens University in Belfast tracked 1,000 middle-aged men for over 10 years.

Those who had orgasms **twice a week or more** had half as many heart attacks.

(*British Journal 1997*) & Life Magazine

SEX CAN LEAD TO A LONGER LIFE

"a low frequency of sexual activity predicts CVD independently of ED"

The American Journal of Cardiology Volume 105, Issue 2, Pages 192-197 (15 January 2010) abstract below

The American Journal of Cardiology Volume 105, Issue 2, Pages 192-197 (15 January 2010

7 SYSTEMS PLAN

Harvard Health Let

Pill-free ways to improve your sex life

Exercise, smoking cessation, and alcohol moderation can help bring sexual activity back into the bedroom.

Sex is important to health. It revs up metabolism and may boost the immune system. Frequent sexual intercourse is associated with reduced heart attack risk. And it's fun. So why aren't we having more of it? "There are many reasons why sexual activity can diminish in older age, but many sexual problems can be overcome with appropriate interventions, especially if the

having sex. Heart disease can reduce the amount of blood that reaches sex organs. High blood pressure, diabetes, stress, depression, and incontinence can also nudge sex aside. Medications for these and other conditions can interfere with sexual

ment may be more invo
hormone therapy for dec
or sex therapy for inabili
The first line of treatmen
cludes prescription medi
as sildenafil (Viagra), var
tra, Staxyn), tadalafil
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Curr Urol Rep (2015) 16: 16
DOI 10.1007/s11934-015-0482-1

Penile Doppler Ultrasound Predicting Cardiovascular Disease in Men with Erectile Dysfunction

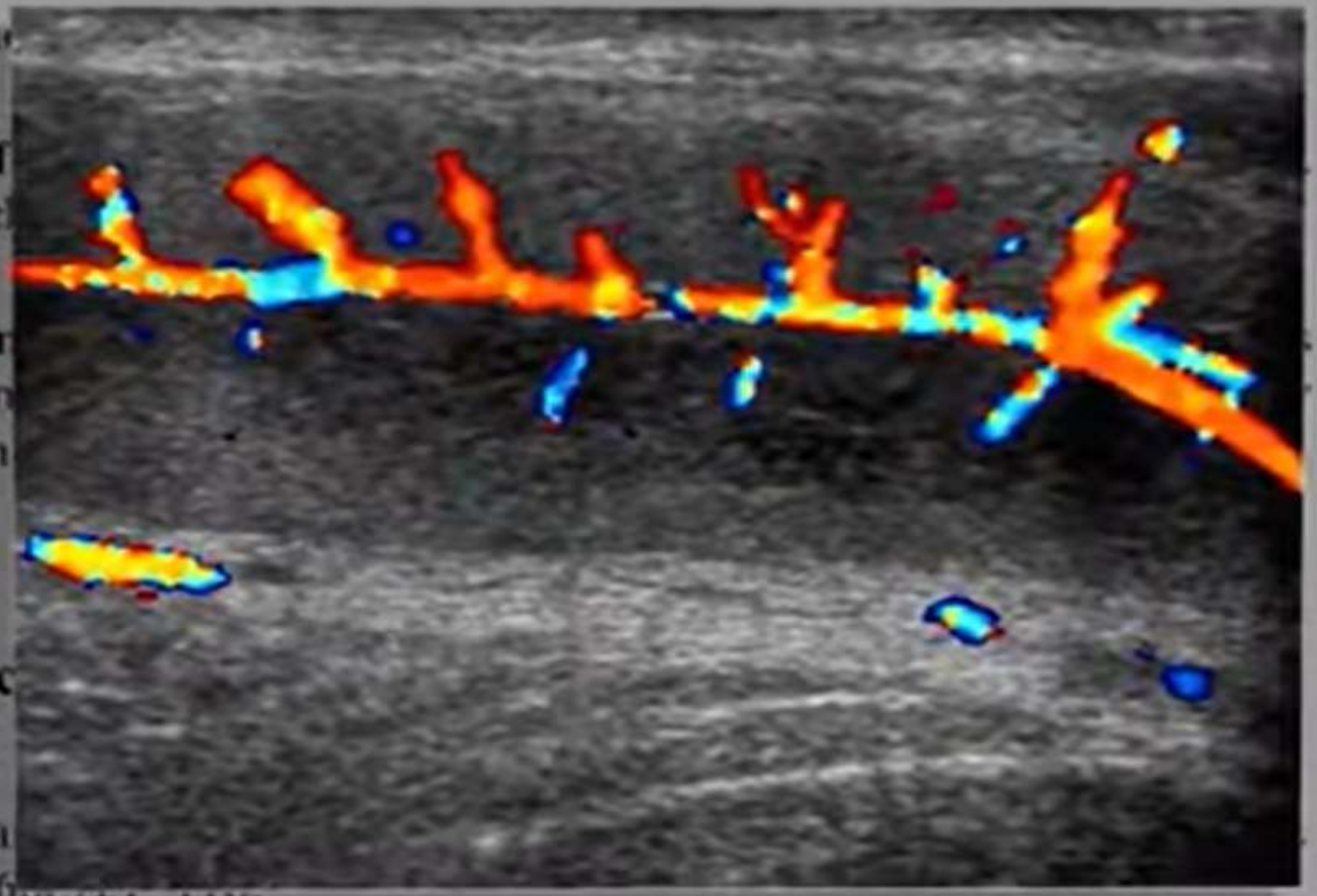
Nikhil Gupta · Amin Herati · Bruce R. Gilbert

Published online: 13 February 2015

Abstract Cardiovascular disease is a major cause of morbidity and mortality in the USA. Traditional risk factors such as obesity, physical inactivity, and diet are used to screen for cardiovascular disease. However, these risk factors miss a significant

in the USA are attributable to ischemic heart disease [1]. Current screening methods, which assess traditional risk factors such as diabetes mellitus type II (DM2), obesity, diet, and physical inactivity, only capture about half of those at high risk for developing cardiovascular disease and fail to identify

dysfunction is often a re-entry point for men into health care after years of neglect. Penile Doppler ultrasound is an important diagnostic tool that not only documents penile vascular function but also has the potential for reducing the devastation of cardiovascular disease by providing early diagnosis and treatment.



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ED: Slight Problems= Heart Problems

- **Men with ED** have an increased risk of **heart-related problems**, including **heart failure, stroke and heart disease**, according to new research
- Even among those with **mild ED**, the risks of certain **heart problems**, as well as the risk of **dying prematurely** from any cause
- Erectile dysfunction appears to be an important **biomarker for heart disease**
- There are a number of **lifestyle choices and supplements** that can contribute to **restoring healthy sexual function.**

European Urology

European Urology 44 (2003) 352–354

Editorial

Is Erectile Dysfunction the "Tip of the Iceberg" of a Systemic Vascular Disorder?

Piero

[a]Institute
[b]Depart
[c]Depart

Atherosclerosis is a systemic disorder that uniformly affects all major vascular beds.

Erectile function is a psychoneurovascular phenomenon which ultimately culminates in an increase of arterial flow within the hypogastric-penile bed with the subsequent activation of the veno-occlusive mechanism of the corpora cavernosa [1]. Most cases of erectile

simultaneously in the same patient. This may occur because arteries supplying various districts (i.e. penis, heart, brain, lower limbs) do have different size. Fig. 1 depicts the hypothetical vascular situation of a patient with isolated ED. A >50% lumen obstruction (i.e. the

European Urology

European Urology 44 (2003) 360–365

Erectile Dysfunction Prevalence, Time of Onset and Association with Risk Factors in 300 Consecutive Patients with Acute Chest Pain and Angiographically Documented Coronary Artery Disease

Fran

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orsi[c]

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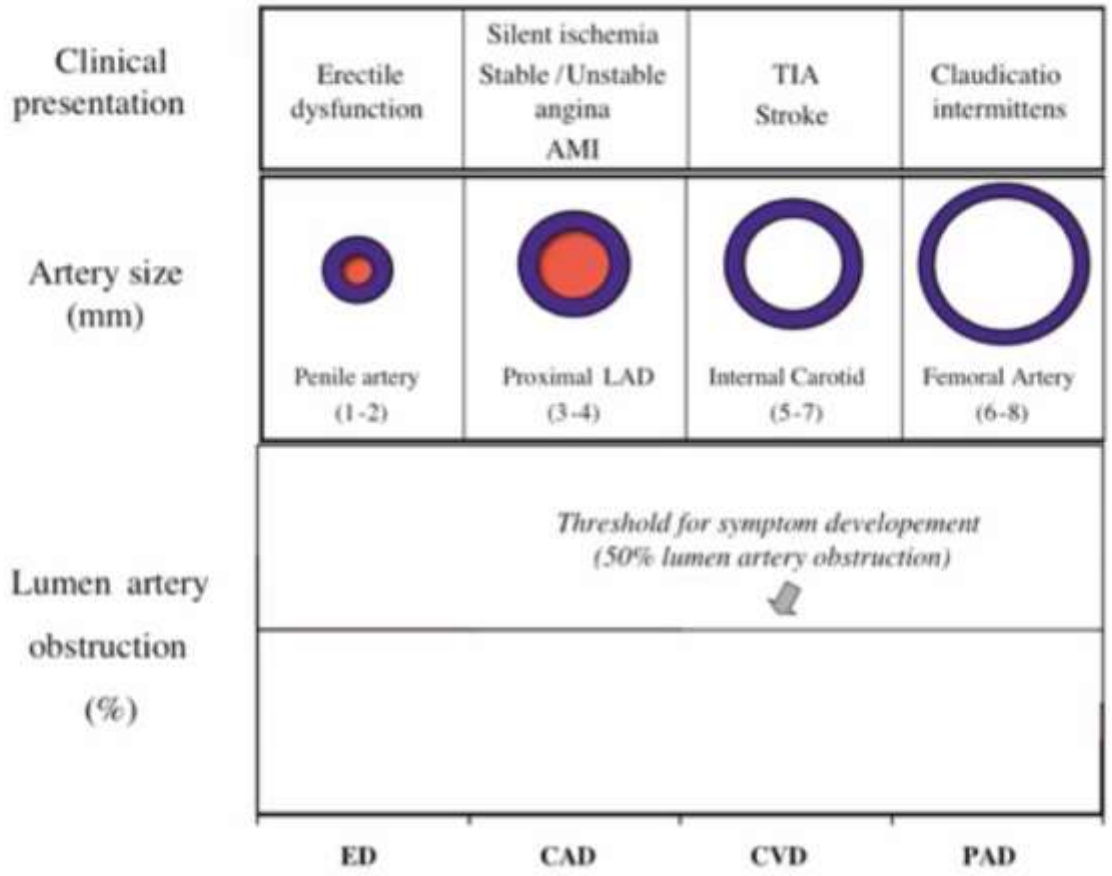
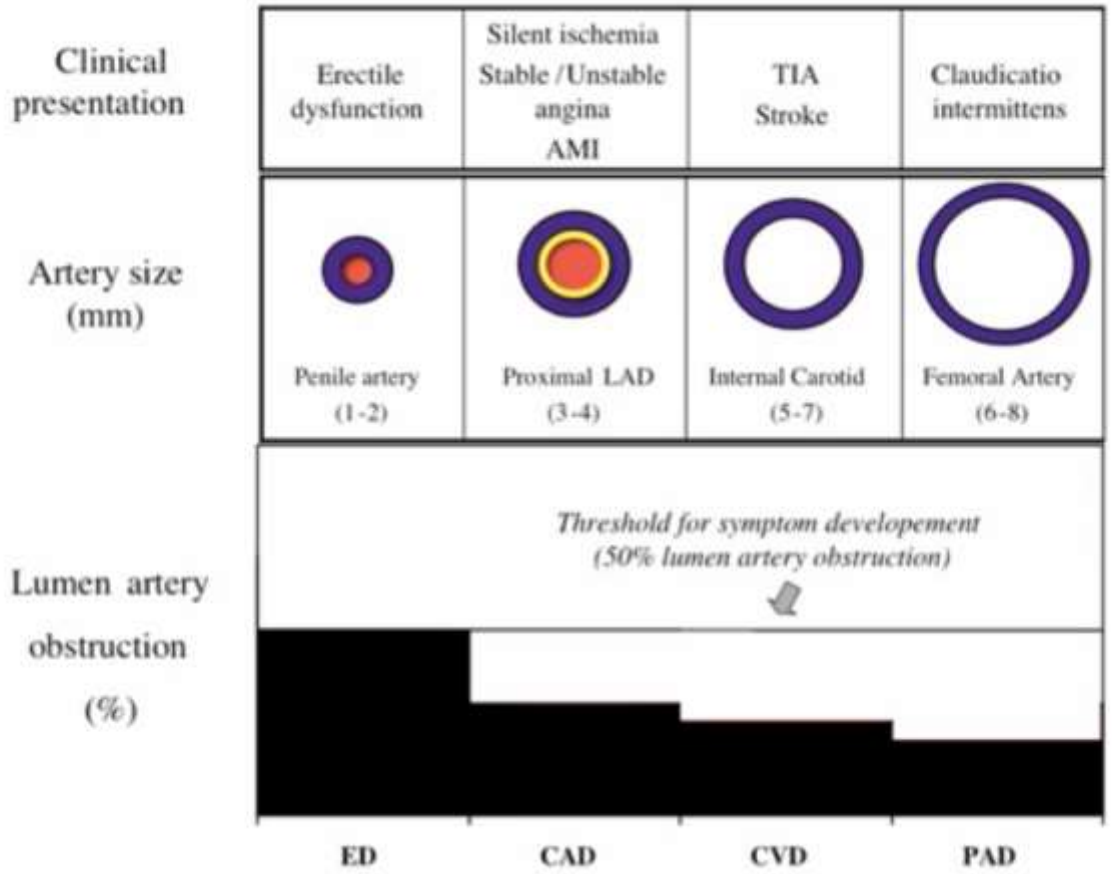
67% reported that they had become impotent well before the onset of CAD symptoms, with a mean time interval of more than 3 years.

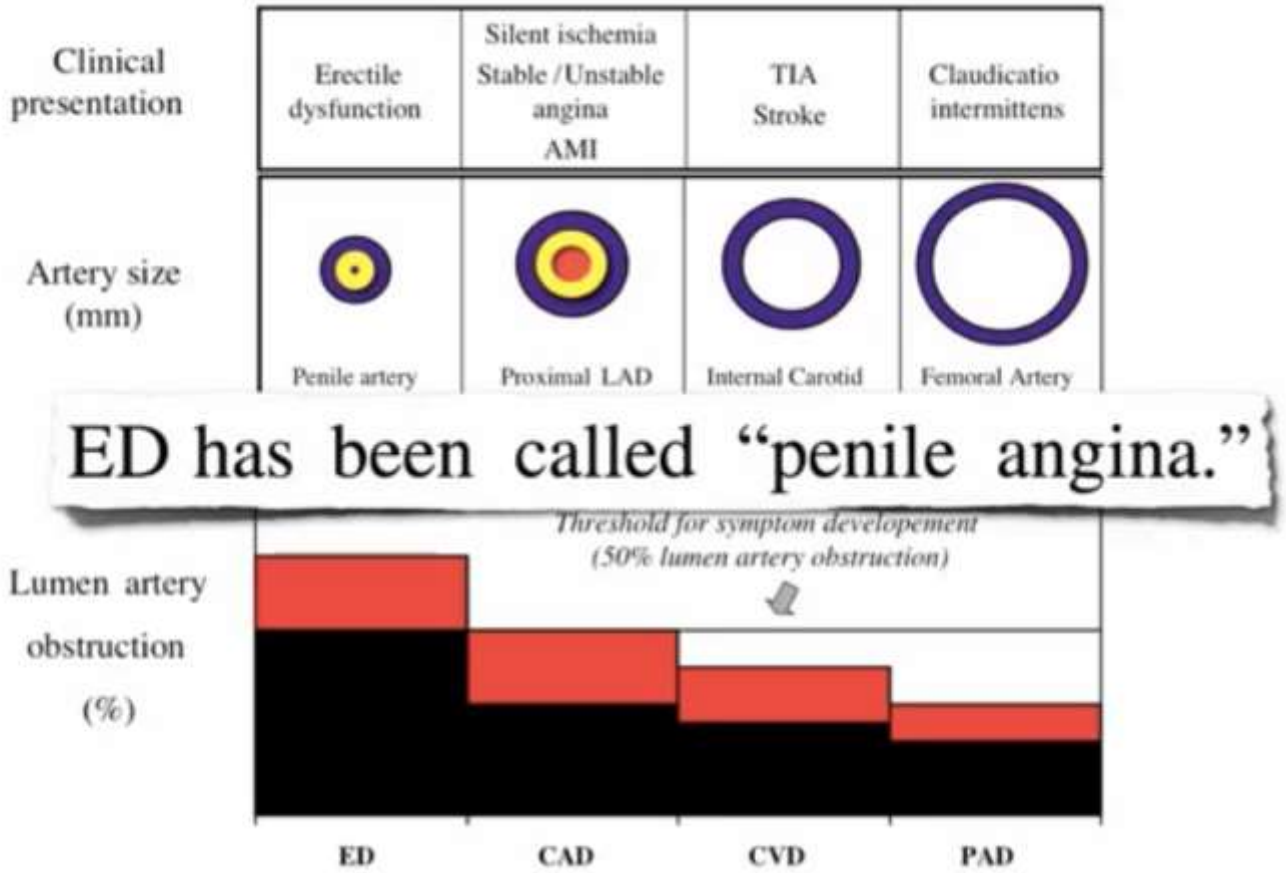
Small Blood Vessels are Affected First

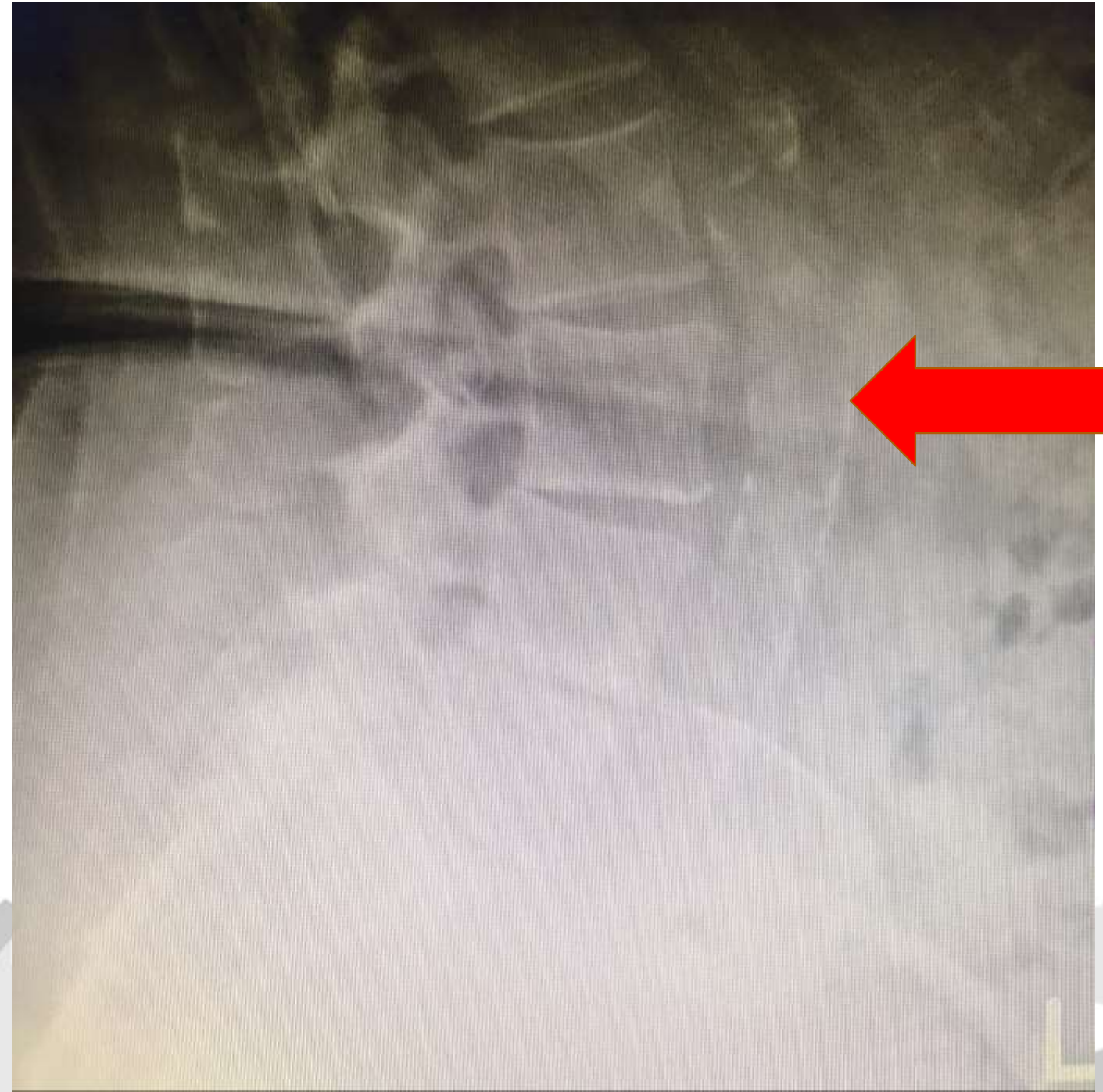


This is when You have ED



This is when you Feel Chest Pain





from the questionnaire responses and categorized as moderate/complete ED versus none/minimal. CVD included a wide range of major end points and was ascertained through self-report, medical records, and the National Death Index. We calculated the age-adjusted incidence rates according to the person-years of follow-up, and Cox proportional hazards models were used to estimate covariate-adjusted, Framingham risk score-adjusted, and ED-adjusted hazard ratios and 95% confidence intervals for sexual function variables and the subsequent risk of CVD. Of the 1,165 men free of CVD at baseline, the age-adjusted CVD incidence rate for moderate/complete ED and none/minimal ED was 17.9/1,000 person-years and 12.5/1,000 person-years, respectively. In multivariate models adjusted for age, covariates, ED, and the Framingham risk score, a low frequency of sexual activity (once a month or less vs ≥2 times weekly) was associated with increased risk of CVD (hazard ratio 1.45, 95% confidence interval 1.04 to 2.01). In conclusion, our results suggest that a low frequency of sexual activity predicts CVD independently of ED and that screening for sexual activity might be clinically useful. (Am J Cardiol 2010;105:192–197)

Longitudinal studies have shown that erectile dysfunc-
n (ED) is a risk factor for incident cardiovascular disease
VD)[1–4] and CVD mortality.[5] However, little is known
out how or whether other aspects of sexual health, in

Methods

The Massachusetts Male Aging Study (MMAS) is
ulation-based, longitudinal cohort study of aging, healt

Controversies in Sexual Medicine

Is Sex Just Fun? How Sexual Activity Improves Health

Emmanuele A. Jannini, MD,* William A. Fisher, PhD,† Johannes Bitzer, MD,‡ and Chris G. McMahon, MBBS FAChSHM§

*Course of Endocrinology and Medical Sexology, Department of Experimental Medicine, University of L'Aquila, L'Aquila, Italy; †Department of Psychology, Department of Obstetrics and Gynecology, University of Western Ontario, London, ON, Canada; ‡Department of Obstetrics and Gynecology, University Hospital Basel, Basel, Switzerland; §Australian Centre for Sexual Health, Sydney, Australia

DOI: 10.1111/j.1743-6109.2009.01477.x

ABSTRACT

Introduction. With nonscientific, religious, or magic arguments, sexual activity has been regarded in the past as dangerous to health. This opinion is now rejected, and intercourse is generally considered healthy. However, while some aspects of the equation "more sex equals more health" have been demonstrated, others still need robust data for confirmation.

Methods. Four scientists (an endocrinologist, a psychologist, a gynecologist, and a urologist) with expertise in the area of sexual medicine were asked to contribute with their opinions.

Main Outcome Measure. Expert opinion supported by currently available literature.

Results. Expert 1, who is Controversy's section editor, demonstrates that sexual activity stimulates testosterone production. He infers that this physiological stimulus to androgenic production is one of the reasons why sexual activity improves general health. He is partially supported by the psychological findings in the couple having sex dissected by expert 2 and by the experimental evidences discussed by expert 3, who found that general benefits of sexual activity are not just for men. Expert 4 critically discusses contrasting findings so far published on the

dangerous to health. This opinion is now rejected, and intercourse is generally considered healthy. However, while some aspects of the equation "more sex equals more health" have been demonstrated, others still need robust data for confirmation.

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Conclusion. Readers of *The Journal of Sexual Medicine* will judge if safe, satisfactory, and frequent sexual activity can be prescribed as a medicine in order to improve both general and sexual health of individuals and of the couples.

Jannini EA, Fisher WA, Bitzer J, and McMahon CG. Is sex just fun? How sexual activity improves health. J Sex Med 2009;6:2640–2648.

Key Words. Sexual Activity; Testosterone; Estrogen; Prostate Cancer; Depression

ehavioral therapy), pharmaco-
din, sildenafil, tadalafil), and
prostheses, surgery, vacuum
re able to restore LH bioac-
ently testosterone (T) levels

al stress associated with long-
ring lack of sexual activity) may
nic disturbance of the GnRH
ich in turn causes the pituitary
H molecules with reduced bio-
wer biological activity of LH
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cells. This may represent an
n. As demonstrated for the
tion of many metabolic func-
starvation, the impossibility of

activity is started anew—no matter what the cause of the erectile impairment or how it was treated. For this reason, we can hypothesize that sexual activity is be able to "feed" itself through activation of the hypothalamic–pituitary–testicular axis which results in increased T levels, increased readiness for the next sexual encounter, and for the reactivation of the endocrine axis itself.

More sex means more physiologically produced T. More T correlates with both psychological and general health. In fact, full, satisfactory sexual intercourse is not only associated with indices of ameliorated hormonal function, but also with the improvement of the corresponding physical and psychological parameters [19–21]. A possible answer to the methodological doubts exposed by Dr. Fisher in his piece on the correlation between

followed a fixed temporal pattern. If it is postulated that plasma testosterone levels over each 24 h period fit a curve described by a sine wave, in which both amplitude and wavelength could vary, then the marked differences in measurements carried out at fixed times might be explained. Although it has been established by means of repeated sampling (e.g. every 4 h, see Nieschlag & Ismail, 1970) that changes do indeed occur over periods of 24 h, it has not so far been demonstrated that the patterns are consistent from one day to another in any one individual. Moreover, in the study of Nieschlag & Ismail (1970) it was clear that there was considerable temporal variation between the patterns obtained in different individuals.

In the subject studied herein, samples were provided from 5 to 35 min (generally

The act of coitus was invariably associated with increased plasma testosterone levels compared with control values irrespective of whether sexual intercourse occurred in the morning or in the evening (see Table 1). Furthermore, regardless of whether the control samples were collected before or after coitus (see Table 1), testosterone values in the preorgasmic samples were always higher. The average increase was 86·5 ± 18·5 ng/100 ml and was highly significant ($P < 0{\cdot}001$). The postorgasmic sample, collected within 35 min of the preorgasmic specimen, was increased over the latter in seven and reduced in nine out of 16 events and the change, representing an average increase of 10·1 ng/100 ml during coitus, was not significant.

Precise information on the relationship existing between circulating testosterone levels and male libido is not yet available. Nor is it clear by what mechanism the increased plasma testosterone levels associated with coitus are produced. It is, however, possible that intercourse could occur in response to rising testosterone levels occasioned by changes in the amplitude of the underlying nyctohemeral rhythm. Our present results suggest that the increase in circulating testosterone levels are likely to be associated with the act of coitus itself rather than with the desire for, or anticipation of sexual activity. This view is supported first by the relatively frequent finding of low control levels of testosterone on the days on which intercourse took place and secondly by the fact that many of the peaks of plasma testosterone activity noted in the control samples were independent of sexual activity. The choice of the time of collection of the control samples might not have been optimal to demonstrate pre-coital alterations in testosterone levels in view of the possible

The results of the first [illegible] samples collected daily at 22.00 h varied between [illegible] = 321·5 ± 14·3 (S.E.M.)). Peak values were detected at irregular intervals which bore no apparent relationship to sexual activity, the latter being denoted by triangles.

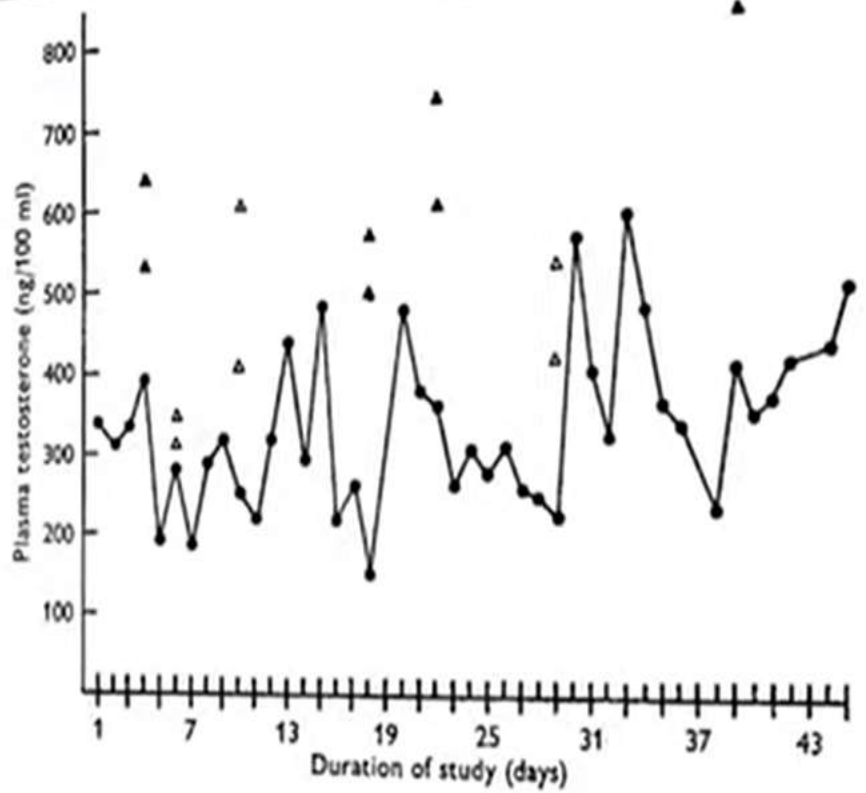


Fig. 1. Plasma testosterone levels in a male subject – first study. Horizontal black bar, menstruation of partner; ●——●, control measurements at 22.00 h each day; ▲, measurements in morning coital blood samples; △, measurements in evening coital blood samples.

Testosterone levels were invariably higher in the evening coital samples when compared with the control sample collected on the same day; however, the interval of time elapsing between the collection of the morning coital and the control samples varied from 8 to 12 h, and any differences observed were not included in the comparisons made (see Table 1).

The results of the second study are shown in Fig. 2. Control blood samples were collected daily at 08.00 h and again at 20.00 h. On only [illegible] level of testosterone in

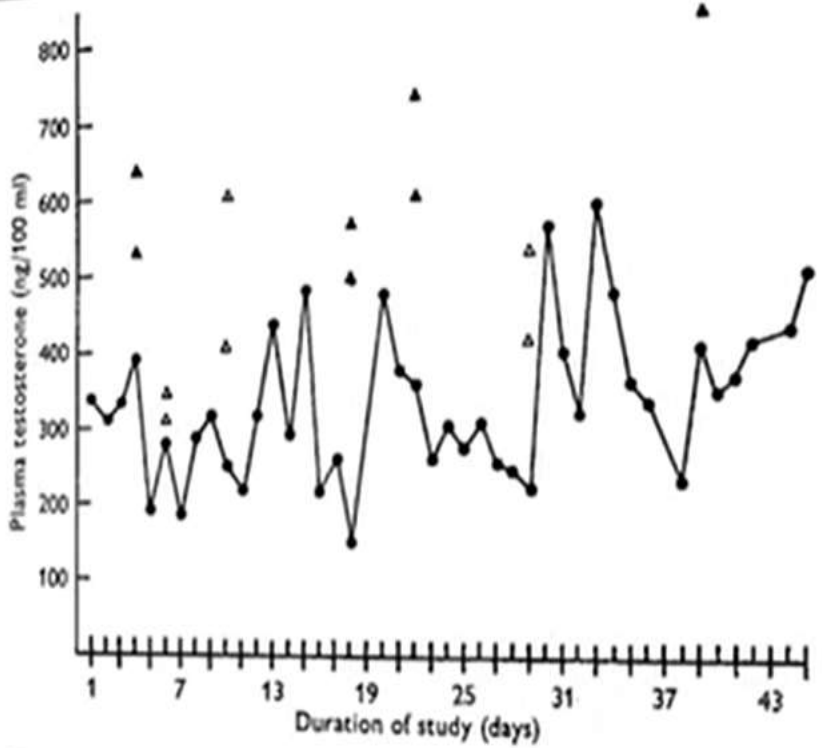
study 2), it is not clear whether changes from low to high levels (or vice versa) followed a fixed temporal pattern. If it is postulated that plasma testosterone levels over each 24 h period fit a curve described by a sine wave, in which both amplitude and wavelength could vary, then the marked differences in measurements carried out at fixed times might be explained. Although it has been established by means of repeated sampling (e.g. every 4 h, see Nieschlag & Ismail, 1970) that changes do indeed occur over periods of 24 h, it has not so far been demonstrated that the patterns are consistent from one day to another in any one individual. Moreover, in the study of Nieschlag & Ismail (1970) it was clear that there was considerable temporal variation between the patterns obtained in different individuals.

In the subject studied herein, samples were provided from 5 to 35 min (generally less than 15 min) before orgasm, and within 5 min after orgasm. The act of coitus was invariably associated with increased plasma testosterone levels compared with control values irrespective of whether sexual intercourse occurred in the morning or in the evening (see Table 1). Furthermore, regardless of whether the control samples were collected before or after coitus (see Table 1), testosterone values in the preorgasmic samples were always higher. The average increase was $86{\cdot}5 \pm 18{\cdot}5$ ng/100 ml and was highly significant ($P < 0{\cdot}001$). The postorgasmic sample, collected within 35 min of the preorgasmic specimen, was increased over the latter in seven

In contrast to the changes noted with coitus, there was no significant change in plasma testosterone levels in relation to masturbation.

Precise information on the relationship existing between circulating testosterone levels and male libido is not yet available. Nor is it clear by what mechanism the increased plasma testosterone levels associated with coitus are produced. It is, however, possible that intercourse could occur in response to rising testosterone levels occasioned by changes in the amplitude of the underlying nyctohemeral rhythm. Our present results suggest that the increase in circulating testosterone levels are likely to be associated with the act of coitus itself rather than with the desire for, or anticipation of sexual activity. This view is supported first by the relatively frequent finding of low control levels of testosterone on the days on which intercourse took place and secondly by the fact that many of the peaks of plasma testosterone activity noted in the control samples were independent of sexual activity. The choice of the time of collection of the control samples might not have been optimal to demonstrate pre-coital alterations in testosterone levels in view of the possible fluctuations in the circadian rhythm. In this connexion it has been reported that

The results of the first study are shown in Fig. 1. Control blood samples collected daily at 22.00 h varied between 145 and 565 ng/100 ml ($\bar{x} = 321{\cdot}5 \pm 14{\cdot}3$ (S.E.M.)). Peak values were detected at irregular intervals which bore no apparent relationship to sexual activity, the latter being denoted by triangles.



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The results of the second study are shown in Fig. 2. Control blood samples were collected daily at 08.00 h and again at 20.00 h. On only three out of 43 days did the level of testosterone in the evening control sample exceed that

mation was [illegible]
in variance and make it possible to include
males in the same analysis. Data were analyzed using repeated measures analysis of variance, with gender as a between-subjects factor and time of evening and presence/absence of coitus as within-subjects factors.

The means are shown in Fig. 1. Testosterone increased across the evening on sex days and decreased on nonsex days. Only the time by sex interaction was statistically significant, $F(1, 6) = 8.46$, $p < 0.05$. Newman–Keuls tests on pairs of means in the interaction indicated testosterone in the early evening did not differ between sex and nonsex days, while late evening testosterone was lower on nonsex than on sex days ($p < 0.01$) and lower than early evening testosterone on either kind of day ($p < 0.05$). There were no effects of interest beyond the time by sex interaction. There was no overall mean difference between early and late evening ($F < 1.0$) or between sex and nonsex days ($F < 1.0$) and no interaction involving gender ($F < 1.0$). As expected, testosterone concentrations were higher for males than females, $F(1, 6) = 12.26$, $p < 0.05$.

DISCUSSION

Testosterone increased from before to after coitus, in contrast to changes across the evening on days when there was no coitus. The effect was the same for males and females.

worked alone on an island and [illegible]
partner did show anticipatory increases in testosterone (1). A more complete study would include testosterone measurements from both established and newly acquainted pairs, perhaps during one-night encounters among the new pairs.

The present results could be related to changes in testosterone observed in dyadic encounters involving competition and dominance. Testosterone increases with competitive success and decreases with failure (2,3,8,21,22). Testosterone has been reported to increase before the beginning of an important tennis match (3). Coitus is not usually regarded as a competitive event, but one's mental state following coitus could nevertheless be something like that of a winner (14). This interpretation suggests testosterone might increase in both participants in any encounter, sexual or otherwise, where they feel they have made important gains.

The effect we observed could be related to exercise, which at strenuous levels over short periods of time will increase testosterone concentrations (6). The exercise in coitus, variously described in interviews with our subjects as like wrestling, bike riding, horseback riding, doing push-ups, and nothing else, does not seem to us intense enough to have produced increases in testosterone. Effects of exercise can to some extent be evaluated by comparing the present study

partner did show anticipatory increases in testosterone (1). A more complete study would include testosterone measurements from both established and newly acquainted pairs, perhaps during one-night encounters among the new pairs.

The present results could be related to changes in testosterone observed in dyadic encounters involving competition and dominance. Testosterone increases with competitive success and decreases with failure (2,3,8,21,22). Testosterone has been reported to increase before the beginning of an important tennis match (3). Coitus is not usually regarded as a competitive event, but one's mental state following coitus could nevertheless be something like that of a winner (14). This interpretation suggests testosterone might increase in both participants in any encounter, sexual or otherwise, where they feel they have made important gains.

The effect we observed could be related to exercise, which at strenuous levels over short periods of time will increase testosterone concentrations (6). The exercise in coitus, variously described in

Beard growth was measured quantitatively by collecting and weighing the shavings from the head of a Philips Philishave razor after a single shave once every 24 h. Activity data were recorded on a 0–5 scale with respect to physical and mental exercise, nervousness, sleep, libido and intercourse.

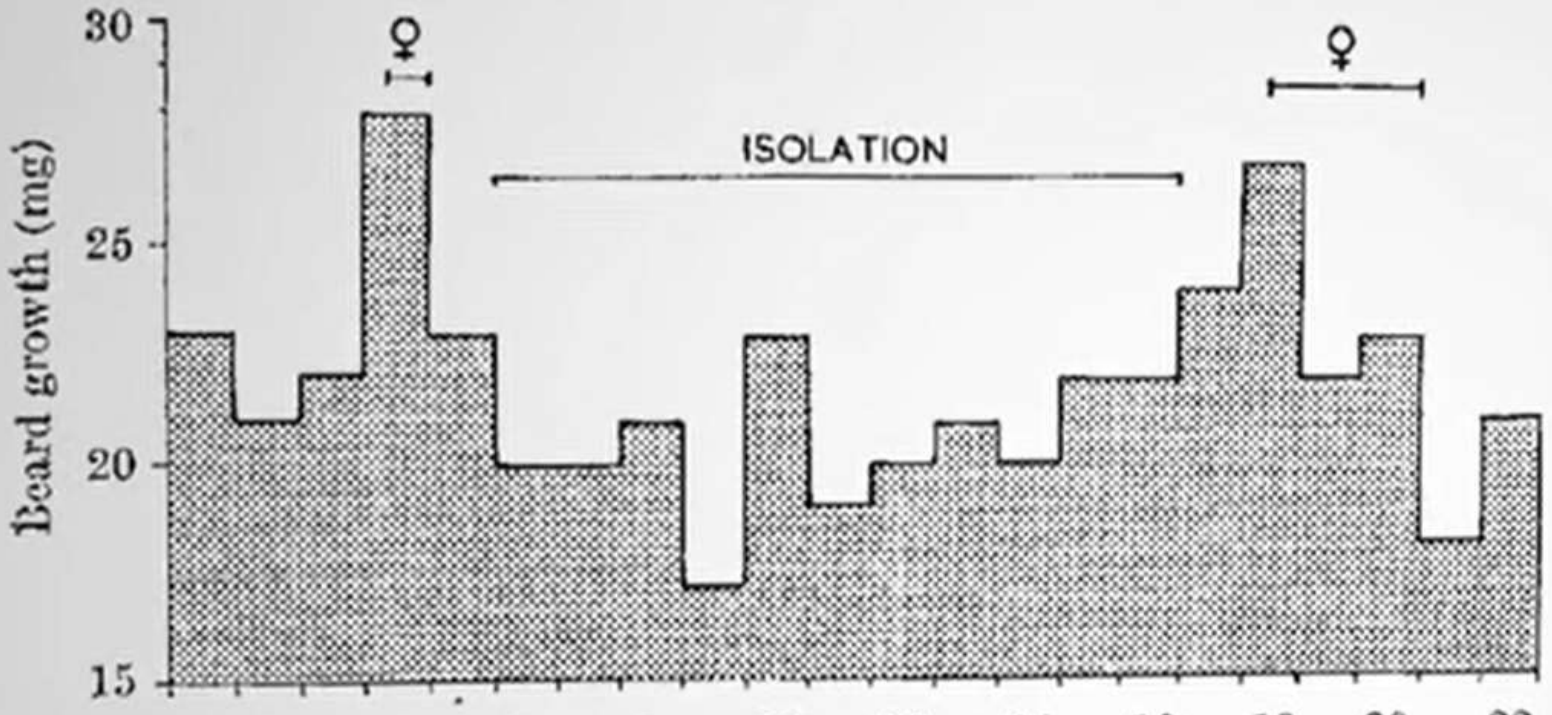
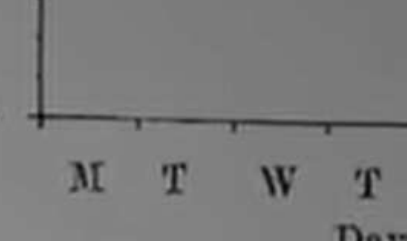


Fig. 1.

Fig. 1 illustrates the changes in beard growth during a short stay on the island. The day of return to the main-



for androgens because it w
control. An attempt was t
rate of beard growth with
activity, the rate of sebum
glands of facial skin[2]. Th
in general, there was good
indices of androgenic activ

A variety of compounds,
testosterone, androsterone
were taken sub-lingually
measured. All the samples
also included. The results
had a stimulatory effect o
producing the greatest incre
same order of magnitude a
intercourse. Although the
cortisone also stimulated
the beard may respond to

In conclusion, it seems t

Human Metabolism, University of Sheffield Medical School, Sheffield, UK

Summary

Epidemiological studies have found that men with low or low normal endogenous testosterone are at an increased risk of mortality than those with higher levels. Cardiovascular disease accounts for the greater proportion of deaths in those with low testosterone. Cancer and respiratory deaths in some of the studies are also significantly more prevalent. Disease-specific studies have identified that there are higher mortality

Introdu

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Sex and death: are they related? Findings from the Caerphilly cohort study

George Davey Smith, Stephen Frankel, John Yarnell

Abstract

Objective: To examine the relation between frequency of orgasm and mortality.
Study design: Cohort study with a 10 year follow up.
Setting: The town of Caerphilly, South Wales, and five adjacent villages.
Subjects: 918 men aged 45-59 at time of recruitment between 1979 and 1983.
Main outcome measures: All deaths and deaths from coronary heart disease.
Result: Mortality risk was 50% lower in the group

assumed to be shared by their subjects—renders the whole area apparently uninteresting. This is an instance of a more general phenomenon of epidemiologists studying what interests other epidemiologists, and not always being drawn to areas of more general public concern. There may be more exciting issues for the public than determining exactly how many servings of fruit and vegetables a day may confer enhanced health, or discovering that smoking is even worse for people than was once thought.

A few exceptions to the general epidemiological

Caerphilly cohort study

George Davey Smith, Stephen Frankel, John Yarnell

Abstract

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Abstract

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Setting: The town of Caerphilly, South Wales, and five adjacent villages.

Subjects: 918 men aged 45-59 at time of recruitment between 1979 and 1983.

Main outcome measures: All deaths and deaths from coronary heart disease.

Result: Mortality risk was 50% lower in the group with high orgasmic frequency than in the group with low orgasmic frequency, with evidence of a dose-response relation across the groups. Age adjusted odds ratio for all cause mortality was 2.0 for

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A few exceptions to the
silence on the association b
and later mortality exist. In th
study of ageing, frequency o
inversely associated with
enjoyment of intercourse

confidence interval 1.1 to 3.5, test for trend P = 0.02). With adjustment for risk factors this became 1.9 (1.0 to 3.4, test for trend P = 0.04). Death from coronary heart disease and from other causes showed similar associations with frequency of orgasm, although the gradient was most marked for deaths from coronary heart disease. Analysed in terms of actual frequency of orgasm, the odds ratio for total mortality associated with an increase in 100 orgasms per year was 0.64 (0.44 to 0.95).

Conclusion: Sexual activity seems to have a protective effect on men's health.

Introduction

mortality among women.[7] T
with a perception that the qu
of more importance to men
with quality is seen among
study early cessation of sexua
be associated with an increa
men over a 5 year follow up.[10]
found to be a risk factor for
case-control study of women
tion and impotence in hu
underlying factor.[11] From a
assumption that Catholic pri
renders another epidemiolo
A retrospective cohort a
priests in the United State

Main Outcome Measures. We reported literature data on the prevalence of unfaithfulness and on related psyc biological, sexual, and risk factors.

Results. Some surveys reported that 1.5–4% of married men had extramarital coitus in any given year, others t 23.2% of men have cheated during their current relationship. Different studies reported a lifetime prevalence unfaithfulness between 15% and 50%. With respect to factors related to unfaithfulness, several authors reported t men with extramarital affairs more frequently have a dysfunctional primary relationship, in both relational and sex terms. In addition, parenthood, as well as conflicts within the family, seem to be associated with a higher risk having an affair. Furthermore, unfaithful men display a higher androgenization, larger testis volume, lower pre lence of hypoactive sexual desire, and better sexual functioning. Only few studies have evaluated the correlat between infidelity and cardiovascular risk, reporting that having an extramarital affair could have a negative imp on cardiac morbidity and mortality.

Conclusions. Several interpersonal, sexual, and biological factors are associated with having extramarital affa Unfaithfulness in men seems to be associated with a higher risk of major cardiovascular events.

isher AD, Banc E, Rastrelli G, Corona G, Monami M, Mannucci E, and Maggi M. Sexual and cardiovascular correlates male unfaithfulness. J Sex Med 2012;9:1508–1518.

Key Words. Unfaithfulness; Sexual Dysfunction; Major Cardiovascular Events; Psychobiological Correlates

bove.

d from Being Unfaithful

t relational intimacy and sexu-
spects of human well-being, as
life and overall health [84,85].
l studies have demonstrated an
between sexual activity and
ng a favorable effect of rela-
d sexuality on overall health
ar, the Duke First Longitudinal
25-year investigation, involving
94 years, found that the fre-
tercourse was a significant pre-
in men [87]. Conversely, a

tionship between extramarital affairs and risk for MACE. This result is surprising, considering that unfaithful men are a sort of high-ranking male with a better hormonal milieu and vascular function [39,76]. Extramarital sex may be hazardous and stressful because the lover is often younger than the primary partner, and probably sex occurs more often following excessive drinking and/or eating [96,97]. Of interest and concern is the possibility of an enhanced physiological response to coitus with an extramarital partner [91]. It is possible that a secret sexual encounter in an unfamiliar setting may significantly increase blood pressure and heart rate, leading to an increased myocardial oxygen demand [91]. Moreover, the physiological response to coitus might trigger the fracture or

om Being Unfaithful

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3
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2
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1

Is; $n = 5$ anterior MIs; $n = 4$ no specifi-
diabetes mellitus was known in 6 cases,
s, and cardiac arrhythmia in 4 cases. In
tion had been performed several years
e history revealed angina pectoris com-
nented myocardial insufficiency. On the
provided by witnesses, it was possible
romes listed in Table 6, which occurred
he fatal event. In accordance to the pro-
ath sounds were reported in 15 and spon-

Course of the Fatal Event and Circumstances

Most of the deaths occurred during or after sexual intercourse ($N = 39$; $n = 4$ women; $n = 35$ men). Ten men died during self-masturbation and 5 died as a result of manual penis stimulation by the sexual partner. Three cases of death occurred during oral sex, 1 during striptease, 4 during erotic body massage, 2 while visiting a brothel, and 3 during foreplay and immediately before sexual intercourse. Ejaculation before the fatal event was reported in 19 cases, no ejaculation in 23, and no statement was given in 26 cases. The majority of the deaths occurred during extramarital intercourse ($N = 39$), such as with a mistress ($n = 10$) or prostitute ($n = 29$). In 13 of the cases, the wife or usual partner of the man was involved. Therefore, most of the deceased were found in brothels ($n = 21$), prostitute apartments ($n = 6$), hotels ($n = 3$), or the mistress' apartment ($n = 5$). Only 19 of the fatal events occurred in the victim's home ($n = 16$) or the home of longtime partner ($n = 3$). In 3 cases, death occurred in a car. One person died in an ambulance after visiting a brothel. As the information on

37 (16.0%)	1	1	0.21
80 (16.5%)	0.92 (0.59 to 1.42)	0.95 (0.60 to 1.50)	
52 (26.4%)	1.47 (0.89 to 2.44)	1.40 (0.82 to 2.39)	
19 (8.2%)	1	1	0.24
53 (10.9%)	1.19 (0.68 to 2.09)	1.30 (0.72 to 2.35)	
33 (16.8%)	1.69 (0.90 to 3.20)	1.53 (0.77 to 3.01)	

or systolic blood pressure, current smoking, FEV_1/height^2, blood cholesterol, fibrinogen, social class, paternal social class, self reported
n, ECG defined ischaemia, angina.

ss common in those with a low frequency of course compared with those reporting high or frequency (age adjusted OR 0.82, 95% CI 0.25 to se not taking antihypertensives and reporting a y of sexual intercourse, stroke was slightly more e adjusted OR 1.23, 95% CI 0.60 to 2.53). But in confidence intervals were wide and included no

amined the relation between frequency of sexual and fatal and all first coronary heart disease ring up to 20 years (see table 3). Death was more hose reporting an intermediate or low frequency tercourse (intermediate frequency age adjusted

Assuming a sexually active adult life of 50 years and a lifetime average frequency of sexual intercourse of once a week, only one out of 580 men might be expected to suffer a sudden death attributable to sexual intercourse. any association between sexual activity and triggering of an acute stroke. The occurrence of acute stroke immediately after sexual intercourse has been reported by previous case studies, and these tend to be attributable to vasospasm,[12 13] cerebral haemorrhage or subarachnoid haemorrhage.[1] In cerebral haemorrhage and subarachnoid haemorrhage, acute rises in blood pressure are of importance in triggering an event. It has been shown that male sexual intercourse induces transient increases in heart

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A preliminary study of sexual activity as a distraction for young drivers

Cindy Struckman-Johnson[a,*], Samuel Gaster[a], Dave Struckman-Johnson[b]

[a] Department of Psychology 414 East Clark St. University of South Dakota, Vermillion, SD 57069, USA
[b] Department of Computer Science 414 East Clark St. University of South Dakota, Vermillion, SD 57069, USA

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ABSTRACT

In what may be the first in-depth study of sexual activity as a driving distraction in the US, a sample of 195 male and 511 female college students at a Midwestern university (*M* age = 19.7) participated in an on-line study of sex while driving (SWD). Of these, 64 (32.8%) men and 47 (9.3%) women had engaged in sex while driving (SWD). Nine percent of men and 29% of women had engaged in SWD as a passenger. In most recent SWD incidents, respondents reported that the two most common acts were oral sex (70.3%) and genital touching (60.4%). About 11% engaged in vaginal intercourse. Sexual activity lasted from 1 to 10 min for 42.7% of the respondents. Nearly half (49.1%) were traveling 61–80 mph during sex. Considering respondents' lifetime incidents of SWD, the most common driving errors reported were

activity

A type of distraction by young drivers that, to our knowledge, has not yet been studied in depth is engaging in sexual activity. In his book The *Automobile and American Life*, Heitmann (2009, p. 91) wrote that the automobile has always been equated with freedom for adventure, including sexual adventure. Redshaw (2008, p. 103) opined that there is a cultural connection between cars, speed, and male desir

While it is generally assumed that sexual behavior happens in parked cars (Heitmann, 2009), there is little discussion or documentation in the research literature of sexual activity in moving vehicles.

. An international survey by a Danish headset company Jabra found that 15% of consumers aged 18–65 reported having "performed sex or sexual acts while driving" (Woodyard, 2010). In our prior research on texting among college students (Struckman-Johnson et al., 2014), we discovered incidentally that 40% of men

lark St. University of South Dakota, Vermillion, SD 57069, USA
East Clark St. University of South Dakota, Vermillion, SD 57069, USA

A B S T R A C T

In what may be the first in-depth study of sexual activity as a driving distraction in the US, a sample of 195 male and 511 female college students at a Midwestern university (*M* age = 19.7) participated in an on-line study of sex while driving (SWD). Of these, 64 (32.8%) men and 47 (9.3%) women had engaged in sex while driving (SWD). Nine percent of men and 29% of women had engaged in SWD as a passenger. In most recent SWD incidents, respondents reported that the two most common acts were oral sex (70.3%) and genital touching (60.4%). About 11% engaged in vaginal intercourse. Sexual activity lasted from 1 to 10 min for 42.7% of the respondents. Nearly half (49.1%) were traveling 61–80 mph during sex. Considering respondents' lifetime incidents of SWD, the most common driving errors reported were speeding (37.8%), drifting into another lane (36%), and letting go of the steering wheel (10.8%). Only 1.8% nearly had a crash, and none actually had a crash. Separate regression analyses for male and female respondents revealed that lower intentions to engage in SWD in the future were associated with higher estimates of the probability of a car crash. The authors consider SWD to be an under-reported in-vehicle distraction and encourage more research and prevention efforts.

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ABSTRACT

In what may be the first in-depth study of sexual activity as a driving distraction in the US, a sample of 195 male and 511 female college students at a Midwestern university (*M* age = 19.7) participated in an on-line study of sex while driving (SWD). Of these, 64 (32.8%) men and 47 (9.3%) women had engaged in sex while driving (SWD). Nine percent of men and 29% of women had engaged in SWD as a passenger. In most recent SWD incidents, respondents reported that the two most common acts were oral sex (70.3%) and genital touching (60.4%). About 11% engaged in vaginal intercourse. Sexual activity lasted from 1 to 10 min for 42.7% of the respondents. Nearly half (49.1%) were traveling 61–80 mph during sex. Considering respondents' lifetime incidents of SWD, the most common driving errors reported were speeding (37.8%), drifting into another lane (36%), and letting go of the steering wheel (10.8%). Only 1.8% nearly had a crash, and none actually had a crash. Separate regression analyses for male and female respondents revealed that lower intentions to engage in SWD in the future were associated with higher estimates of the probability of a car crash. The authors consider SWD to be an under-reported in-vehicle distraction and encourage more research and prevention efforts.

be related to speeding and losing control of the vehicle (Braitman et al., 2008). Another unknown is the extent to which drivers and passengers having sex in vehicles act as distractors to other drivers on the roadway.

We think that modest prevention efforts could be easily and effectively accomplished. While texting while driving is viewed as risky but socially acceptable (Atchley et al., 2012), sex while driving appears to be viewed as risky and socially unacceptable. Depending upon state and local statutes, sex while driving may be against the law as a category of public lewdness (Criminal Defense Lawyer, 2013). Basic strategies to remind young people of the accident potential and possible illegality of sex while driving may be sufficient to decrease the behavior. One approach would be to include the dangers of sex while driving in high school health and sex education classes. Prevention messages should be aimed at both boys and girls, as about 30% of the women in our study had had sex in

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Lee, J.D.,

J Sex Med 2011;8:931–935

EDITORIAL

Love Protects Lover's Life

In sexual medicine, transforming the typical physician–patient relationship into a physician–couple relationship, focusing on the psychosocial fundamental needs and complaints of the couple, is mandatory. We know from reading *The Journal of Sexual Medicine (JSM)* that cardiovascular disease (CVD) is responsible for a significant number of

behaviors [8]. Accordingly, epidemiological st
showed lower morbidity and mortality rate
married compared with unmarried men, c
attention to the association between marital
ables and health [9]. Evidence from several ar
published over the last decades, particu
marital interaction studies, suggest that d

	0.10
3.5)	1.6 (0.7 to 3.3)
2.8)	1.5 (0.8 to 3.0)
	1.0
	0.27

e, smoking, coronary heart disease at
oronary heart disease also adjusted for

se, and other causes were
nt was steepest for deaths
Adjusting for social class,
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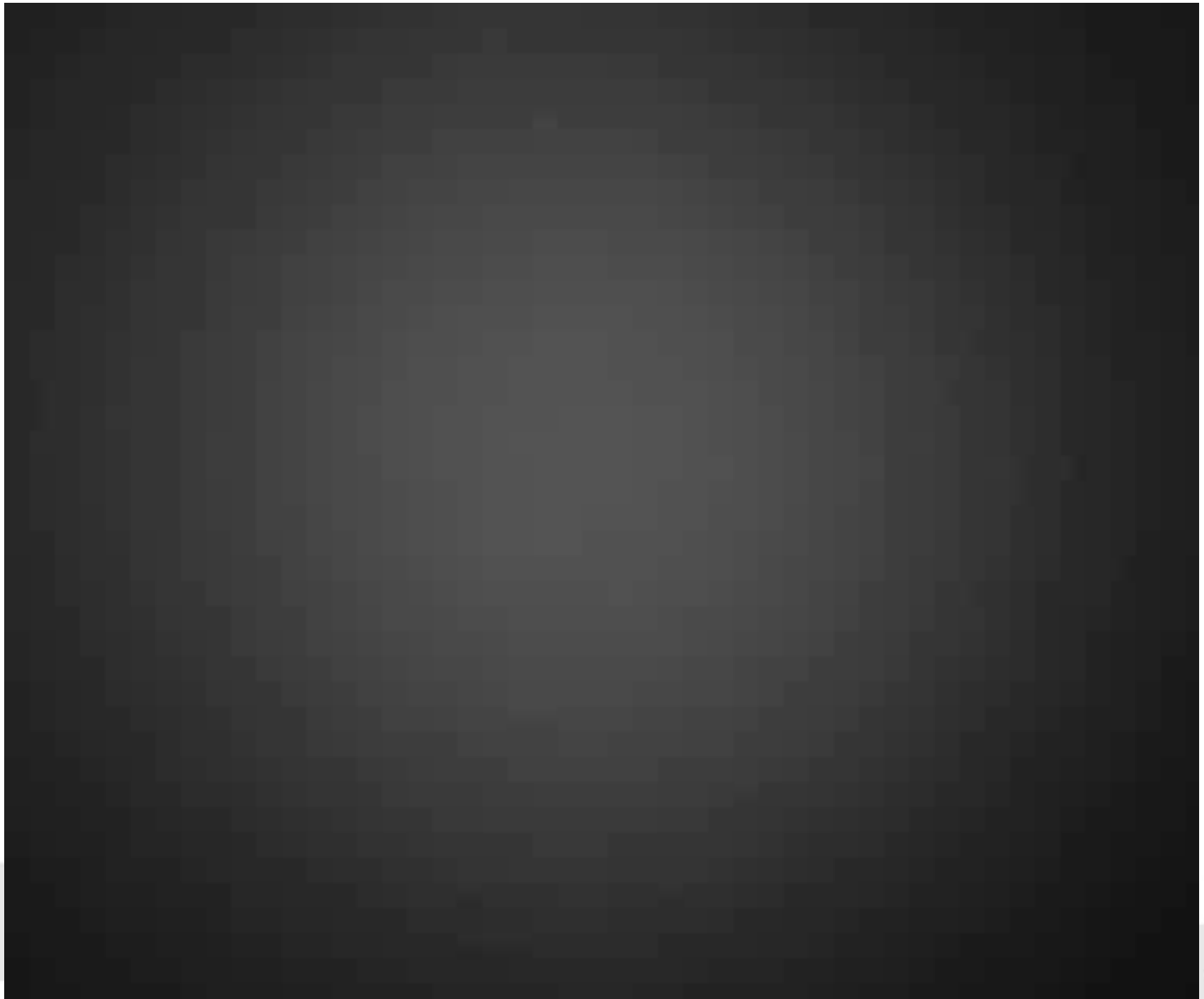
uated the associations to a
2).

create strong, apparently "independent," associations between risk factors and mortality.[22] However, the association between frequency of orgasm and mortality in the present study is at least—if not more—convincing on epidemiological and biological grounds than many of the associations reported in other studies[23-25] and deserves further investigation to the same exten

Intervention programmes could also be considered, perhaps based on the exciting "At least five a day" campaign aimed at increasing fruit and vegetable consumption[26]—although the numerical imperative may have to be adjusted. The disappointing results observed in health promotion programmes in other domains[27] may not be seen when potentially pleasurable activities are promoted.

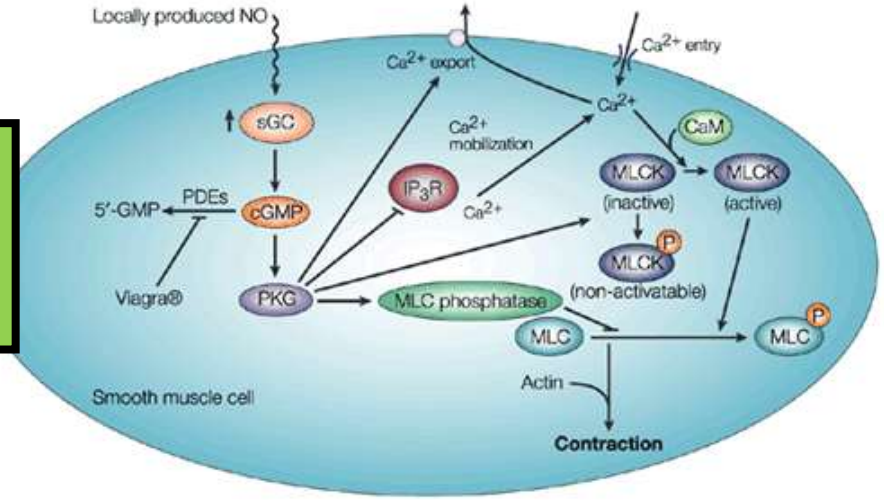
SYSTEMS PLAN

Nitric Oxide Testing



Viagra® Prolongs And Enhances The Effects Of Nitric Oxide

Nitric Oxide

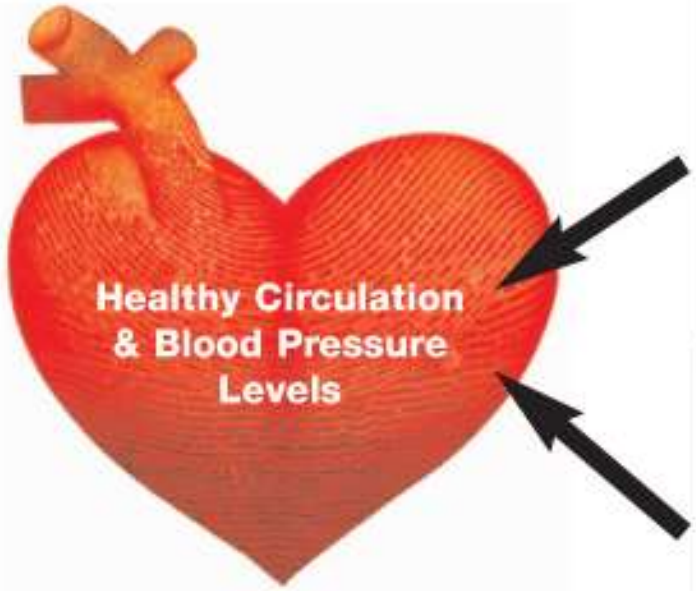


Nature Reviews | Molecular Cell Biology

- If Viagra does not help, you are producing no Nitric Oxide

SYSTEMS PLAN

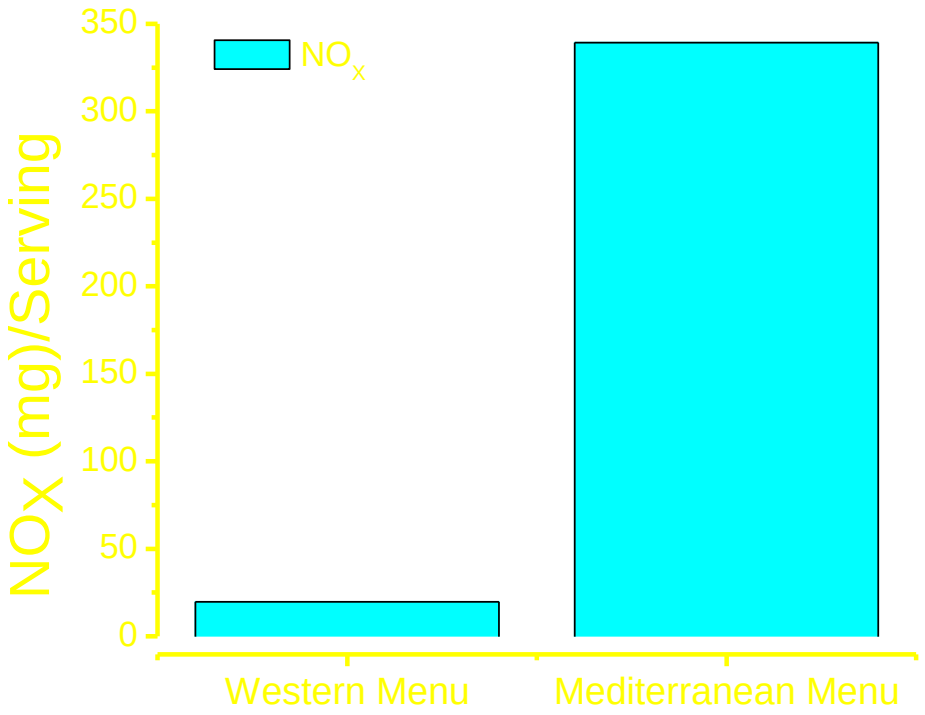
Two Pathways to Produce Nitric Oxide



Pathway	Increased with	Affected by age?
Intake from salivary glands 	Healthy diet having NO potential 	No
Produced by endothelium 	Regular exercise 	Yes Endothelial production declines to 50% of what one needs by age 40. Even exercise cannot restore it all.

Can Diet Change Your NOx Levels?

Western Diet Mediterranean Diet

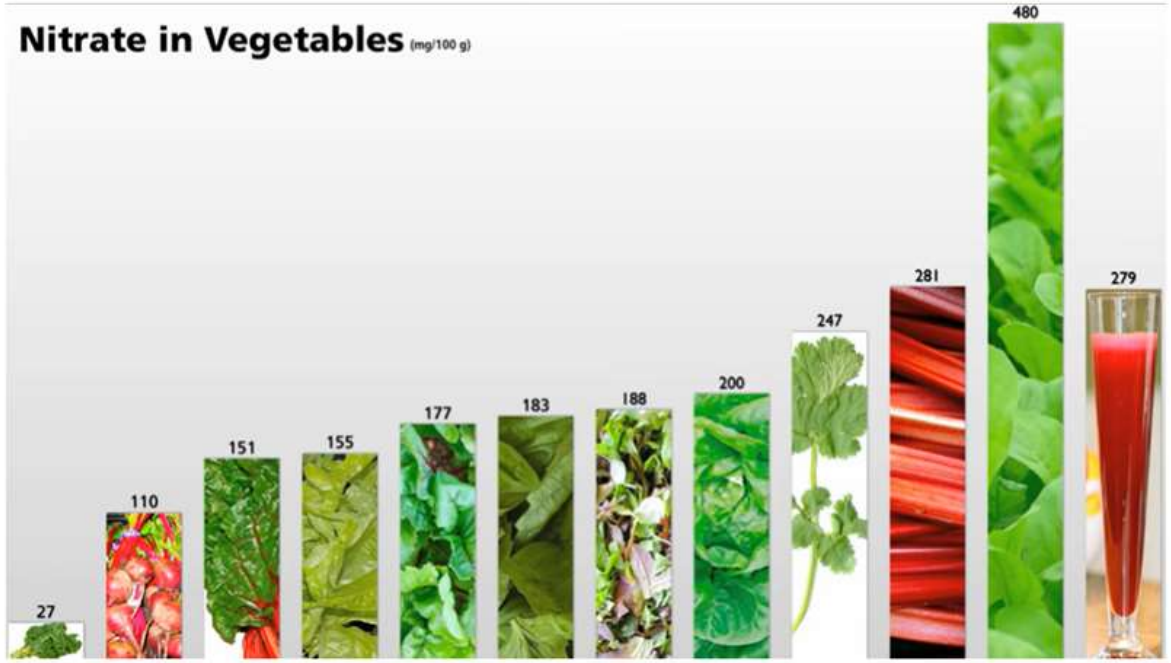


	Western Menu	Mediterranean Menu
Breakfast	Bagel w/ Cream Cheese Black Coffee (12 oz)	Toast w/ Jam and Butter Cappuccino (Espresso+Milk)
AM Snack	Carrot Nut Muffin Diet Coke (12 oz)	Yogurt (Strawberry) Carrot Juice (12 oz)
Lunch	Big Mac Large French Fries Diet Coke (12 oz)	Mediterranean Wrap Garden Vegetable Soup Mineral Water (12 oz)
PM Snack	Snickers Black Coffee (12 oz)	Trail Mix Orange Juice (12 oz)
Dinner	Cheese Pizza (4 slices) Diet Coke (12 oz)	Salmon (Smoked) Red Wine (12 oz)

H. Garg, Master's Thesis

SYSTEMS PLAN

Nitrates in Vegetables



- Beets 110
- Raw beet juice 279
- Rhubarb 281
- Arugula 480

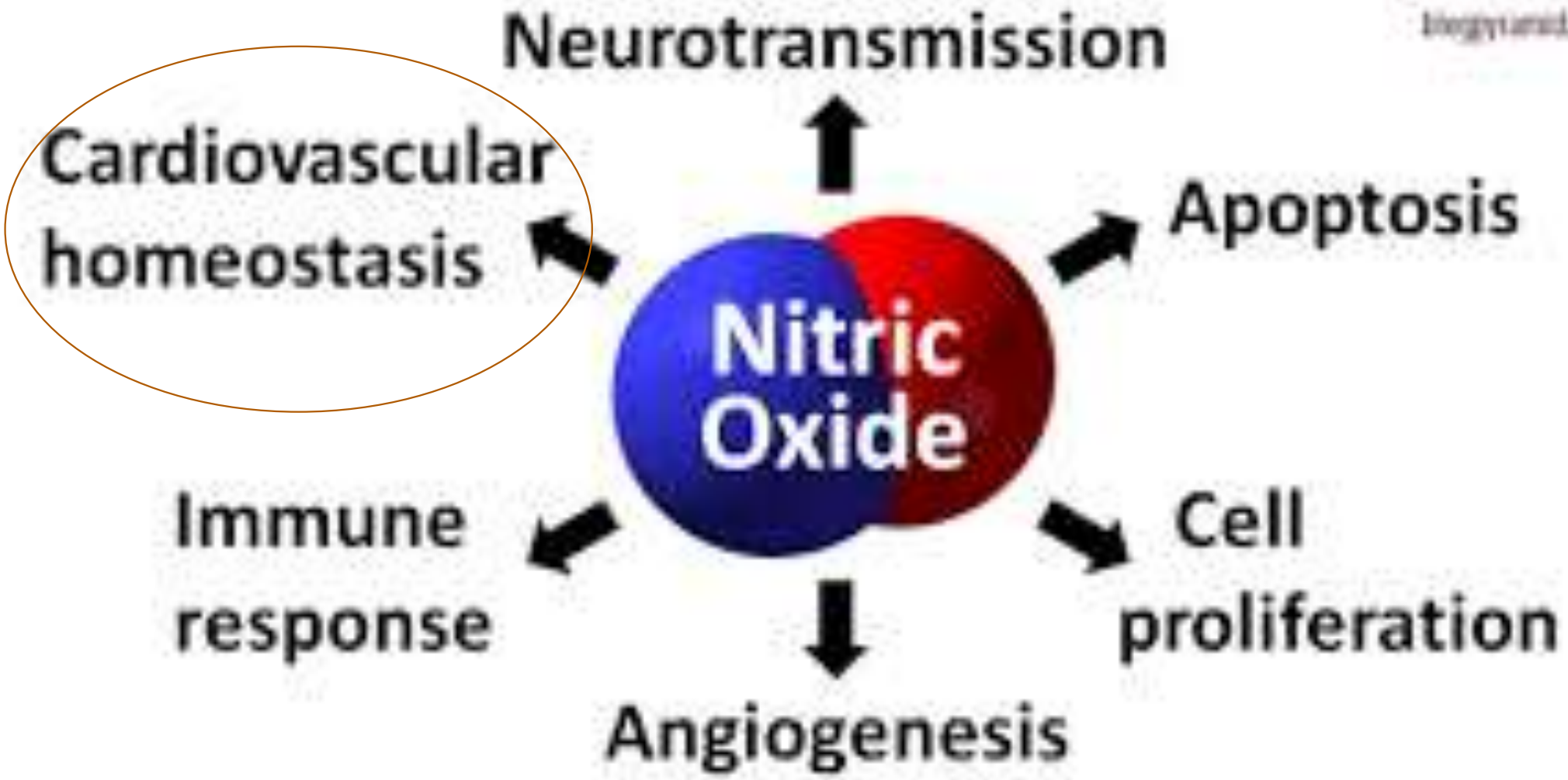
7 SYSTEMS PLAN

Best Foods To Increase Nitric Oxide

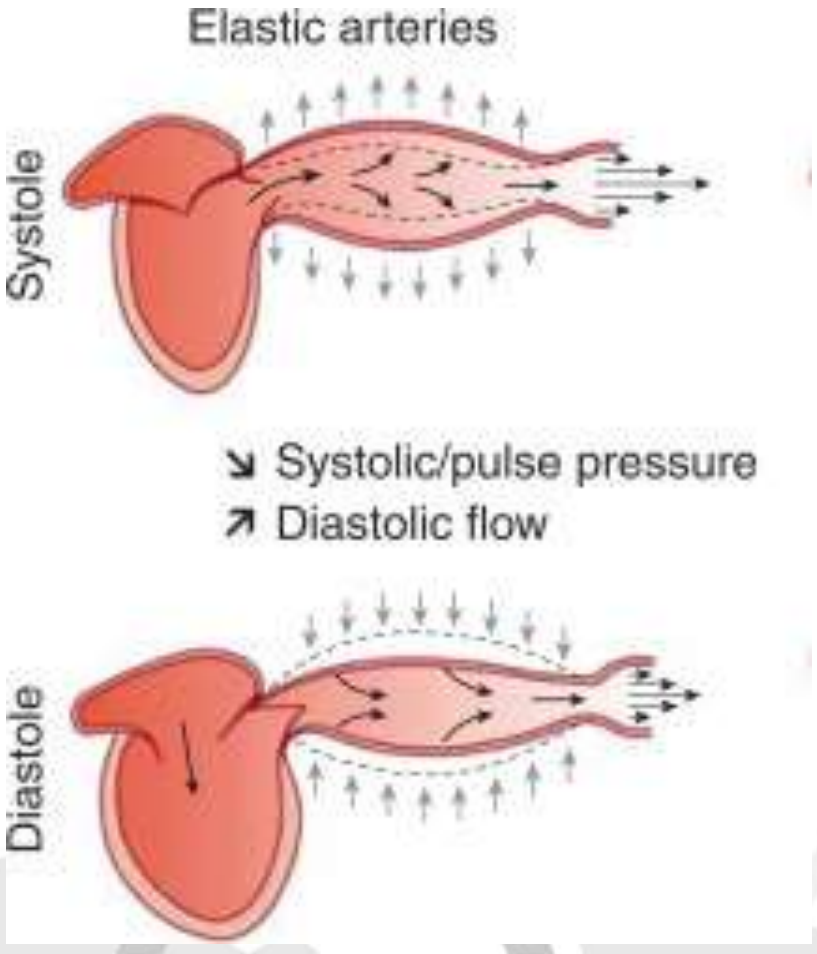
Kale	**6825**
Swiss Chard	**2055**
Arugula	**1452**
Spinach	**1123**
Chicory	**938**
Wild Radish	**814**
Bok Choy	**775**
Collard Greens	**697**
Beets	**632**
Chinese Cabbage	**499**
Lettuce	**388**
Cabbage	**312**
Mustard greens	**226**
Cauliflower, Raw	**167**
Parsley	**150**
Kohlrabi	**136**
Carrot	**127**
Broccoli	**122**

- Eat your green leafy vegetables

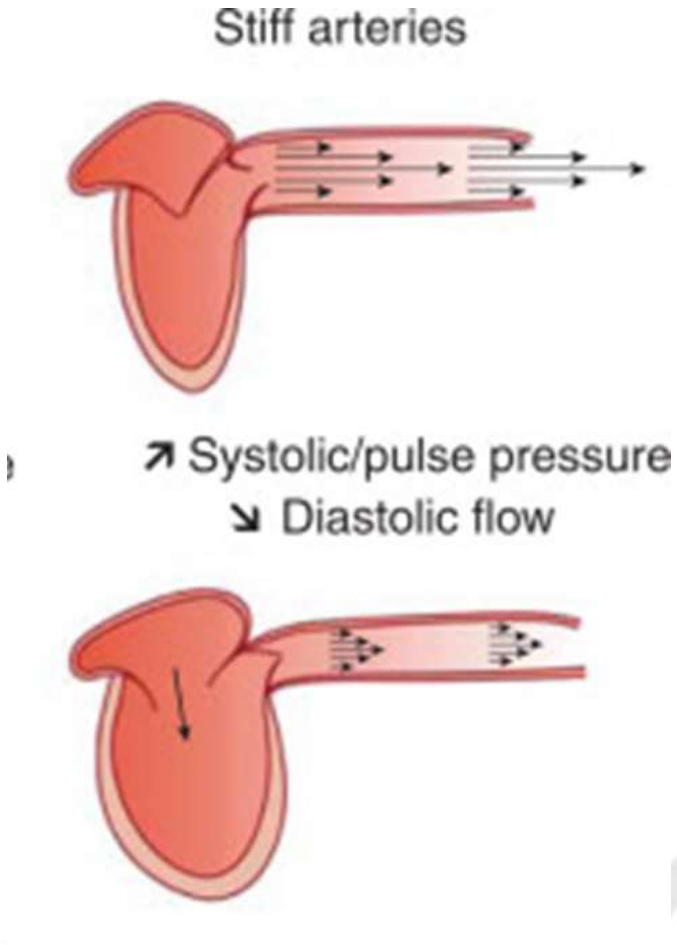
SYSTEMS PLAN


Neurotransmission
Cardiovascular homeostasis
Apoptosis
Nitric Oxide
Immune response
Cell proliferation
Angiogenesis

Healthy Artery

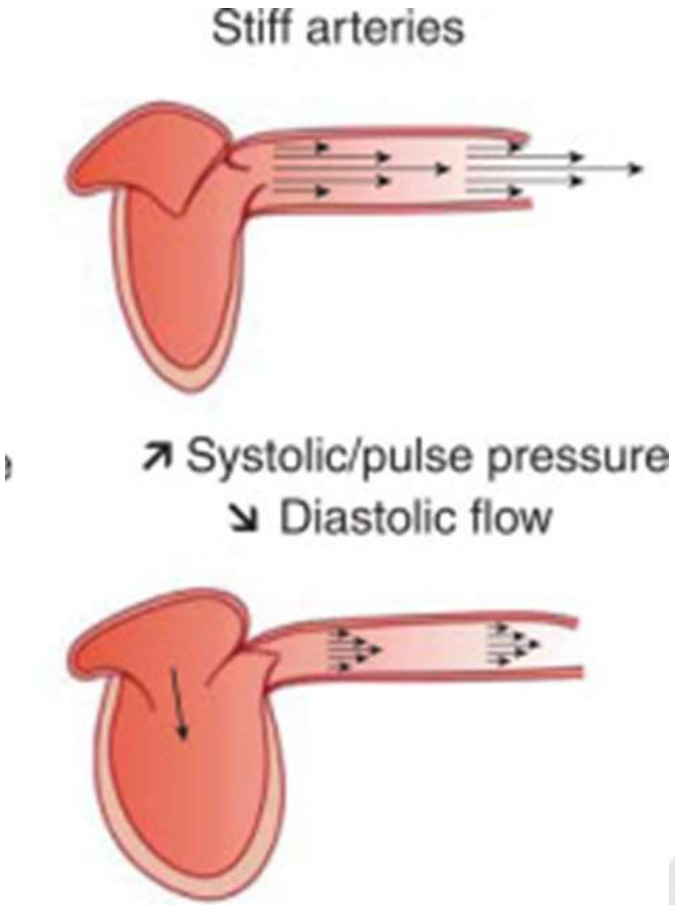


Sick Artery

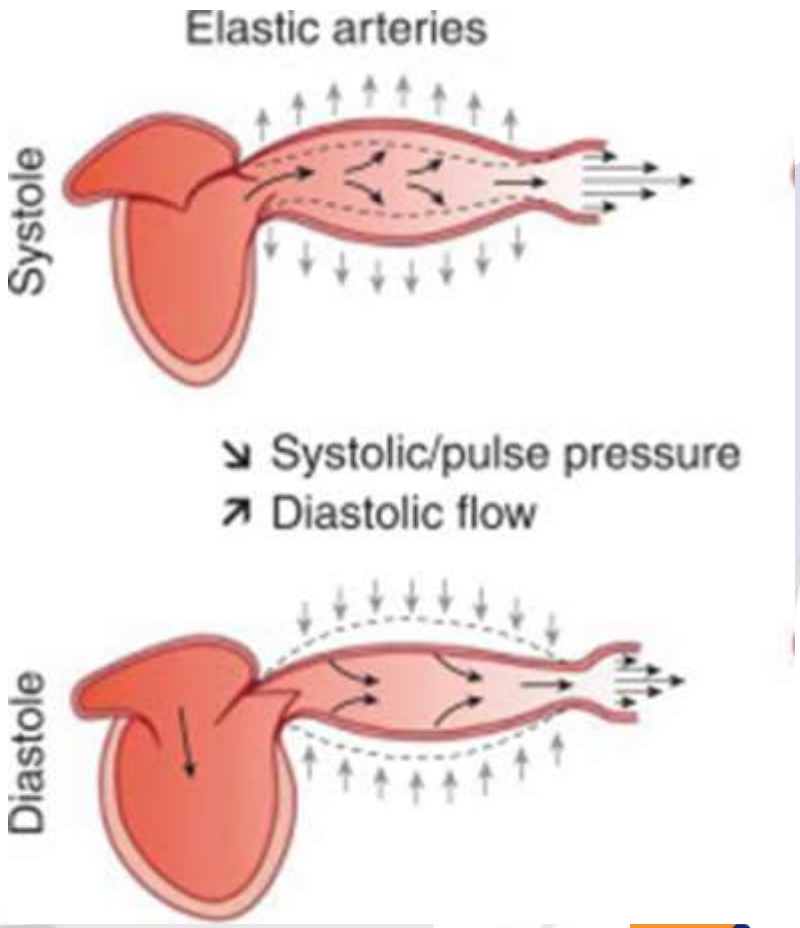


SYSTEMS PLAN

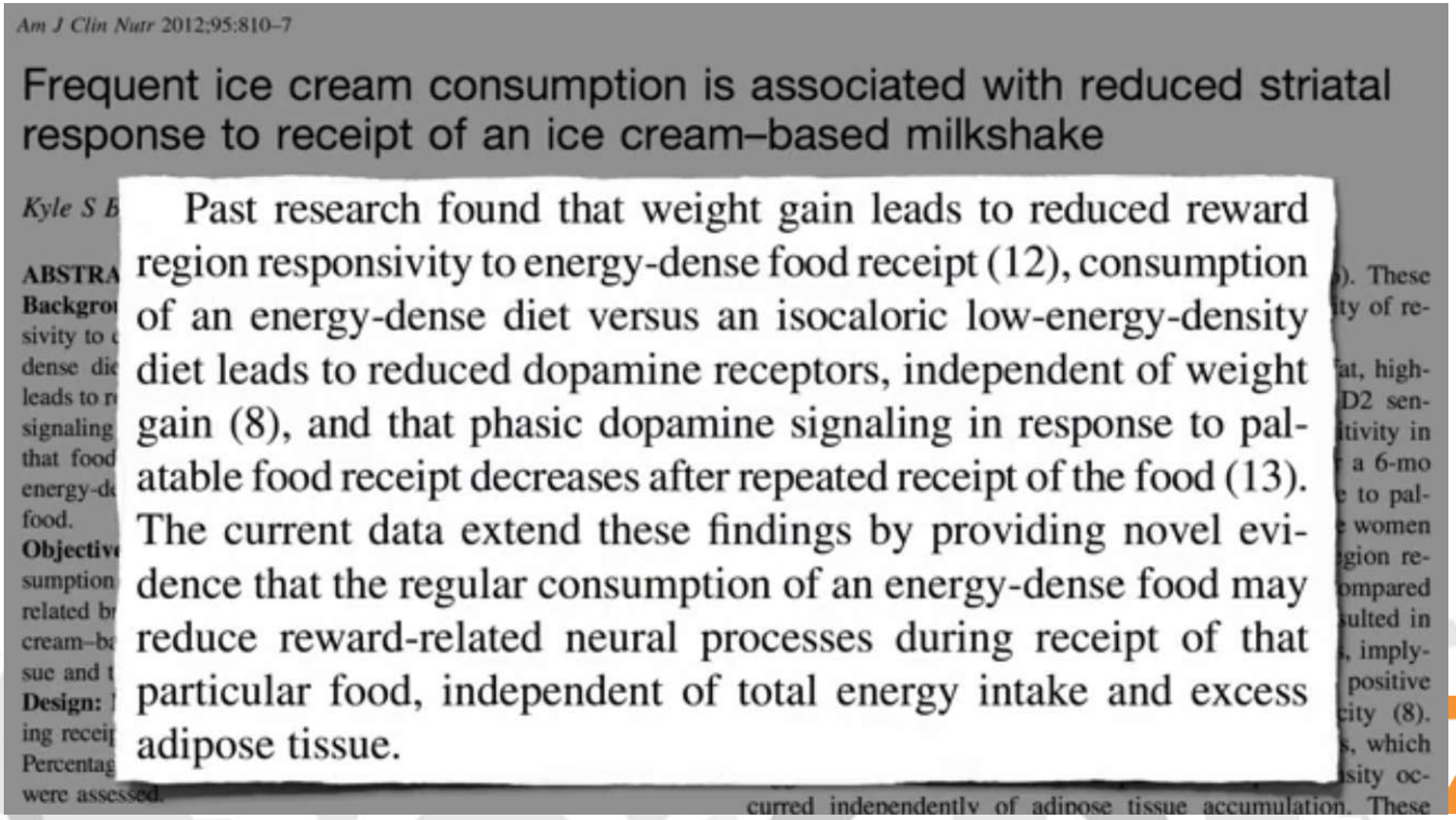
Recent Experiment



Added?


Elastic arteries
Systole
↘ Systolic/pulse pressure
↗ Diastolic flow
Diastole

Repeated Use Of Energy Dense Foods Reduces Reward Response



Am J Clin Nutr 2012;95:810–7

Frequent ice cream consumption is associated with reduced striatal response to receipt of an ice cream–based milkshake

Kyle S B

ABSTRA
Backgro
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dense die
leads to r
signaling
that food
energy-d
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Objectiv
sumption
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sue and t
Design:
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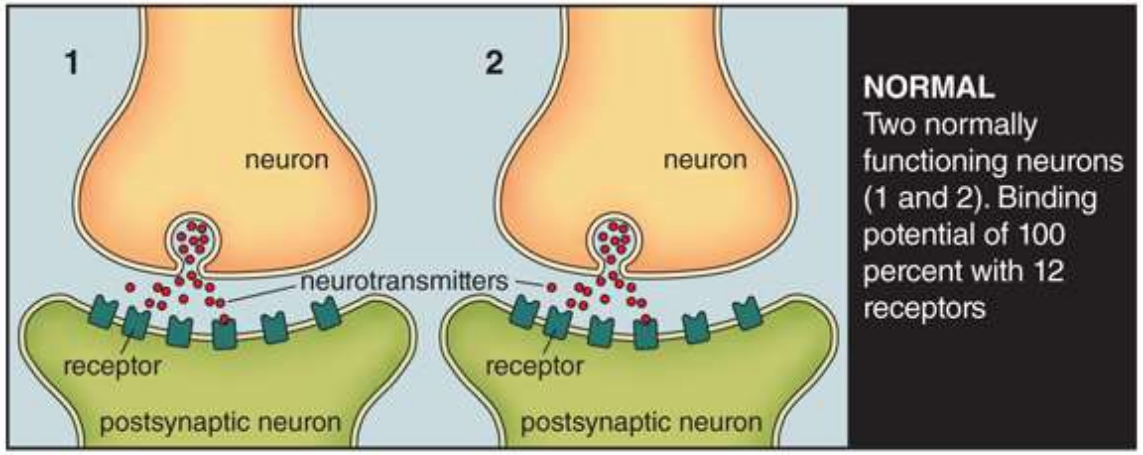
Past research found that weight gain leads to reduced reward region responsivity to energy-dense food receipt (12), consumption of an energy-dense diet versus an isocaloric low-energy-density diet leads to reduced dopamine receptors, independent of weight gain (8), and that phasic dopamine signaling in response to palatable food receipt decreases after repeated receipt of the food (13). The current data extend these findings by providing novel evidence that the regular consumption of an energy-dense food may reduce reward-related neural processes during receipt of that particular food, independent of total energy intake and excess adipose tissue.

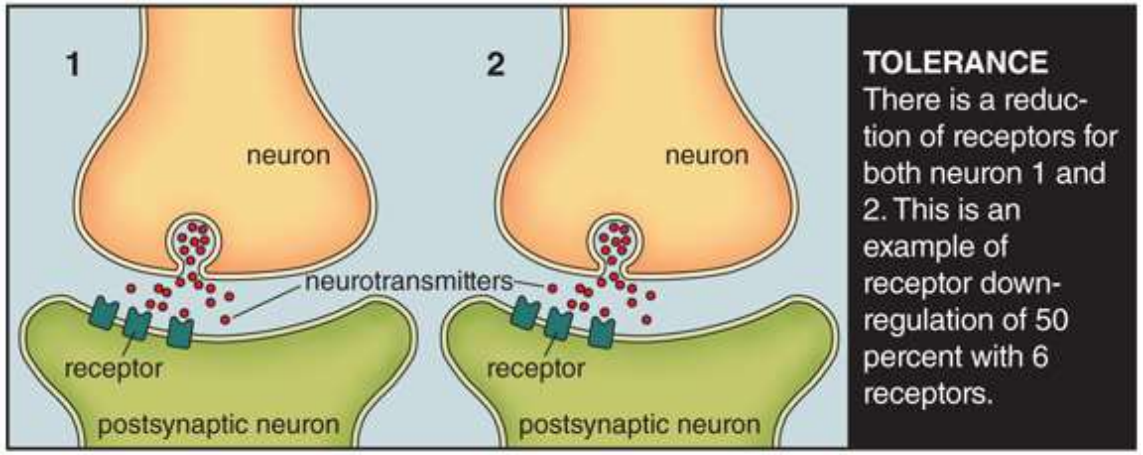
curred independently of adipose tissue accumulation. These

SYSTEMS PLAN

Decreased Pleasure- Enjoyment Of Everything



- Normal brain

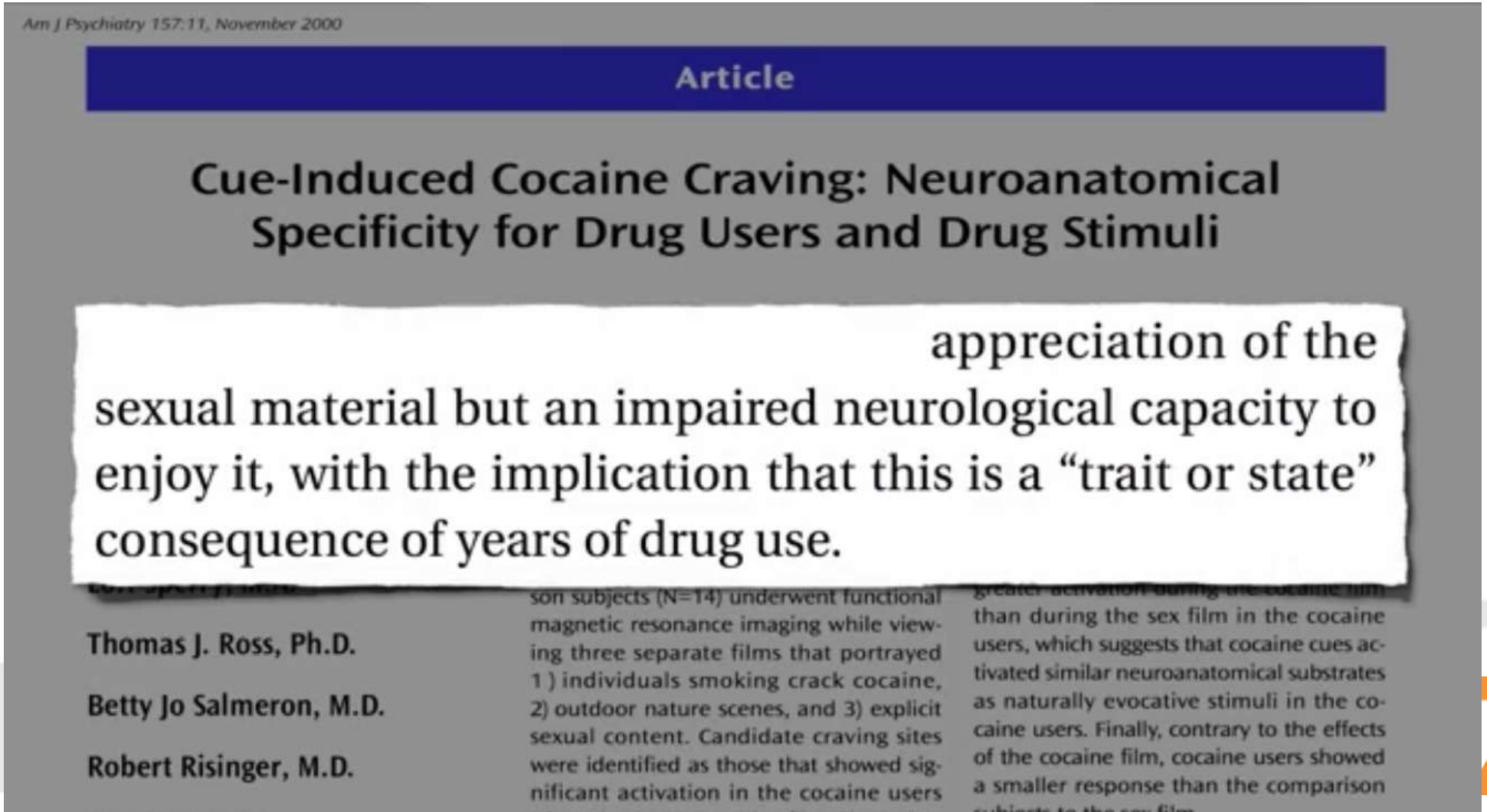


- Obese or addict brain

SYSTEMS PLAN

Decreased Ability To Enjoy Everything

Addicts Don't Enjoy Sex As Much



Am J Psychiatry 157:11, November 2000

Article

Cue-Induced Cocaine Craving: Neuroanatomical Specificity for Drug Users and Drug Stimuli

appreciation of the sexual material but an impaired neurological capacity to enjoy it, with the implication that this is a "trait or state" consequence of years of drug use.

Thomas J. Ross, Ph.D.

Betty Jo Salmeron, M.D.

Robert Risinger, M.D.

son subjects (N=14) underwent functional magnetic resonance imaging while viewing three separate films that portrayed 1) individuals smoking crack cocaine, 2) outdoor nature scenes, and 3) explicit sexual content. Candidate craving sites were identified as those that showed significant activation in the cocaine users

than during the sex film in the cocaine users, which suggests that cocaine cues activated similar neuroanatomical substrates as naturally evocative stimuli in the cocaine users. Finally, contrary to the effects of the cocaine film, cocaine users showed a smaller response than the comparison

SYSTEMS PLAN

The More You Weigh, The Less The Reward, The Less Pleasure

Obes Facts 2012;5:155–164

Brain PET Imaging in Obesity and Food Addiction: Current Evidence and Hypothesis

Patricia Iozzo[a] Le
Uberto Pagotto[b]

[a]Institute of Clinical Ph rinology
Unit, Department of C , Alma Mater
University of Bologna,

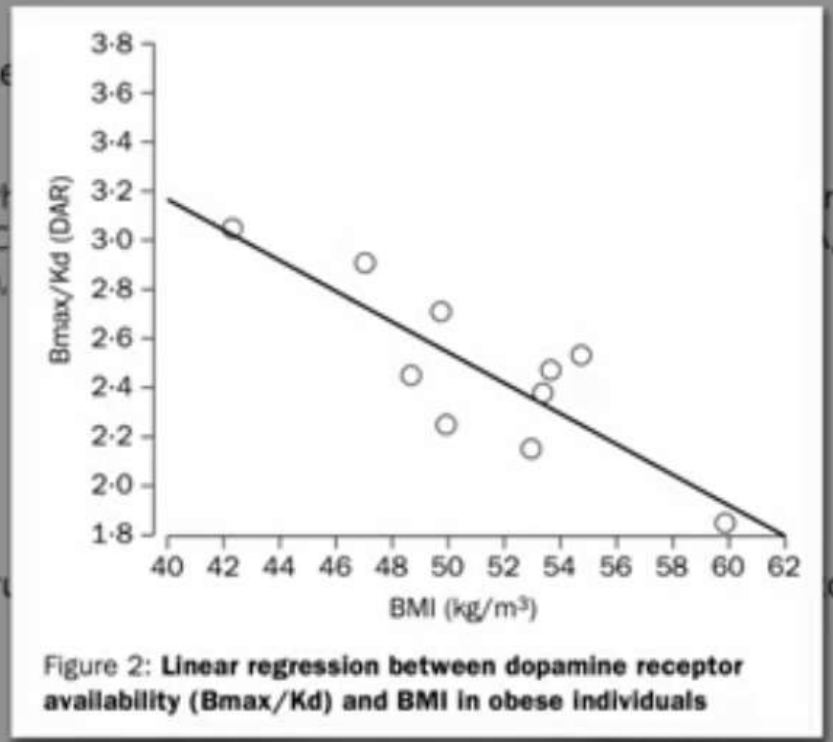


Figure 2: **Linear regression between dopamine receptor availability (Bmax/Kd) and BMI in obese individuals**

Key Words
Food addiction · Dru ose · 18F-FDG · Obesity

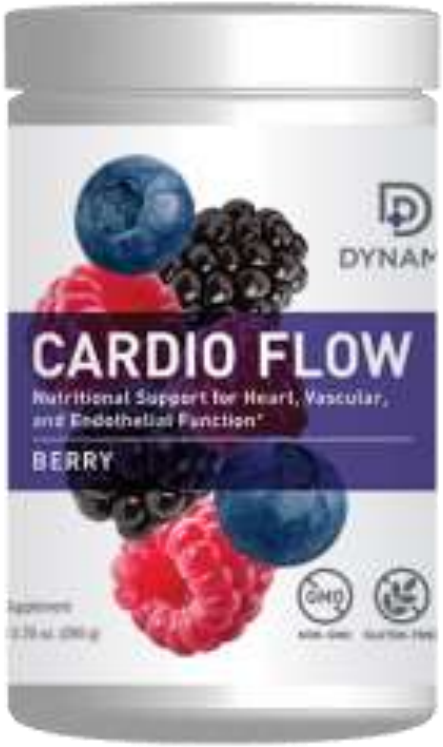
Abstract

Action Steps To Increase Nitric Oxide

- Have a healthy diet 7SP (increases Nitric Oxide)
- Exercise
- Sun light on skin
- Breathe through your nose (NO is produced when you breathe through your nose not your mouth)
- Avoid mouth wash (blocks production of NO in gut)
- Try Arginine (ED has been successfully treated with the amino acid Arginine)

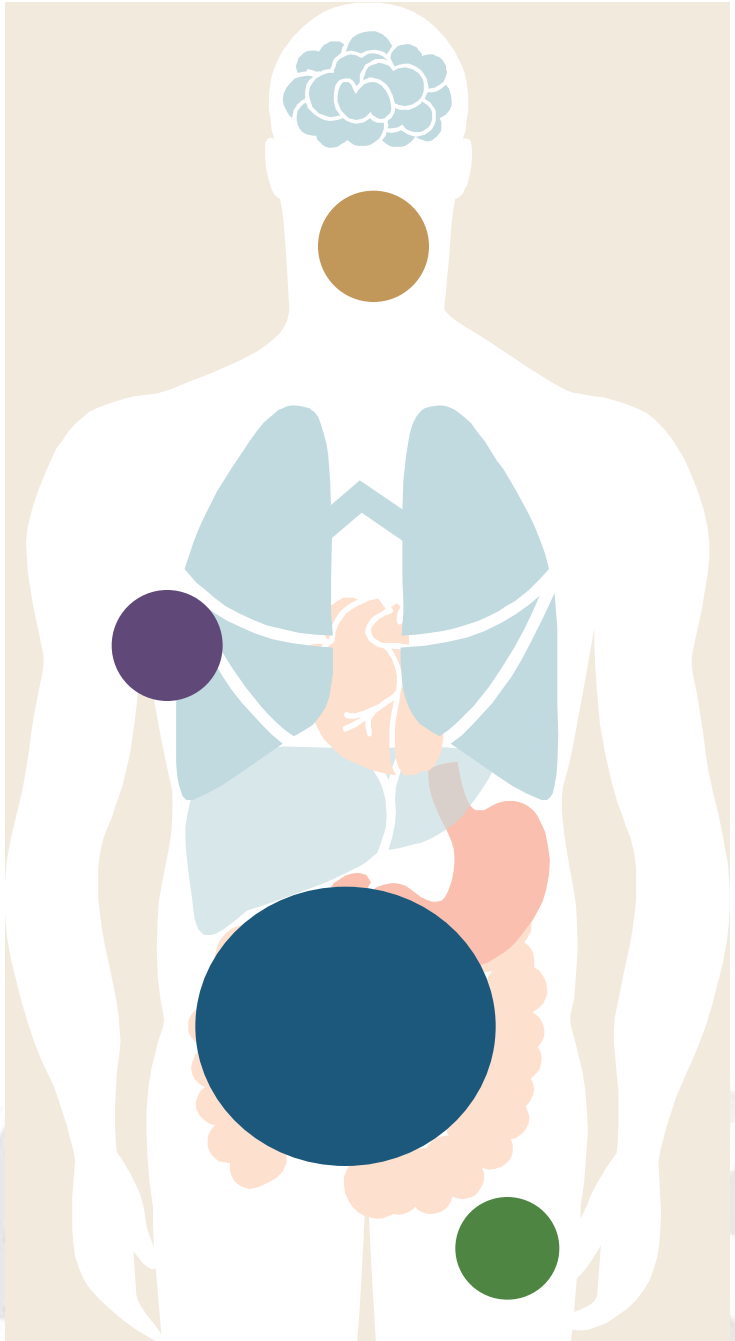
Support For Vessel Health and Nitric Oxide

- L-Arginine
- Beet Root Powder
- Taurine
- Magnesium



Deb

Chapter 6:
DEFENSE SYSTEM



1. Tonsils
2. Lymph
3. Bone Marrow
4. Gut Lymph Tissue

Startling Facts

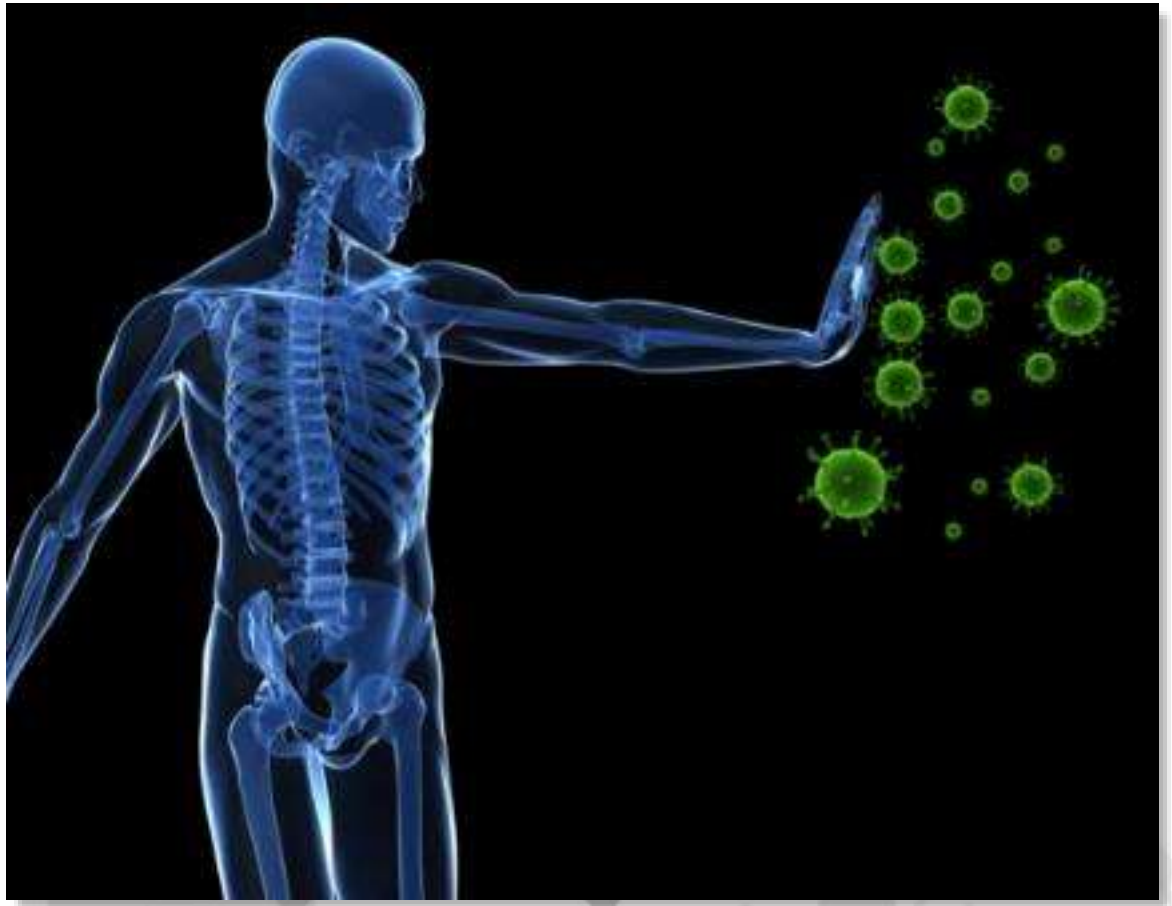
- Autoimmune diseases affect **8% of the population** (approximately 24 million Americans) and are the third leading cause of death.
- Silent inflammation affects up to **75%** of all Americans

"By 2050…antibiotic-resistant bacteria could kill an estimated **10 million** people each year. Shockingly, this would surpass even cancer."

—Julia Calderone

We Will Take A Close Look At This System

Defense System Balance



Under Function

- Colds • Infection
- Bronchitis • Flu

Over Function

- Allergies and Asthma
- Inflammation
- Autoimmune disease

7 SYSTEMS PLAN

Defense System

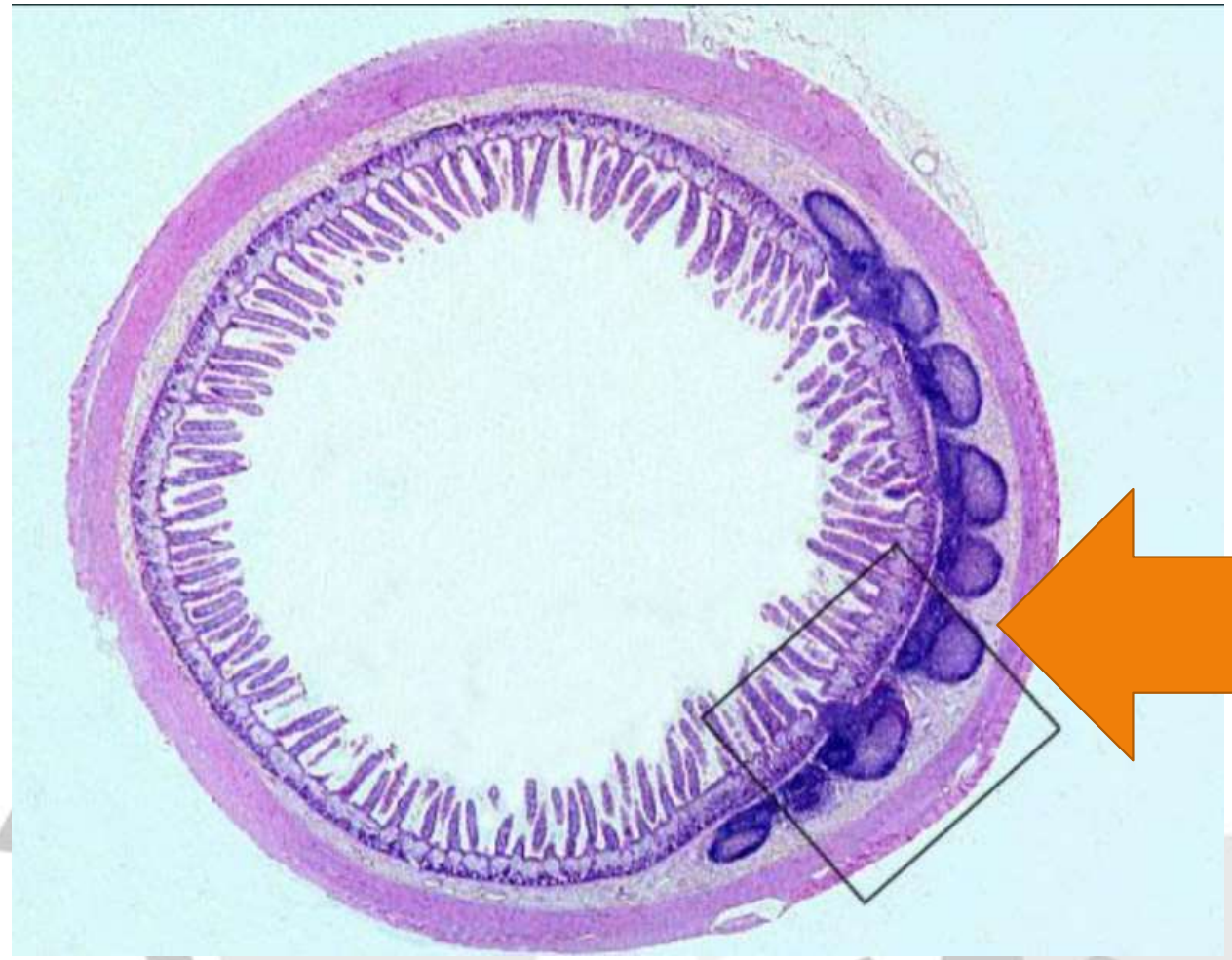
Patty

- Dx RA
- Pain in her feet so bad she cannot wear shoes
- Pain in her wrist - difficult to use her mouse
- Fearful of losing her job
- “Can change help?”

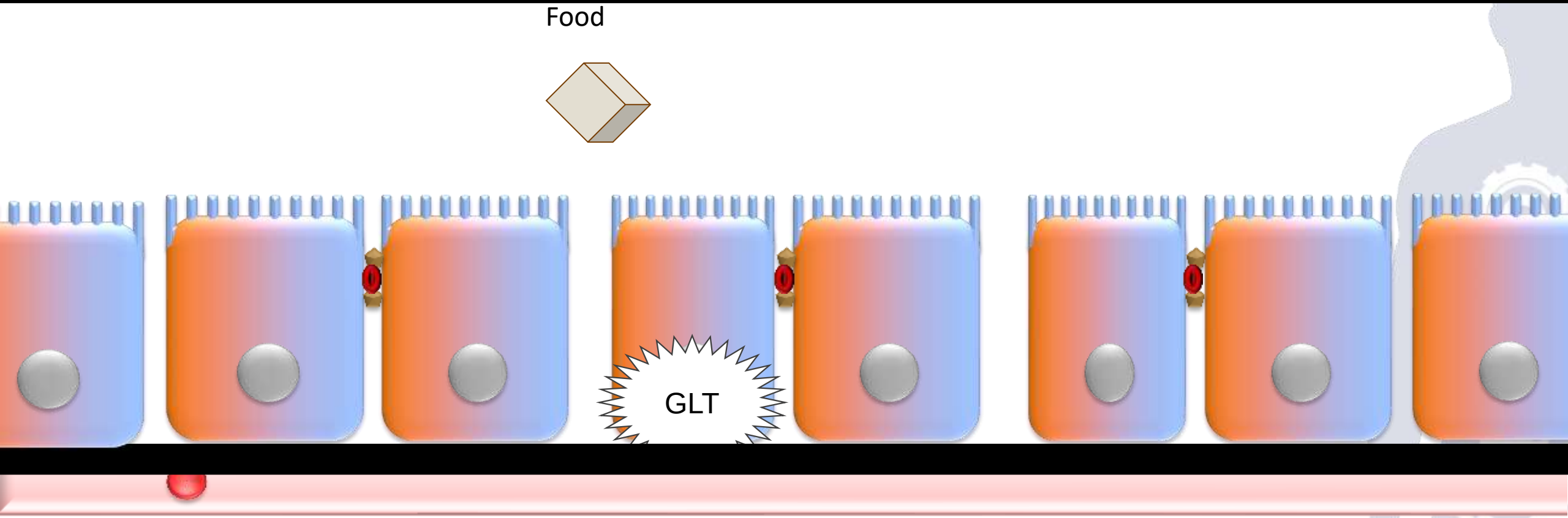
Drug Side Affects

- inflammation of the mouth and lips,
- nausea,
- vomiting,
- upset stomach,
- abdominal pain,
- dizziness,
- tired feeling,
- headache,
- bleeding gums,
- blurred vision, and
- leukopenia (low number of white cells in blood).
- stomach pain,
- loss of appetite,
- dark urine,
- jaundice (yellowing of the skin or eyes).
- dry cough,
- shortness of breath,
- diarrhea,
- white patches or sores inside your mouth or on your lips,
- blood in your urine or stools,
- urinating less than usual or not at all,
- fever,
- chills,
- body aches,
- flu symptoms,
- sore throat and headache with a severe blistering/peeling/red skin rash,
- pale skin,
- easy bruising or bleeding,
- weakness,
- clay-colored stools, or

Gut Lymphatic Tissue

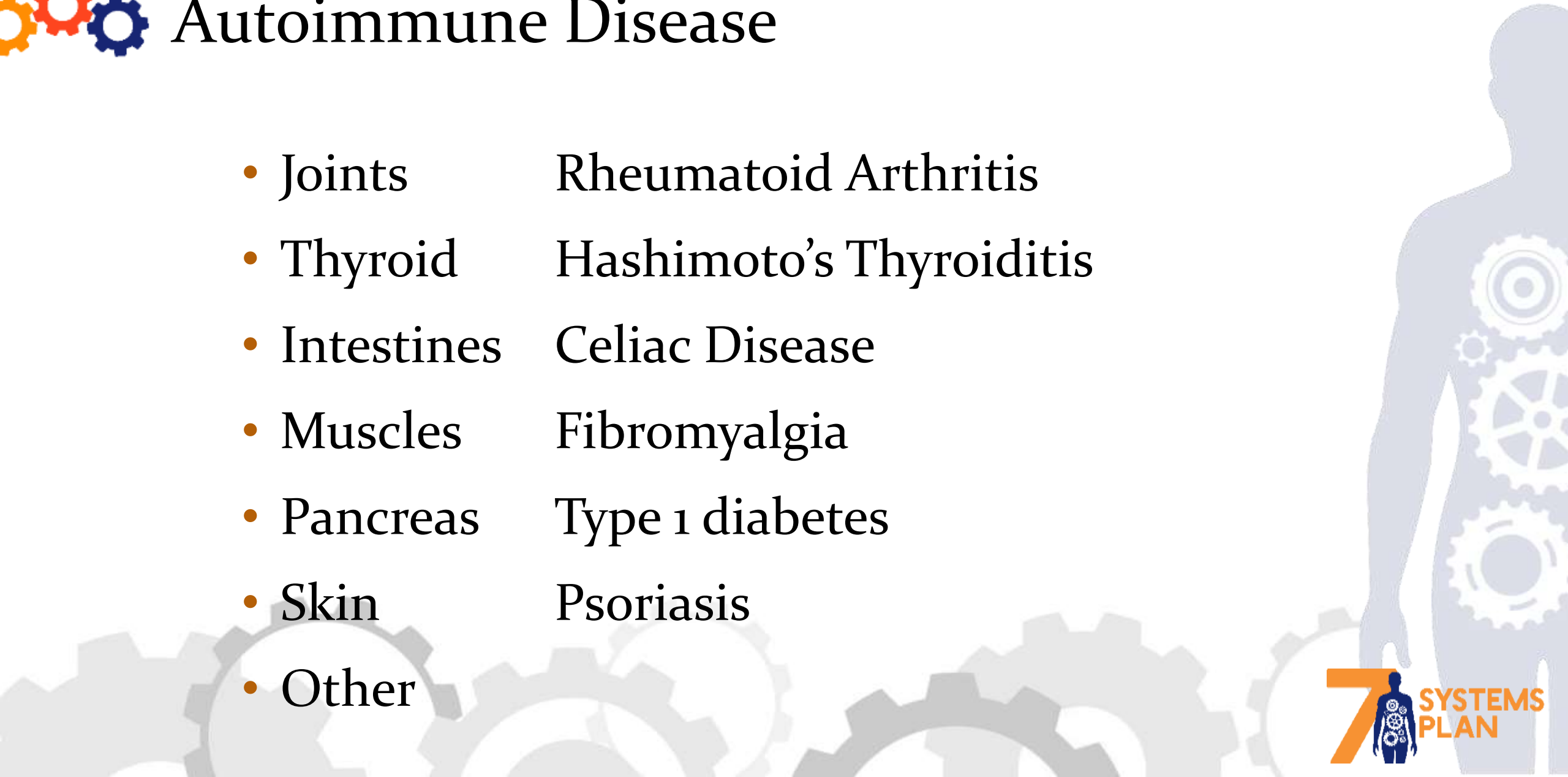


Unhealthy Gut (Leaky Gut)

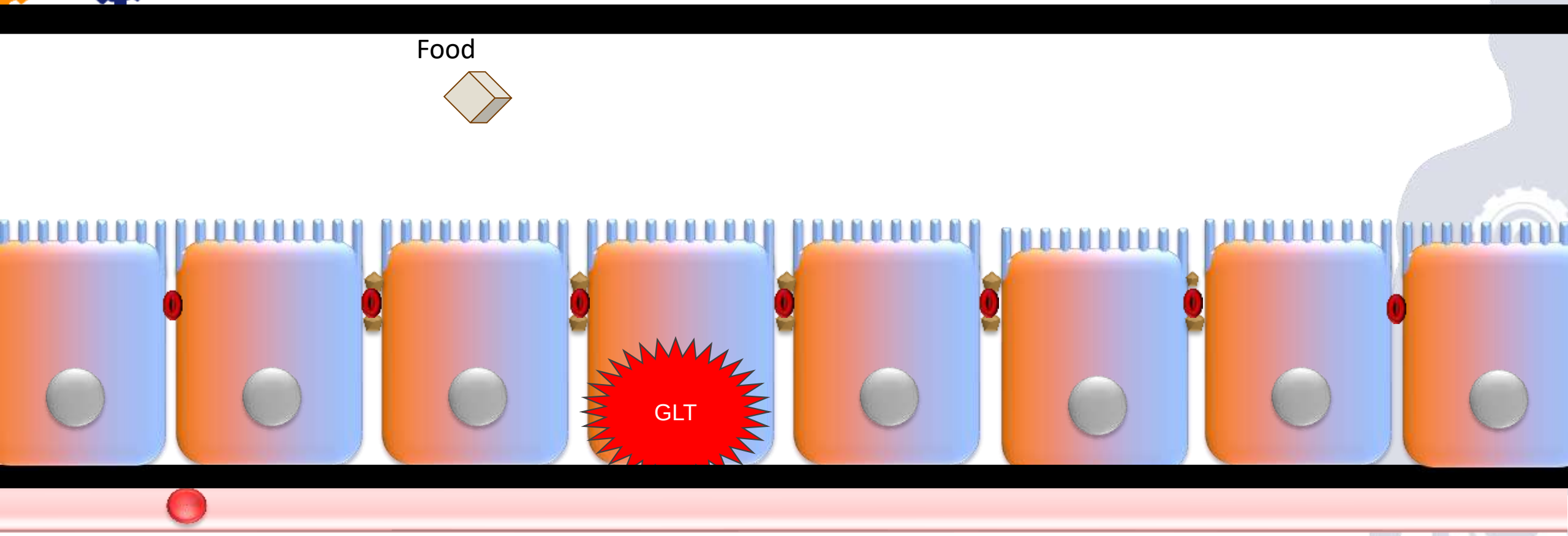


Autoimmune Disease

- Joints — Rheumatoid Arthritis
- Thyroid — Hashimoto's Thyroiditis
- Intestines — Celiac Disease
- Muscles — Fibromyalgia
- Pancreas — Type 1 diabetes
- Skin — Psoriasis
- Other



Healed Healthy Gut



Defense System

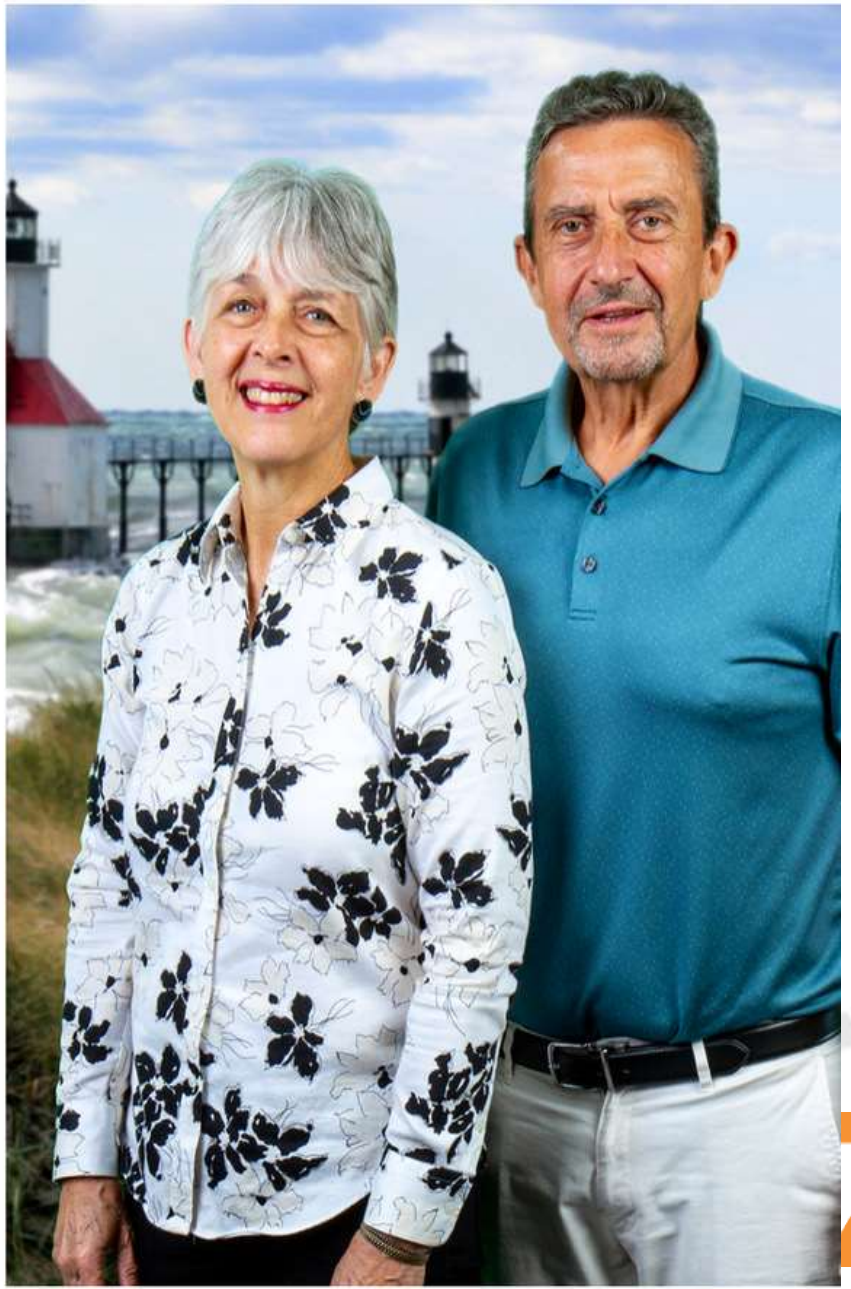
6 months later:
"I could only wear sandals because of the swelling in my feet from RA. My hands were so painful I could hardly do my job. Dr. Luse put me on his 7 Systems Plan. My RA and CTS are now gone and I have lost 65 lbs."

"I am convinced—you can make a difference in your health by the choices you make. I am so grateful for your guidance!"
Patti, Atlanta GA

7 SYSTEMS PLAN

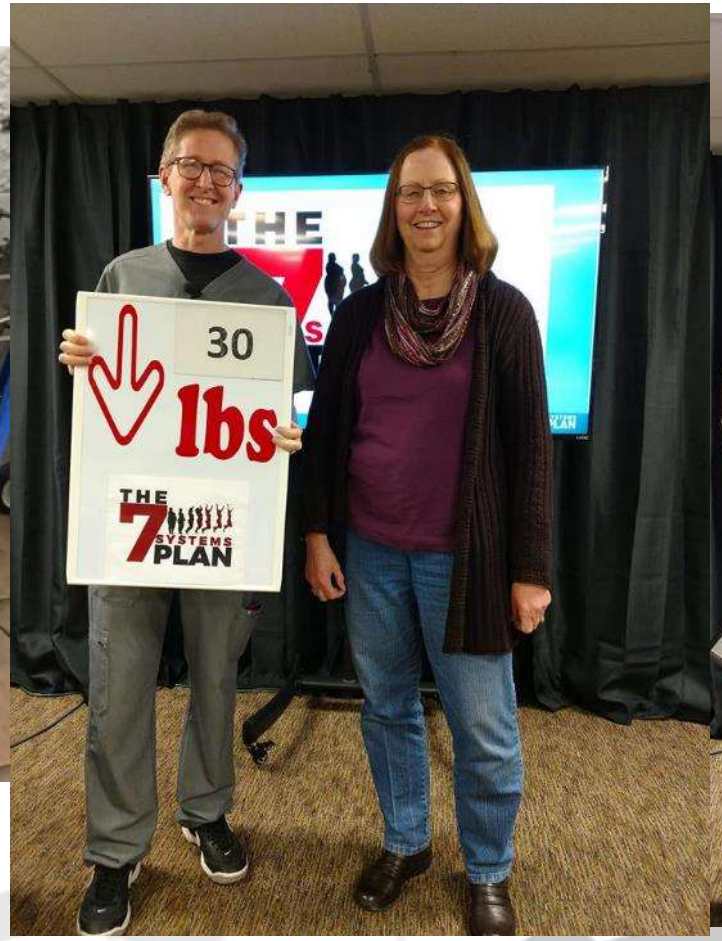
June 2018
242

June 2019
175



SYSTEMS PLAN

Marla- Fibromyalgia Gone



7 SYSTEMS PLAN

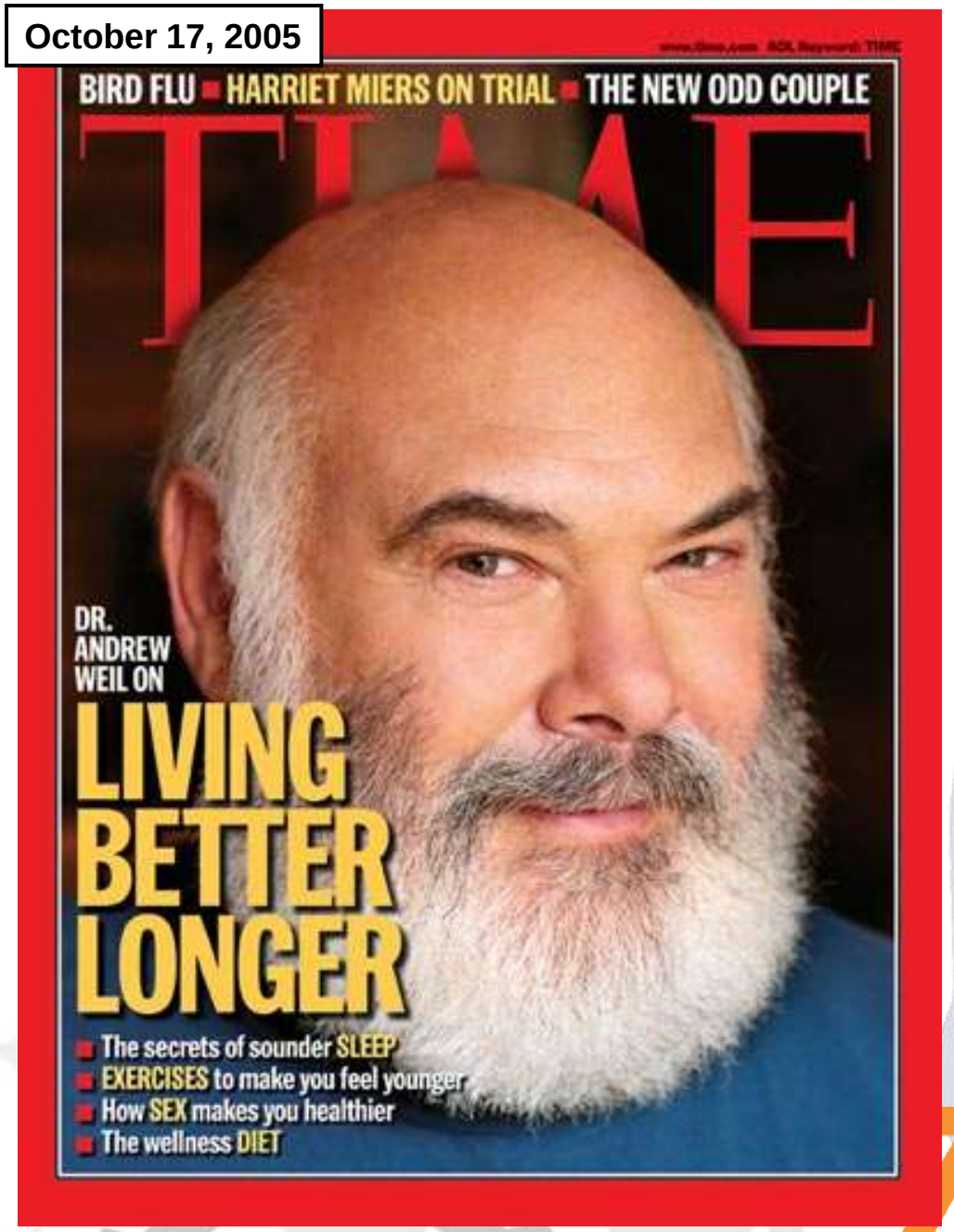
Kurt- Migraines Gone

SYSTEMS PLAN

Acute Inflammation Can Save Your Life

- Acute inflammation is the body's response to injury or serious illness or infection
- Most of the time, inflammation is a lifesaver.
- Enables our body to fend off disease–causing bacteria, viruses and parasites.

The word inflammation suggests "fire within," ... Normal inflammation is the healing system's response to localized injury and attack.



Time Magazine, October 17, 2005 p. 65

SYSTEMS PLAN

If a Shark Bites You, You Need Inflammation

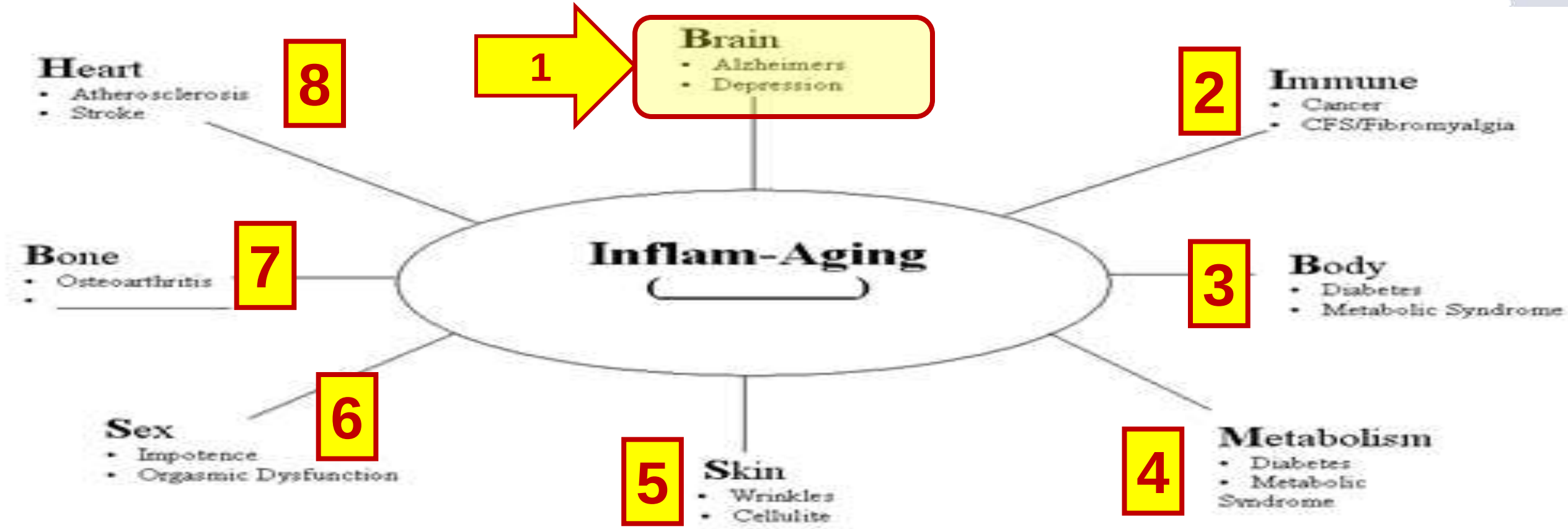
- Blood vessels constrict to stop bleeding
- Fibrinogen and clotting factors increase to stop bleeding
- White blood cells fight infection
- Pain reminds you “don’t swim with sharks”

Two Phases of an Immune Response

1. Initiation

2. Resolution

Chronic Disease is Inflammation



Inflammation is the Cause and the Effect of Illness and the Disease of Aging

Triggers for Inflammation

- Drugs
- Chemicals
- Stress
- Hormone imbalance
- Gut problems
- Diet
  - High sugar and omega 6

Omega-6 (Linoleic Acid)

- In **1909**, Americans ate **2 grams** a day of vegetable oil
- By **2010** they were eating an astounding **80 grams** of vegetable oil a day.
- **Now make up 63%** of the American diet
- Found in 600,000 processed foods sold in the U.S. today.
- **720 calories**, one-third of most people's calories
- YouTube June 13, 2020

2006 New Anti-obesity Drug

- Large randomized trials with **Rimonabant** have demonstrated efficacy in treatment of overweight and obese individuals with weight loss significantly greater than a reduced calorie diet alone.

Other Benefits

- Cardiometabolic:
  - increased levels of HDL
  - reduced triglycerides
  - reduced weight circumference
  - improved insulin sensitivity
  - decreased insulin levels
  - improvements in HBA1C

Mechanism

- **Blocks the metabolism of seed oils** in your body
- **Blocks the endocannabinoid system that cause overeating** (the opposite of munchies)
- (**LA stimulates** the endocannabinoid system)

One Side Effect

- Caused people to want to kill themselves
- Withdrawn from the market

A Better Way Than Drugs

- Stop eating seed oils and eliminate the munchies

YouTube June 13, 2020

Cure AMD Foundation 2020

Metabolic Syndrome and Related DisordersVol. 17, No. 1

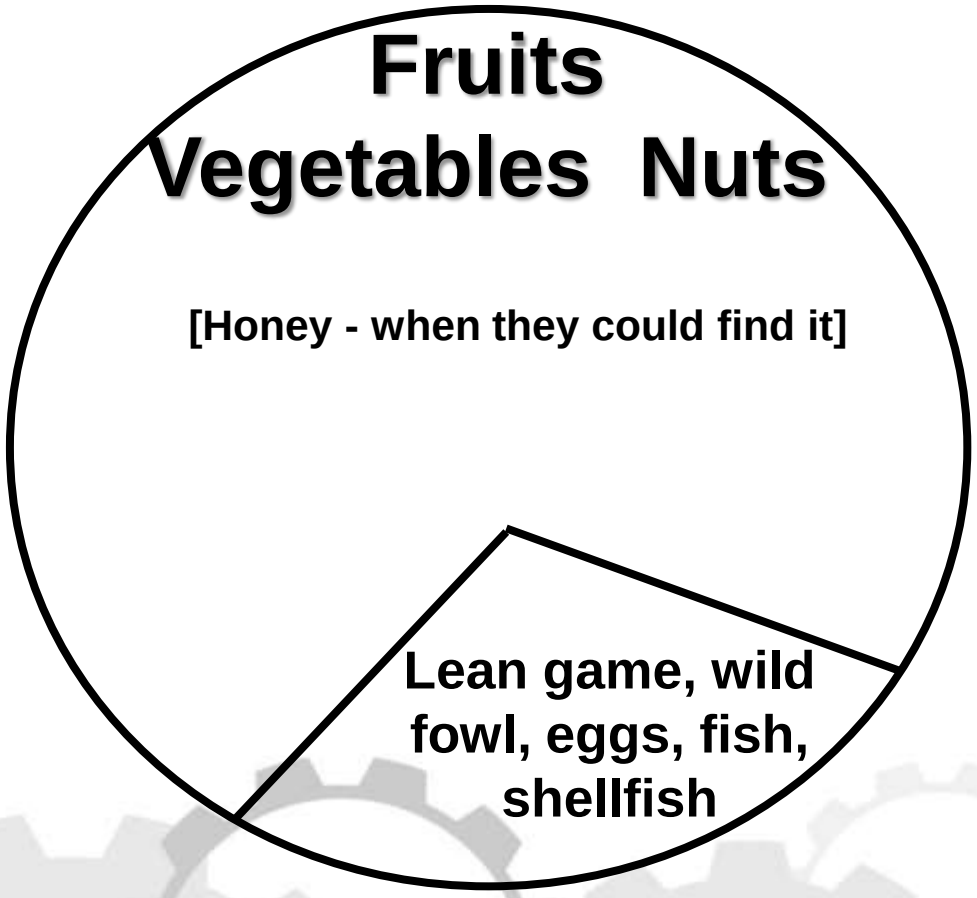
7 Steps to Eliminate Inflammation

1. Calorie restriction
2. **An anti-inflammatory diet**
3. Fix your gut
4. Omega 3, PRMs and D3
5. Exercise
6. Control stress
7. Sleep

Anti-inflammatory Diet:

- Historically, human diets were *naturally* anti-inflammatory.
- Degenerative, inflammatory diseases were not present!

Historical anti-inflammatory diet



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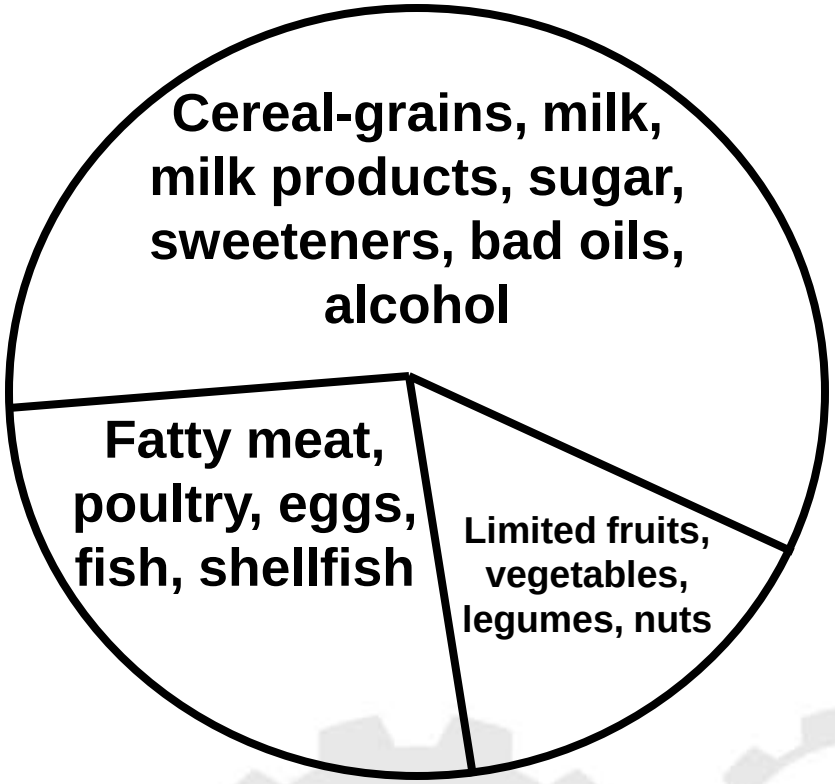
Modern pro-inflammatory diet



Eaton SB, Cordain L. Old genes, new fuels: nutritional changes since agriculture. World Rev Nutr Diet 1997; 81:26-37

7 SYSTEMS PLAN

Polymeal - Brit Med Journal, 2004

Researchers reviewed the literature on dietary factors and the expression of heart disease, which is an inflammatory condition.

They came up with a diet plan called the "**polymeal**," which is estimated to **reduce the expression of heart disease (inflammation) by more than 76%.**

What was in that meal?

Franco OH, Bonneux L, de Laet C, Peeters A, Steyerberg EW, Machenbach JP. The polymeal: a more natural, safer, and probably tastier (than the polypill) strategy to reduce cardiovascular disease by more than 75%. Brit Med J 2004; 329:1447-50

SYSTEMS PLAN

Polymeal Ingredients % reduction in CVD

Fish (4 oz 4xs/wk)

Fruit/veggies (400 g/d)

Garlic (2.7 g/d)

Wine (150 ml/day)

Dark Choc (100 g/d)

Almonds (68 g/d)

Combined effect 76%

Pick the winner

Franco OH et al. The Polymeal: a more natural, safer, and probably tastier (than the Polypill) strategy to reduce cardiovascular disease by more than 75%. BMJ. 2004; 329:1447-50

SYSTEMS PLAN

Polymeal Ingredients % reduction in CVD

Fish (4 oz 4xs/wk)	14% (8-19%)
Fruit/veggies (400 g/d)	21% (14-27%)
Garlic (2.7 g/d)	25% (21-27%)
Wine (150 ml/day)	32% (23-41%)
Dark Choc (100 g/d)	21% (14-27%)
Almonds (68 g/d)	12.5% (10.5-13.5%)
Combined effect	76% (63-84%)

Franco OH et al. The Polymeal: a more natural, safer, and probably tastier (than the Polypill) strategy to reduce cardiovascular disease by more than 75%. BMJ. 2004; 329:1447-50

SYSTEMS PLAN

Study Of 3000 Drinkers

- **Red wine drinkers** had healthier gut **microbiomes** than their counterparts who consumed **other types of alcoholic** beverages.
- They had a **greater variety of bacterial species** in their guts, a tell-tale marker of a healthy microbiome, relative to those who consumed **white wine, beer, or hard liquor**.
- Also had lower levels of obesity and “bad” cholesterol.
- This is **likely due to the array of antioxidant polyphenols**, found in high concentrations in the skin of red grapes known to promote the growth of good gut bacteria, while stifling the growth of the bad.
- Based on this study, **a little red wine goes a long way**.

I Think They Were Wrong

Fish (4 oz 4xs/wk)	**14% (8-19%)**
Fruit/veggies (400 g/d)	**21% (14-27%)**
Garlic (2.7 g/d)	**25% (21-27%)**
Wine (150 ml/day)	**32% (23-41%)**
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Franco OH et al. The Polymeal: a more natural, safer, and probably tastier (than the Polypill) strategy to reduce cardiovascular disease by more than 75%. BMJ. 2004; 329:1447-50

SYSTEMS PLAN

My Winner- Eat 5 Cups Per Day

Fish (4 oz 4xs/wk)	14% (8-19%)
Fruit/veggies (400 g/d)	21% (14-27%)
Garlic (2.7 g/d)	25% (21-27%)
Wine (150 ml/day)	32% (23-41%)
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SYSTEMS PLAN

Eicosanoids

Omega-6 FAs ⇒ pro-inflammatory eicosanoids

(corn, sunflower, cottonseed, safflower, and soybean oils; grains, packaged food)

Omega-3 FAs ⇒ anti-inflammatory eicosanoids

(fish, fish oil, wild game, grass-fed animals, green vegetables, flaxseeds, chia seeds)

Simopoulos AP. Essential fatty acids in health and chronic disease. Am J Clin Nutr 1999; 70(3 Suppl):560S-569S

Omega-3 Stops Asthma, Omega-6 Makes It Worse

Nutrition has a significant effect on your health. Children who ate more omega-3 had fewer symptoms of asthma due to air pollution. I'll share simple strategies to reduce your exposure to air pollution and increase your animal-based omega-3s.

My Doctor Said I have to Eat More Fish

FOOD	RATIO Omega 6:3 (goal 2:1)
Fruit	3:1
Green vegetables	1:1
Sweet potato	4:1
Grass fed meat	2.5:1 (varies)
Wild game	2.5:1 (varies)
The correct fish	1:1
Farm raised salmon	(worse –varies)

- Hands ES. Nutrients in food. New York: Lippincott Williams & Wilkins; 2000
- Enig MG. Know your fats. Silver Spring (MD): Bethesda Press; 2000
- Cordain L. The paleodiet. New York: John Wiley & Sons; 2002

SYSTEMS PLAN

FOOD	RATIO Omega 6:3 (goal 2:1)
Grain-fed meat	5-15:1 or worse
Grain-fed chicken (white)	15:1
Grain-fed chicken (dark)	17:1 (varies)
Grains (cereal, bread, pasta, etc.)	20:1 (varies)
Potato chips (and similar foods with added n-6)	60:1
Seed and seed oils (corn, sunflower, safflower, etc.)	70-100:1 or worse

- Hands ES. Nutrients in food. New York: Lippincott Williams & Wilkins; 2000
- Enig MG. Know your fats. Silver Spring (MD): Bethesda Press; 2000
- Cordain L. The paleodiet. New York: John Wiley & Sons; 2002

Most Addictive Food?

- Stimulates all 3 of the bliss factors
- Carbs, fat and salt
- Chips, fries, pizza

SYSTEMS PLAN

Corn Oil= Inflammation

- Omega 6 to Omega 3
  - Ideal ratio 2:1
  - Corn oil 60:1
  - 1 T corn oil
    - 8 grams of omega 6 fat
    - .1 grams of omega 3 fat

Potentially Inflammatory Foods with Autoimmune Disease

- Gluten
- Dairy
- Eggs
- Soy
- Corn
- Yeast
- Nightshades
- Grains and legumes
- Nuts and seeds

SYSTEMS PLAN

Defense System

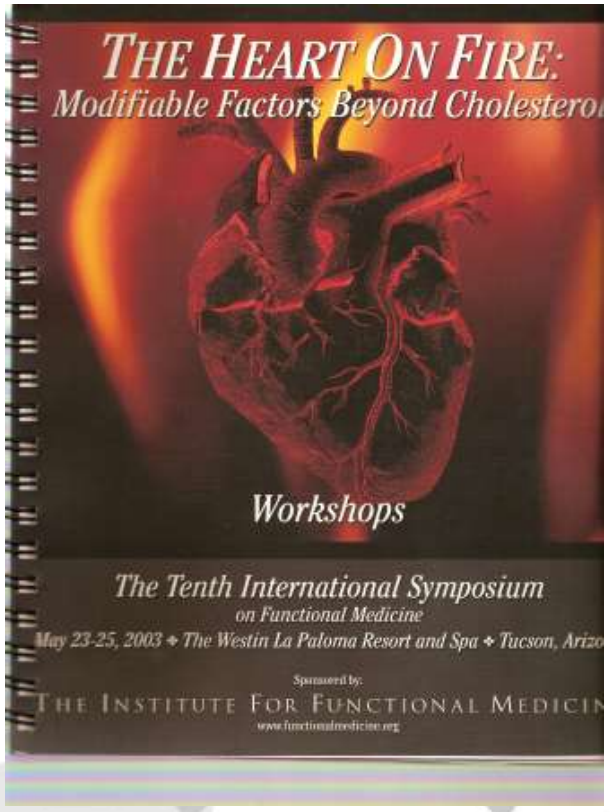
Not Working

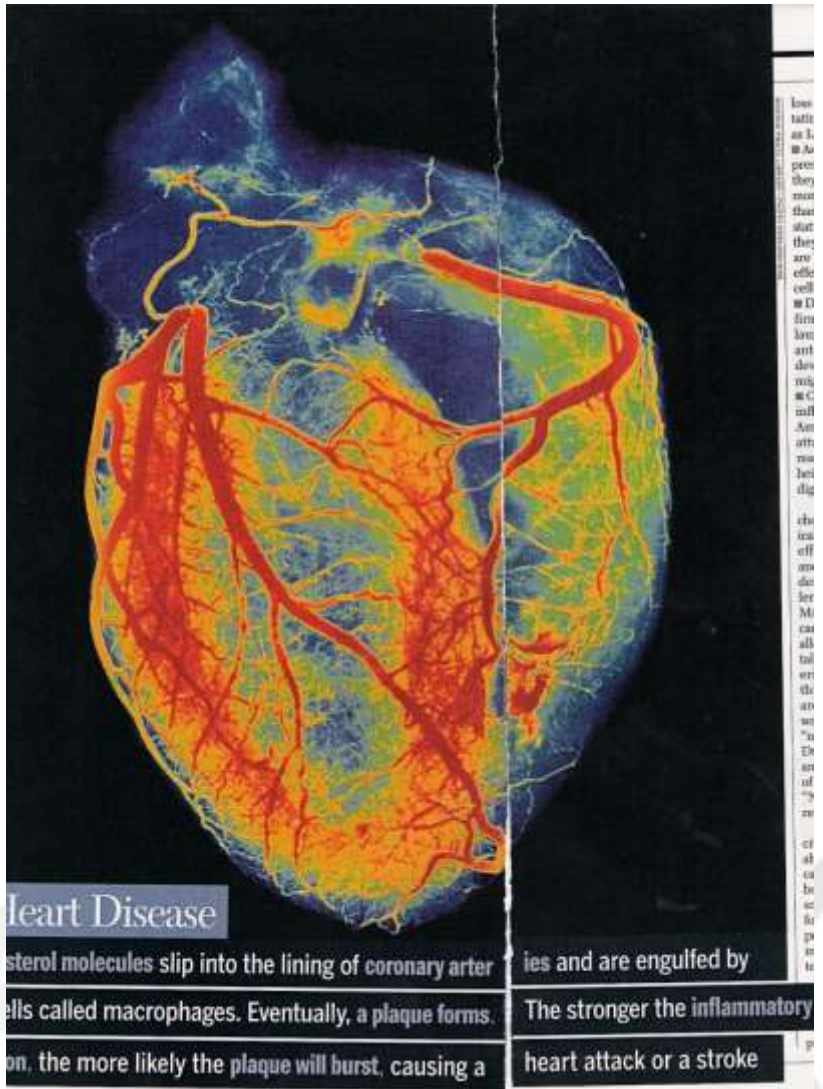
Working

SYSTEMS PLAN

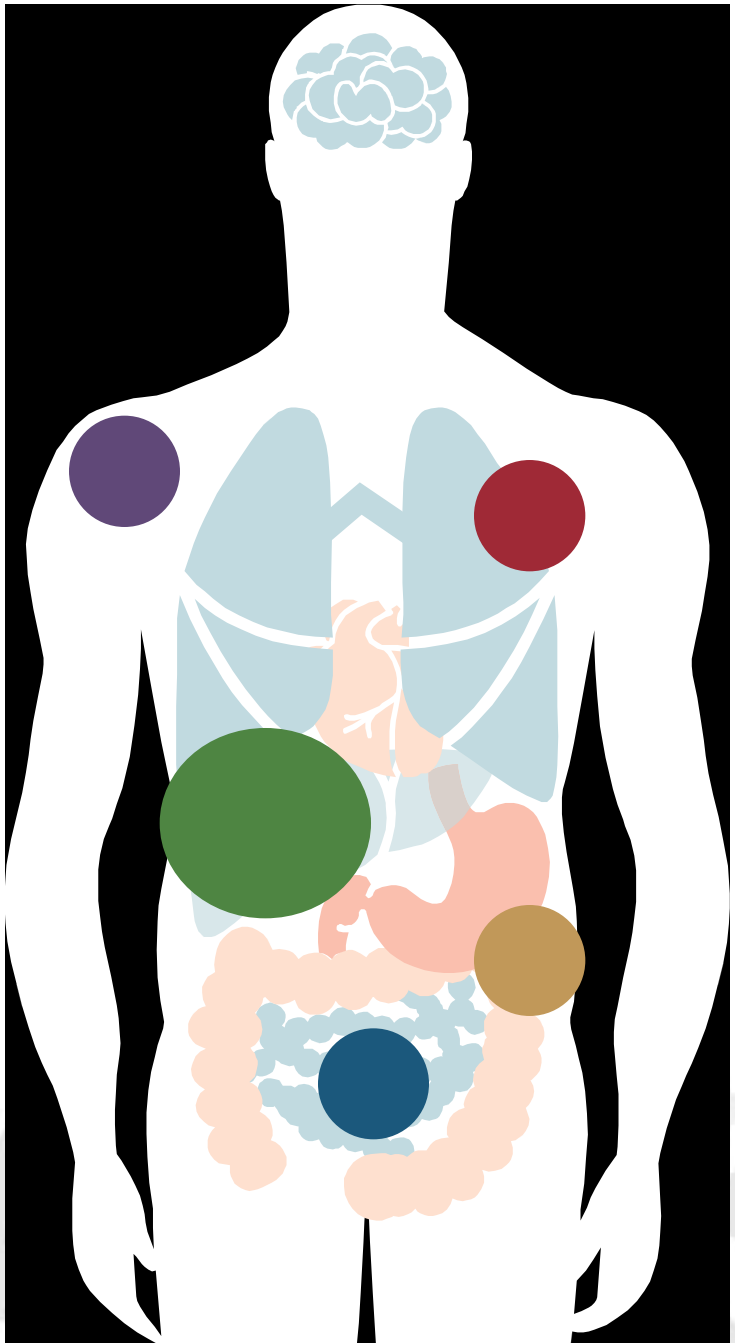
What Food Is This?

Heart Disease Is An Inflammatory Disease





DETOX SYSTEMS



1. Kidneys
2. Skin
3. Liver
4. Colon
5. Lungs

7 SYSTEMS PLAN

"The Environmental Protection Agency has monitored human exposure to toxic environmental chemicals since 1972 when they began the National Human Adipose Tissue Survey. …

- Five of what are known to be the most toxic chemicals were found in 100% of all samples
- Nine more chemicals were found in 91-98% of samples"

http://drhyman.com/downloads/Toxins-and-Obesity.pdf

SYSTEMS PLAN

Nancy

Detox System

- Symptoms
- Job
- Diagnosis
    - Lyme disease
    - RA
    - Fibromyalgia
    - Chronic Fatigue
    - Others

SYSTEMS PLAN

The AGE Less Diet

Gerontotoxins

Gerontotoxins

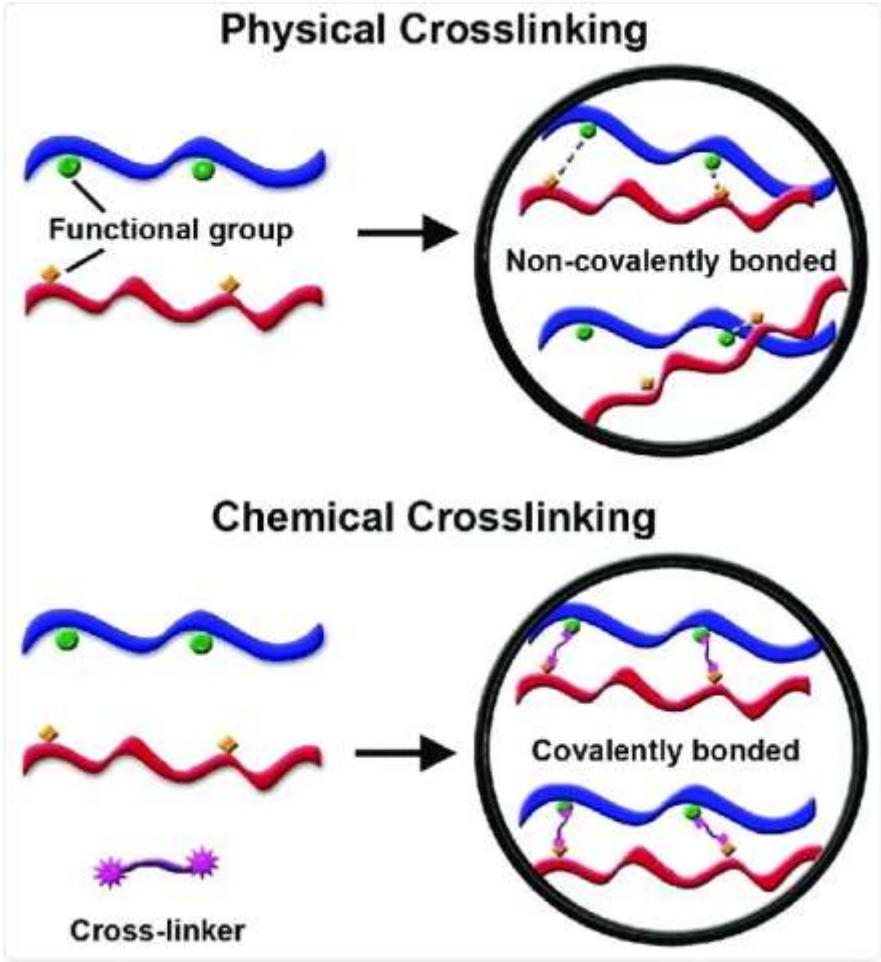
- A group of toxins that cause cells to age
- Example: Advanced Glycation End-products (AGEs)- naturally occurring chemicals in animal-origin foods
- **Cooking accelerates** the generation of more AGEs within them
- **Dry heat cooking** results in the formation of more than **10-100x more** than uncooked

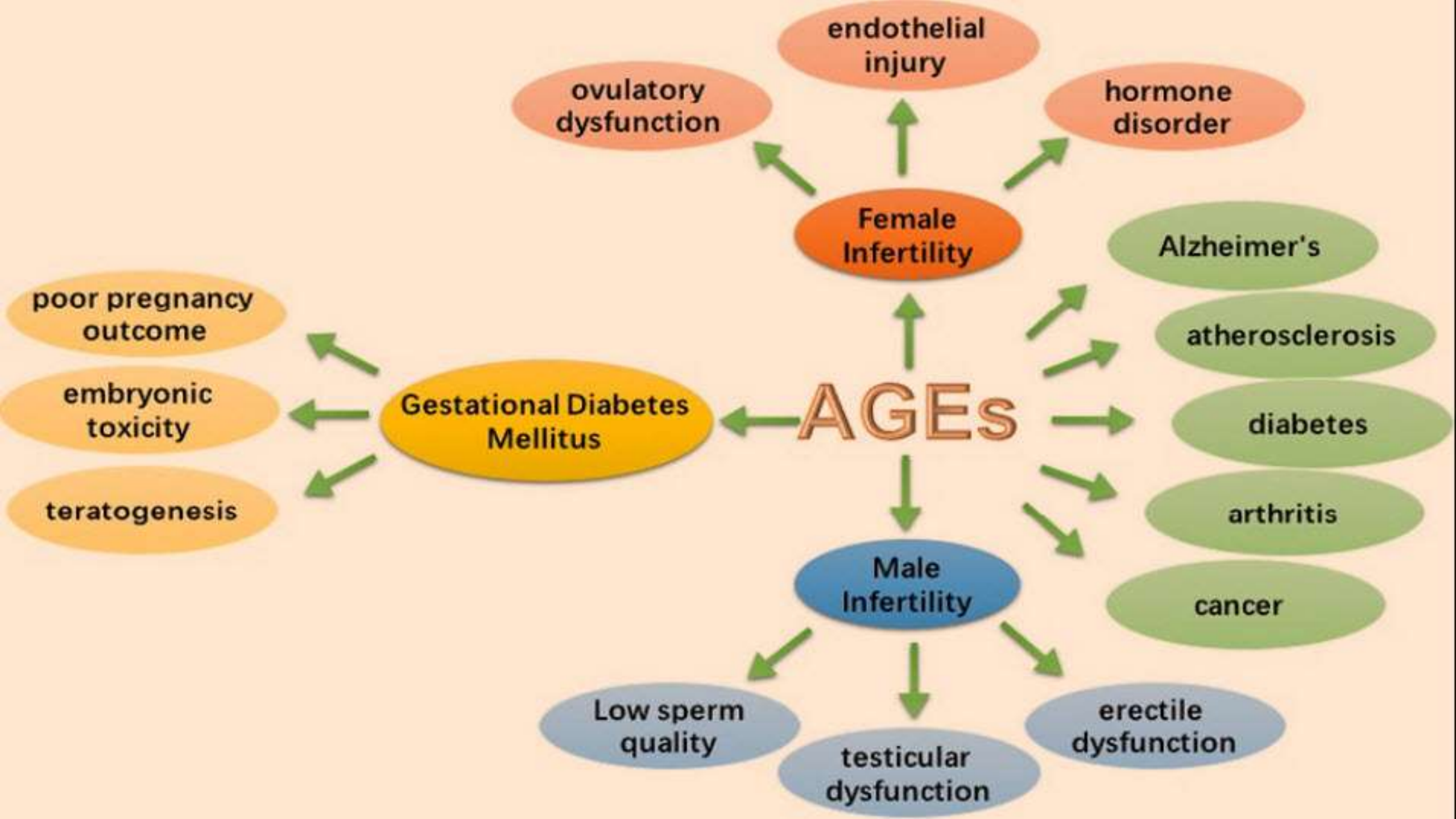
Advanced Glycation End-products (Age)

AGE is an appropriate acronym, as they are considered “gerontotoxins”

AGEs

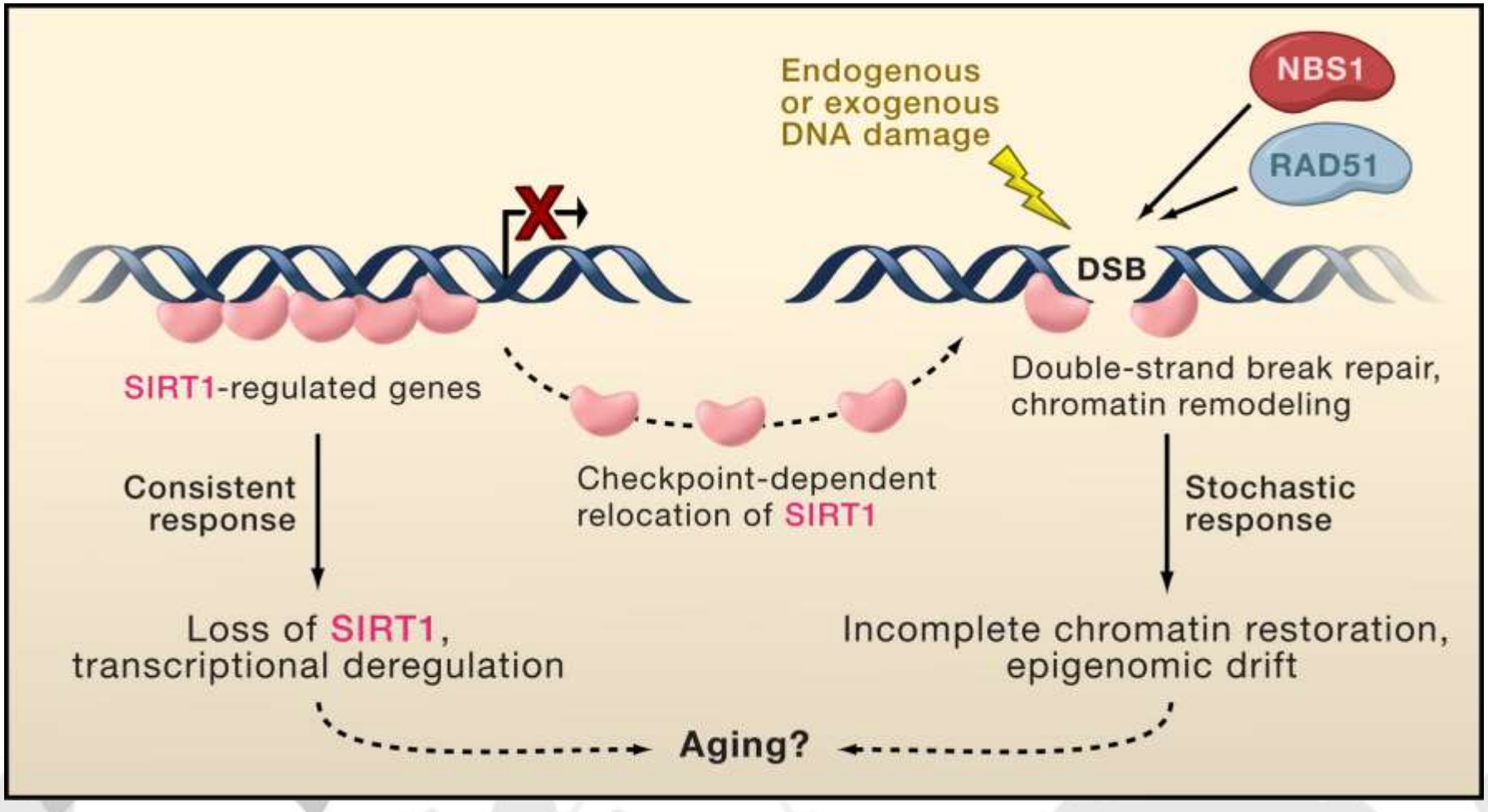
- AGEs are thought to accelerate the aging process by **cross-linking proteins** together, causing:
- tissue stiffness
- oxidative stress
- and inflammation




endothelial injury
ovulatory dysfunction
hormone disorder
Female Infertility
Alzheimer's
poor pregnancy outcome
atherosclerosis
embryonic toxicity
Gestational Diabetes Mellitus
AGEs
diabetes
teratogenesis
arthritis
Male Infertility
cancer
Low sperm quality
testicular dysfunction
erectile dysfunction

DNA

Sirtuins


Endogenous
or exogenous
DNA damage
NBS1
RAD51
DSB
SIRT1-regulated genes
Double-strand break repair,
chromatin remodeling
Consistent
response
Checkpoint-dependent
relocation of SIRT1
Stochastic
response
Loss of SIRT1,
transcriptional deregulation
Incomplete chromatin restoration,
epigenomic drift
Aging?

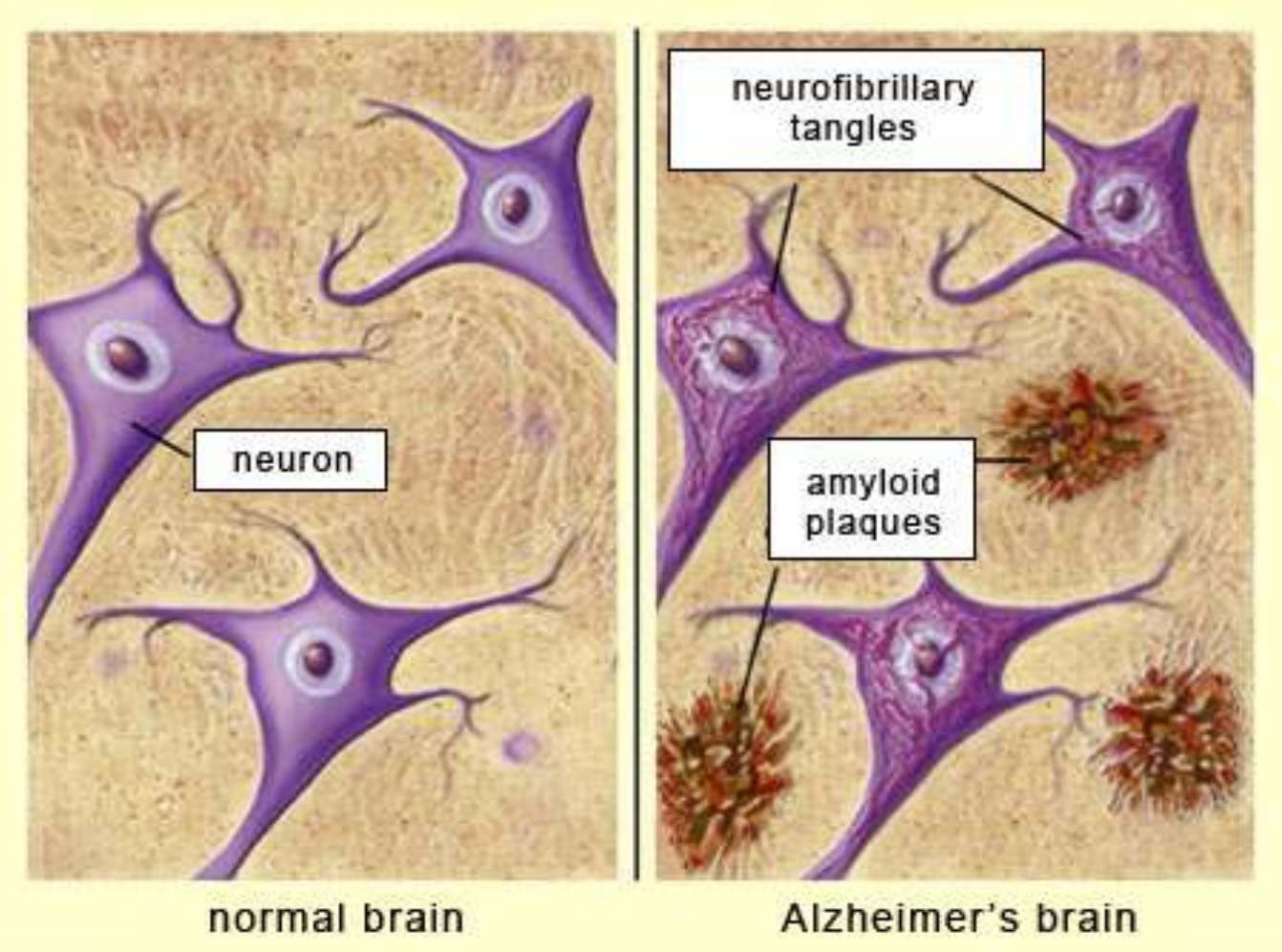
DNA-Thread

Protein-Spool

Sirtuins-Winding

SYSTEMS PLAN

Alzheimer's Plaque and Tangles



Sirtuin Suppression

- Avoiding high-AGE foods is seen as potentially offering a new strategy to combat aging
- **Sirtuin suppression** is both **preventable** and **reversible** by AGE reduction

AGE Content in Food

- Meat 20x more AGEs than highly processed foods
- Meat 150x more than fresh fruits and vegetables
- Poultry (the worst) 20% more AGEs than beef.
- The researchers concluded that even a **modest reduction** in meat intake could realistically **cut daily AGE intake in half.**

Meat Cooked with Dry Heat → AGE

- Dry heat cooking→ meat releases reactive amino-lipids and reducing sugars→ AGE formation

while dairy, grains, fruits, and vegetables the lowest. Within the meat group the CML contents decrease gradually in poultry, pork, fish, eggs, and lamb [2,87]. The reason for this high AGE content in red meats and poultry is probably given by the fact that, when cooked under dry heat, these release high amounts of highly reactive amino-lipids and reducing sugars, like fructose or glucose-6-phosphate, due to the rupture of lean muscle cells. Even if the fat group is the one that contains the most adducts,

Worst to Best Cooking Methods

- Grilling
- Oven-frying
- Frying
- Broiling
- Roasting
- Stewing/steaming

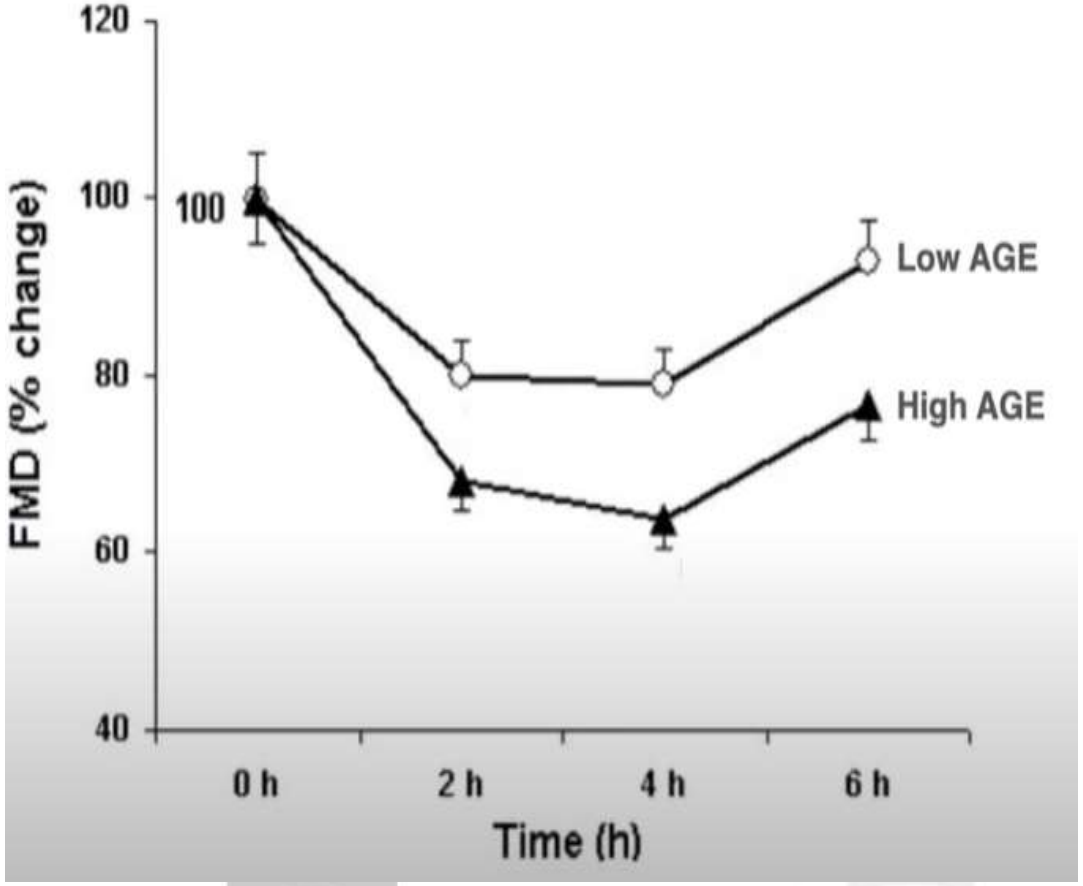
AGE formation, with effects ranging from those caused by oven-frying > frying > broiling > roasting > boiling/poaching/stewing/steaming. For example, cooking meat (e.g., chicken, pork, or beef) by boiling or stewing can reduce the AGE contents to one-half of that prepared by broiling[1,271]. In addition, the water content, cooking method, temperature and time, and food pH are crucial to the final amount of AGEs. Marinating food or meat with

Two Meals Same Calories and Ingredients

Fry One Steam One

The 2 meals were isocaloric, had identical ingredients, and differed only by the temperature and time of cooking. Each meal consisted of 200 g chicken breast, 250 g potatoes, 100 g carrots, 200 g tomatoes, and 15 g vegetable oil and provided 580 kcal, 54 g protein, 17 g fat, 48 g carbohydrates, 60 mg cholesterol, and 10 g fibers. The HAGE meal (15.100 kU AGE) was prepared by frying or broiling at 230 °C for 20 min, whereas the LAGE meal (2750 kU AGE) was prepared by steaming or boiling at 100 °C for 10 min. The subjects were instructed to eat the test meal within 30 min.

Fry→ High AGE→ **Profound** Impairment of Vascular Function in Hours



Our study showed for the first time that the cooking method of a meal influences decisively the extent of postprandial vascular dysfunction in patients with T2DM. It showed that a single "real-life" HAGE meal induces a profound impairment of both macro- and microvascular function (−36.2% and −67.2%, respectively). These changes are significantly greater than those induced by a meal containing the same ingredients but with a five-fold lower AGE concentration (LAGE meal).

SYSTEMS PLAN

500 Foods Tested for AGE Content- Top Five

1. BBQ chicken
2. Bacon
3. Broiled hot dog
4. Roasted chicken thigh
5. Roasted chicken leg

AGE Less Diet

The AGE Less diet is the name given to diet with reduced AGEs. The AGE Less diet involves no caloric restriction and no medication. It involves avoiding the very worst foods (fried bacon) a reduction in very high AGE foods and cooking with moist heat instead of dry heat. It is about using chemistry to produce less AGEs in foods instead of more AGEs. Anybody who is willing

AGE Test: Hemoglobin A1c

- Monitoring hemoglobin A1c levels is essential for all adults who wish to identify excess glycation processes in their bodies and take measures to control and minimize glycation-induced damage.
- Although the standard normal reference is below 5.7, to inhibit and reverse AGEs the optimal goal is <5.0

Reduce AGEs

- Eat less meat (chicken???), a modest reduction can cut AGEs in half
- Avoid dry cooking and high temperatures (fry, grill)
- Use moist cooking methods with lower heat (crock pot, roast)
- Reduce processed foods

Reduce AGE Damage
Scavenge Oxidative Free Radicals

Polyphenols

Peptides

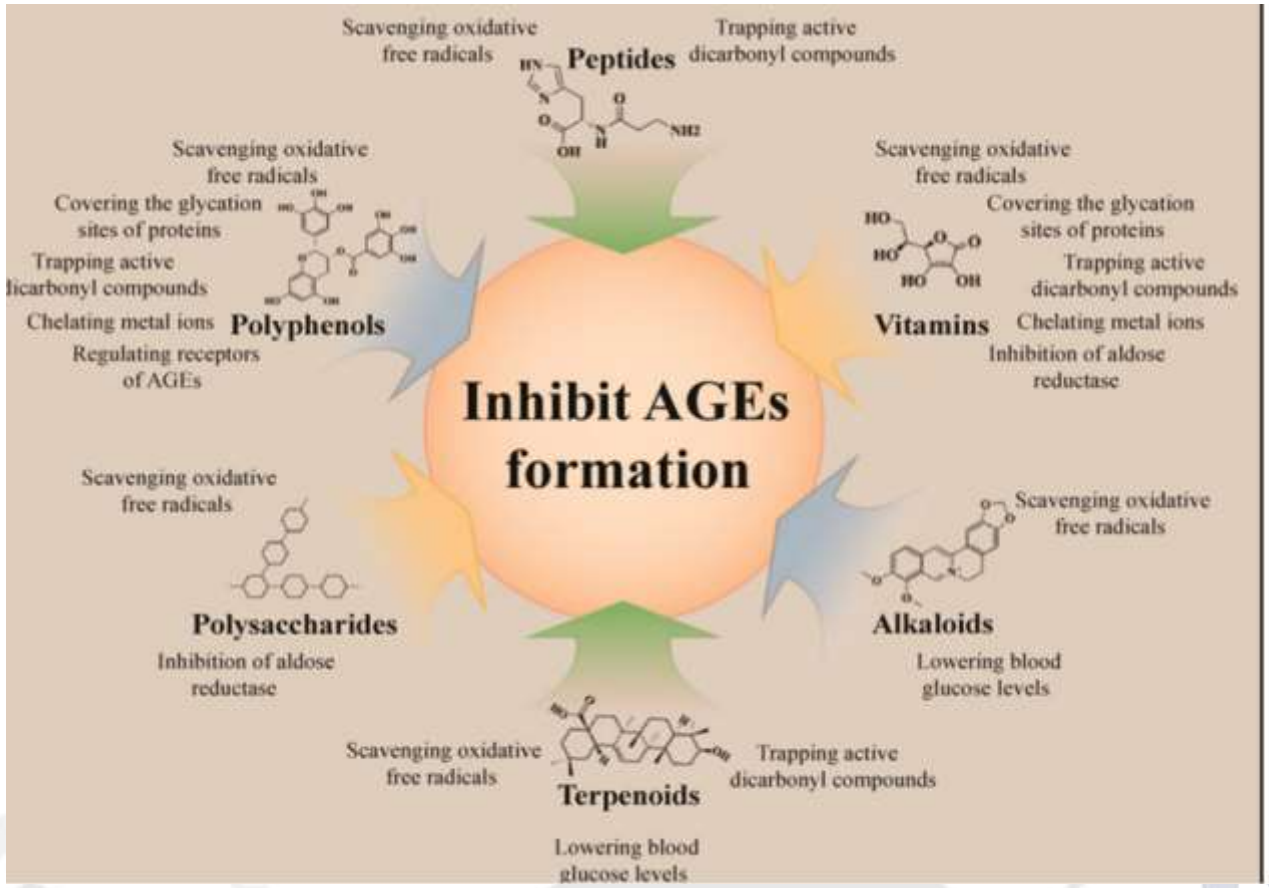
Vitamins

Alkaloids

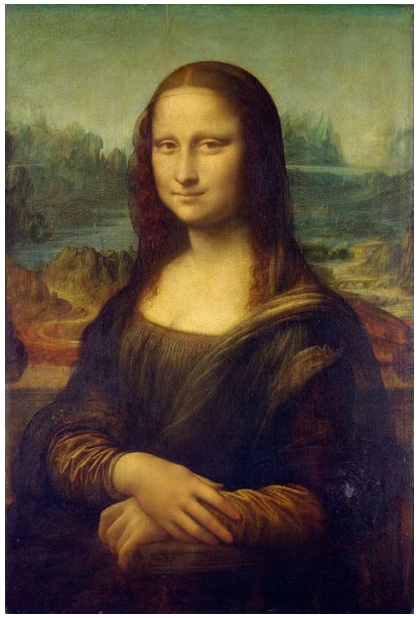
Terpenoids

Polysaccharides

PLANTS



SYSTEMS PLAN



Diagnosing Mona Lisa

Her 7 Systems

SYSTEMS PLAN

SYSTEMS PLAN

MAYO CLINIC Mayo Clinic Proceedings

Submit

LETTER TO THE EDITOR | VOLUME 94, ISSUE 4, P730-731, APRIL 01, 2019

Mona Lisa Decrypted: Another Premise

Lawrence D. Mullany, MD, MBA, FACP

DOI: https://doi.org/10.1016/j.mayocp.2019.01.010 • Check for updates

References

Article Info

Linked Article

Related Articles

To the Editor:

In the September 2018 issue of *Mayo Clinic Proceedings*, Mehra and Campbell[1] gave a lovely and elegant review of the Mona Lisa painting and posited a medical explanation for the mystery of the lady as painted by the great master Leonardo da Vinci. Their insights tied hypothyroidism with attendant hyperlipidemia, lipoma, and xanthelasma as the cause of the enigmatic smile and her gaze. There is merit to this diagnosis, and this should be heavily weighted in the differential diagnosis analysis. Other analysts have attributed this to neurosyphilis,[2] postpartum Bell's palsy,[3] dentition problems,[3] hyperlipidemia,[4] and strabismus.[3]

While painting a study of the great master as a learning exercise, several elements of the composition led me to consider other possibilities for the differential diagnosis.

Bruno Mottin, the curator of the Center for Research and Restoration of Museums of France, and a Canadian team imaged the painting using a new 3-dimensional technology. They noted that the initial da Vinci painting had the left hand “in a clenched rather than relaxed position.” This was later changed to a looser grasp “as if she was going to get up from a chair.”[5] The first iteration would most likely reflect the reality of the moment more accurately.

I submit that the position of the left arm and hand is more in keeping with paresis, which could be recent or from earlier in

The Mystery of the Lady

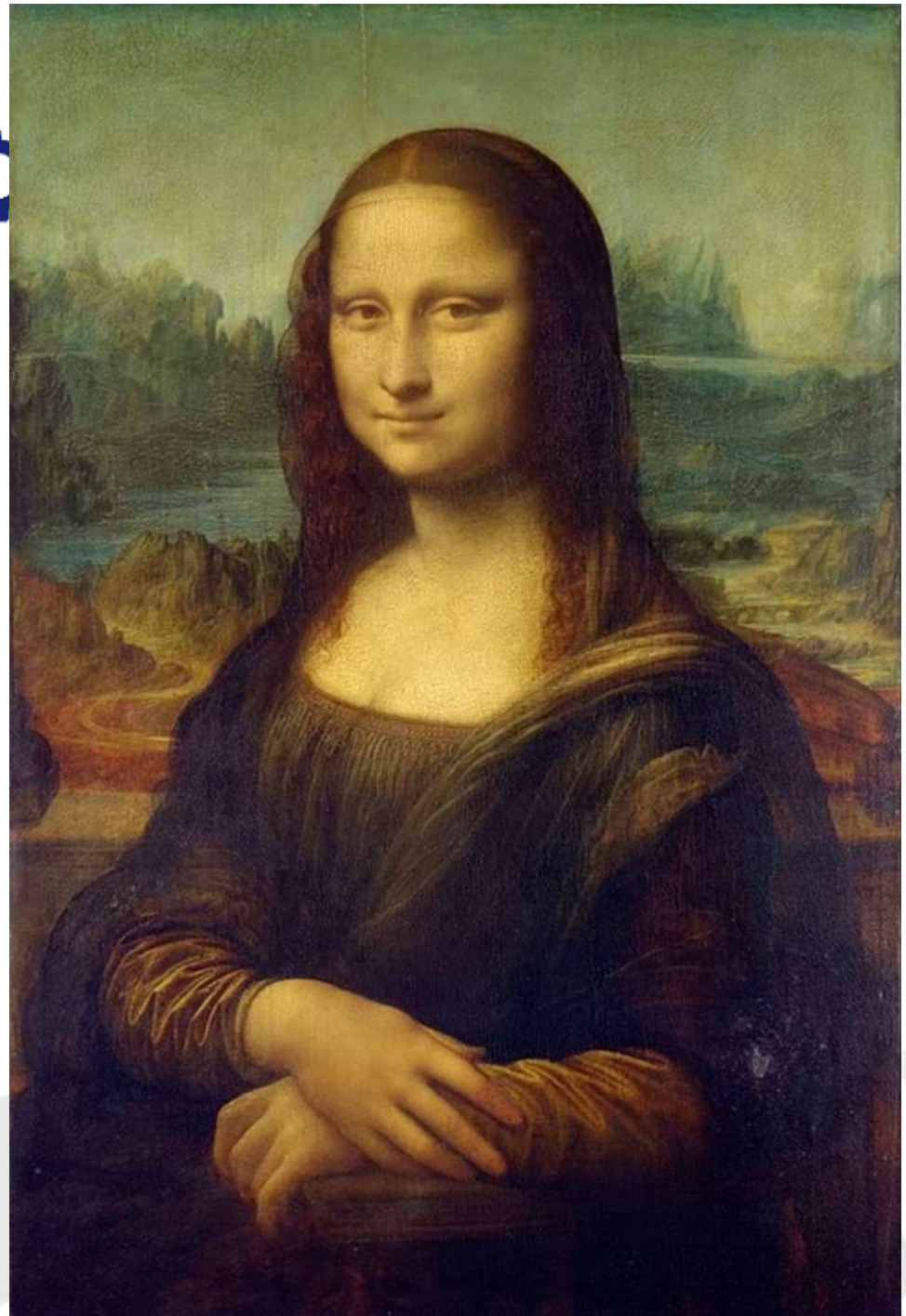
- Some physicians tied hypothyroidism with attendant hyperlipidemia, lipoma, and xanthoma as the cause of the mysterious smile and her gaze.
- Other analysts have attributed this to:
  - neurosyphilis
  - postpartum Bell's palsy
  - hyperlipidemia
  - strabismus

Diagnosis

- Hyperlipidemia
- Hypothyroid

Treatment

- Lipitor (Statin Drug)
- Levothyroxine

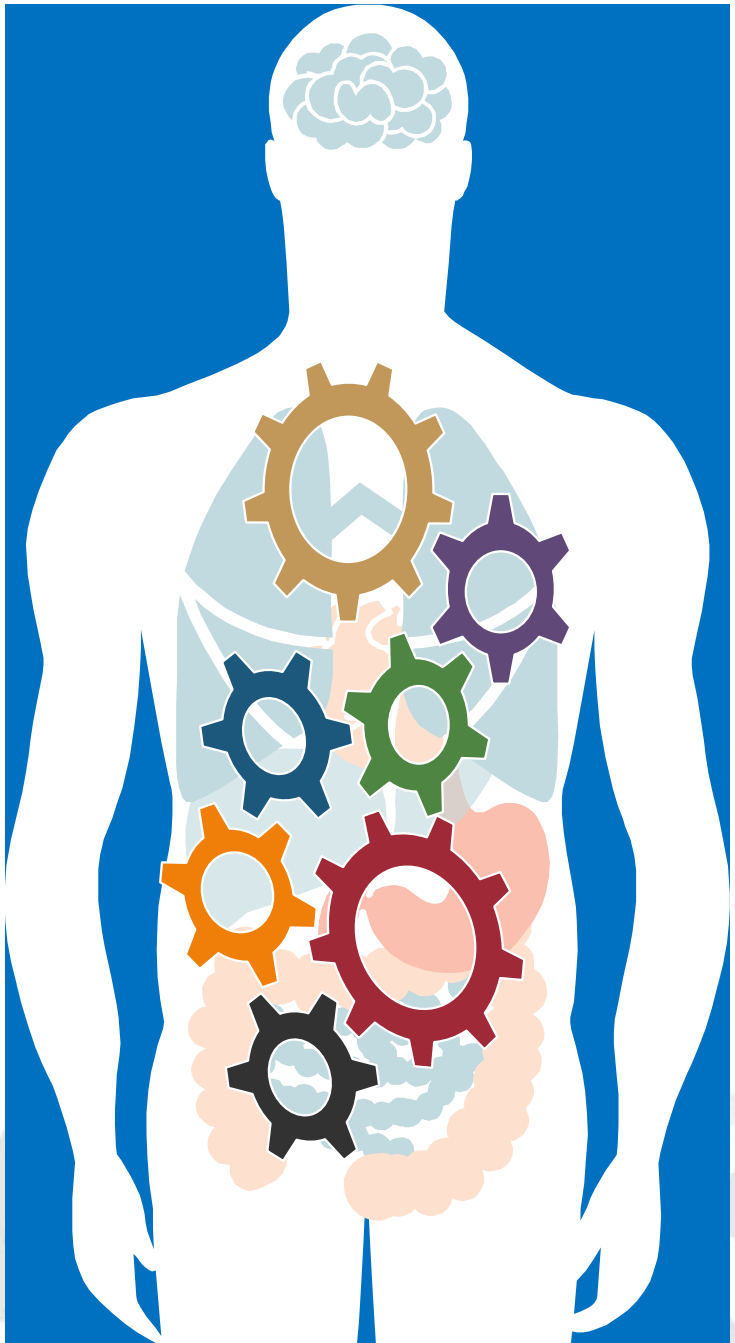


A Second Opinion
7 SYSTEMS PLAN

1. Structure
2. Digestive
3. Delivery
4. Energy
5. Communication
6. Defense
7. Detox

7 SYSTEMS PLAN

7 SYSTEMS PLAN



1. Structure
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7 SYSTEMS PLAN

Structural System

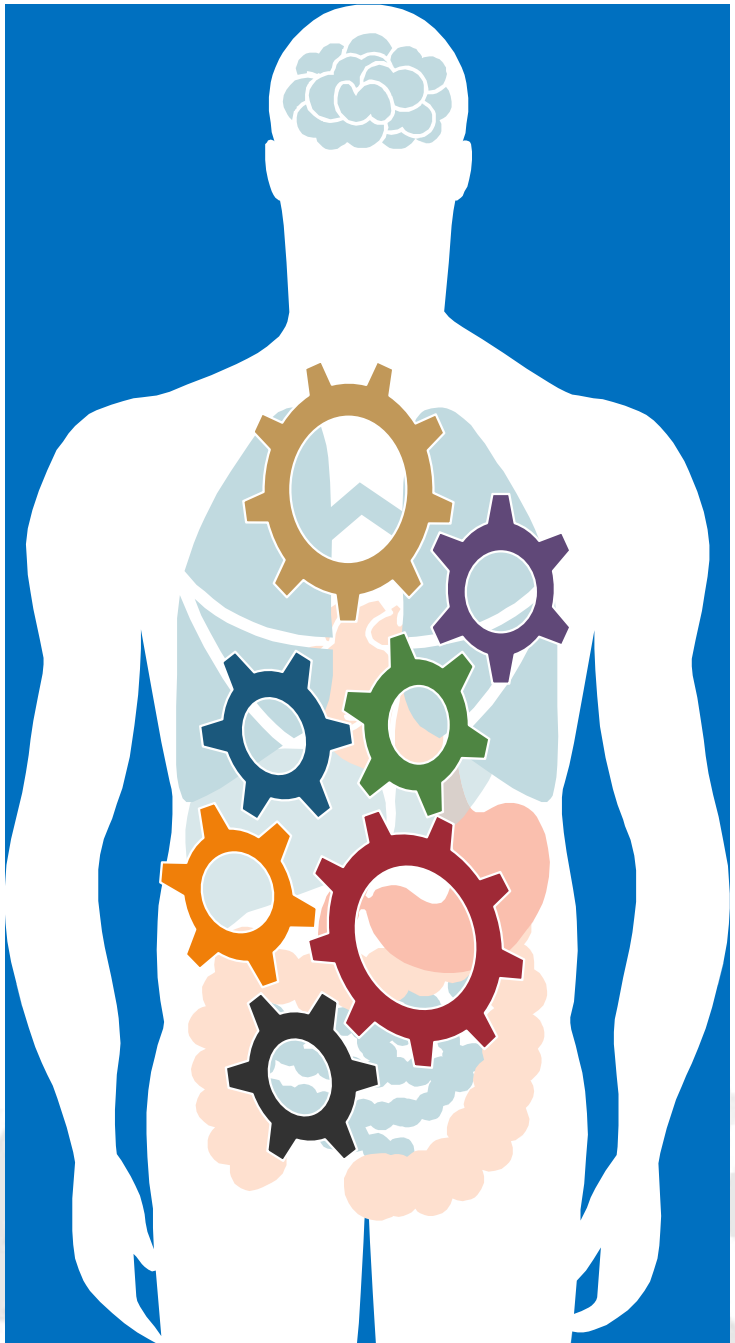
1. Bone
2. Muscle
3. Fat

Candi

Structural System

SYSTEMS PLAN

7 SYSTEMS PLAN



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7 SYSTEMS PLAN

Digestive System

Neurotransmitters

What Makes this Neurotransmitter?

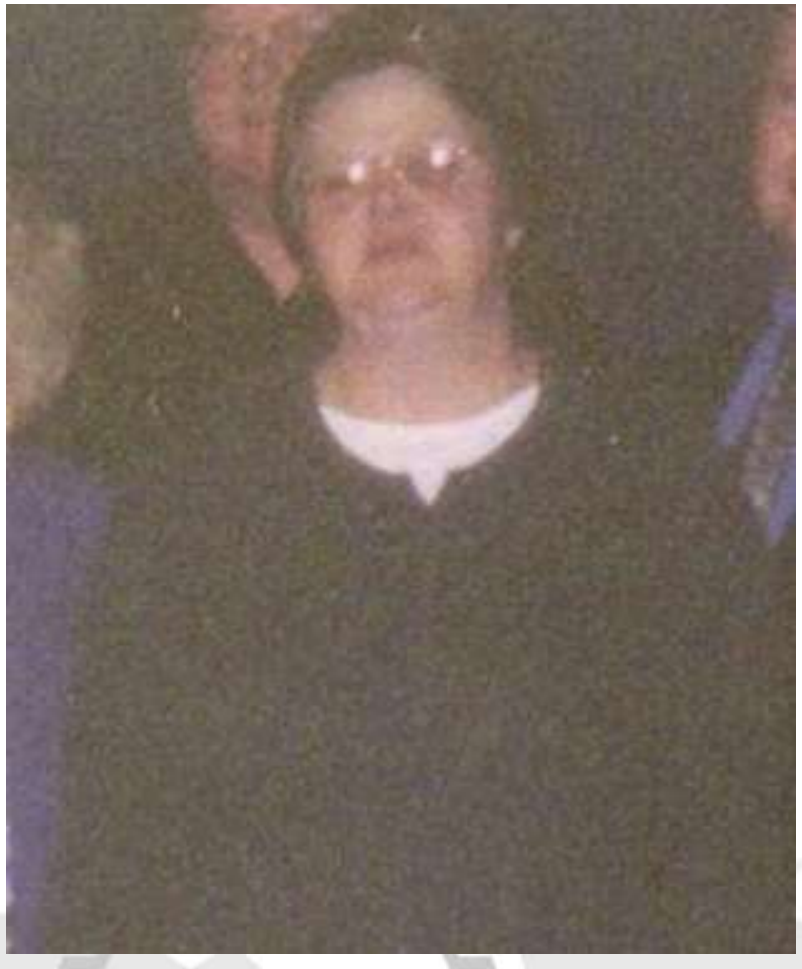
Microbes in the gut make neurotransmitters

Dopamine

Serotonin

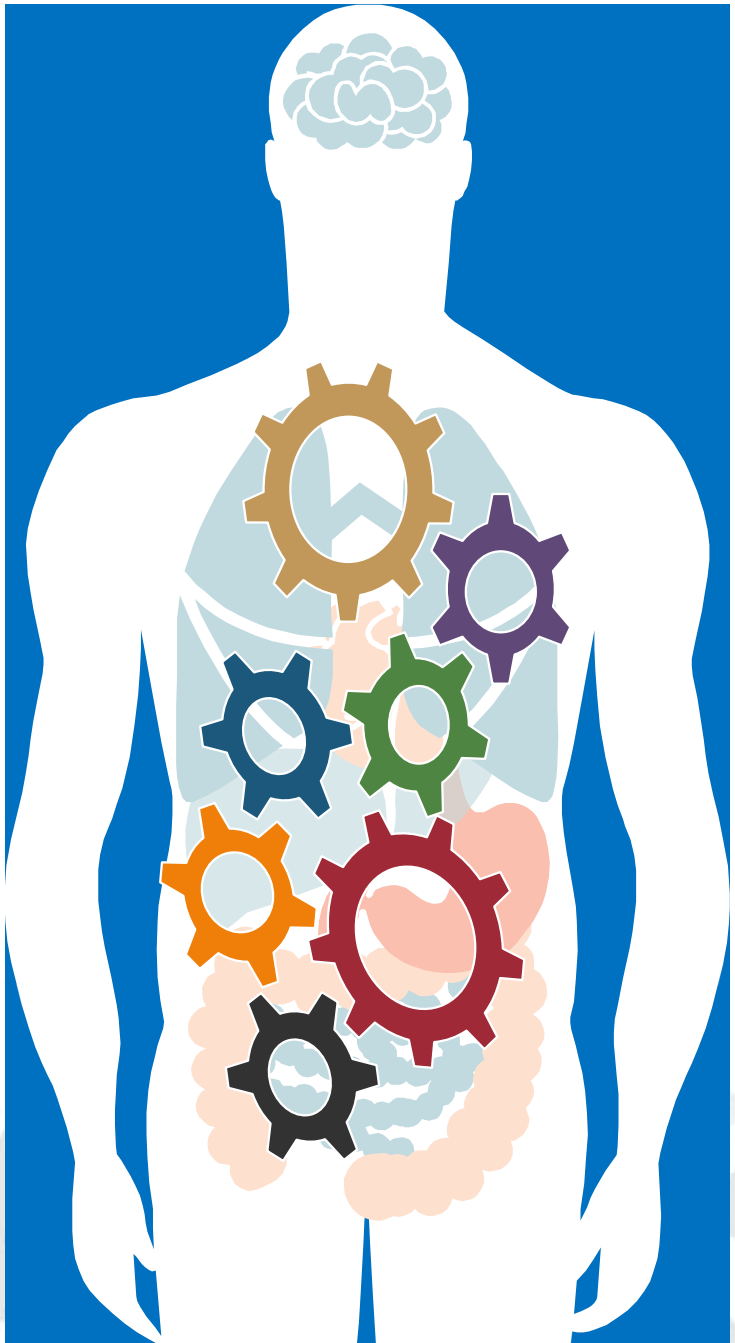
GABA

Sharon



Diane

7 SYSTEMS PLAN



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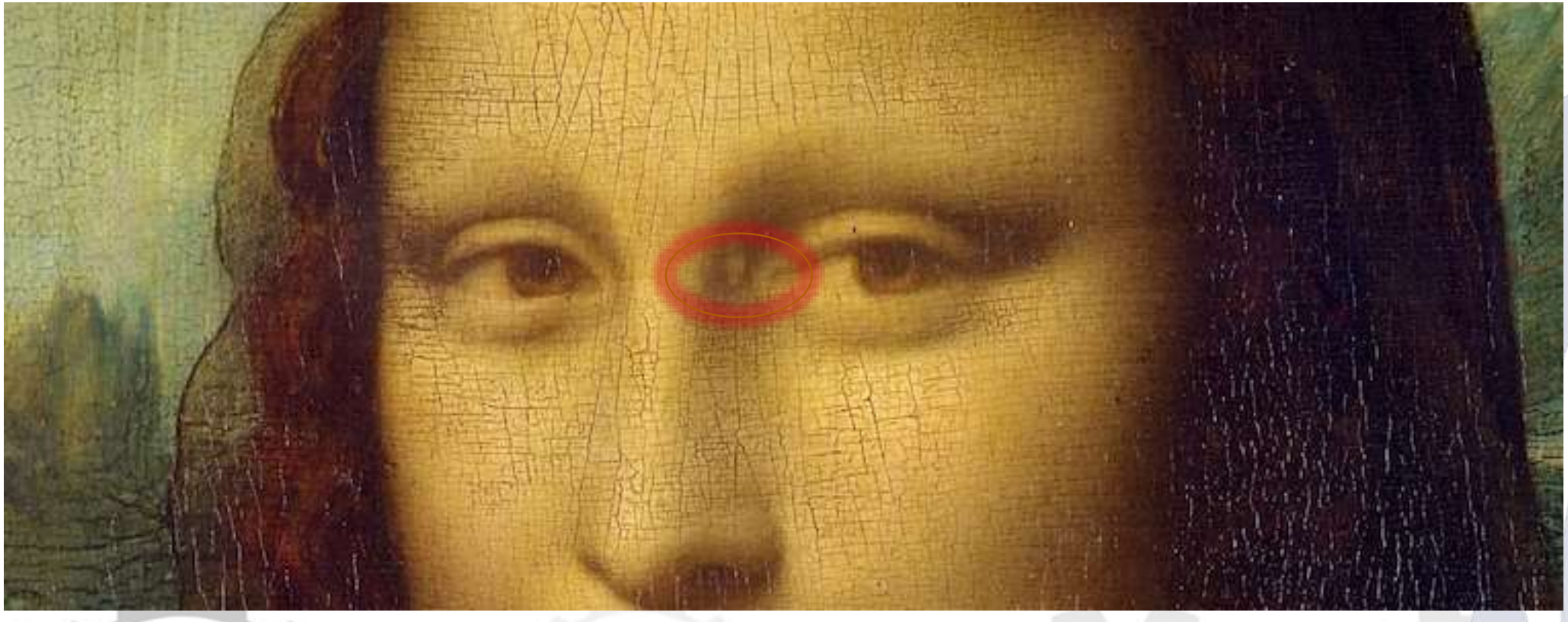
7 SYSTEMS PLAN

Delivery System



Xanthoma

Ear Lobe

Ear Lobe

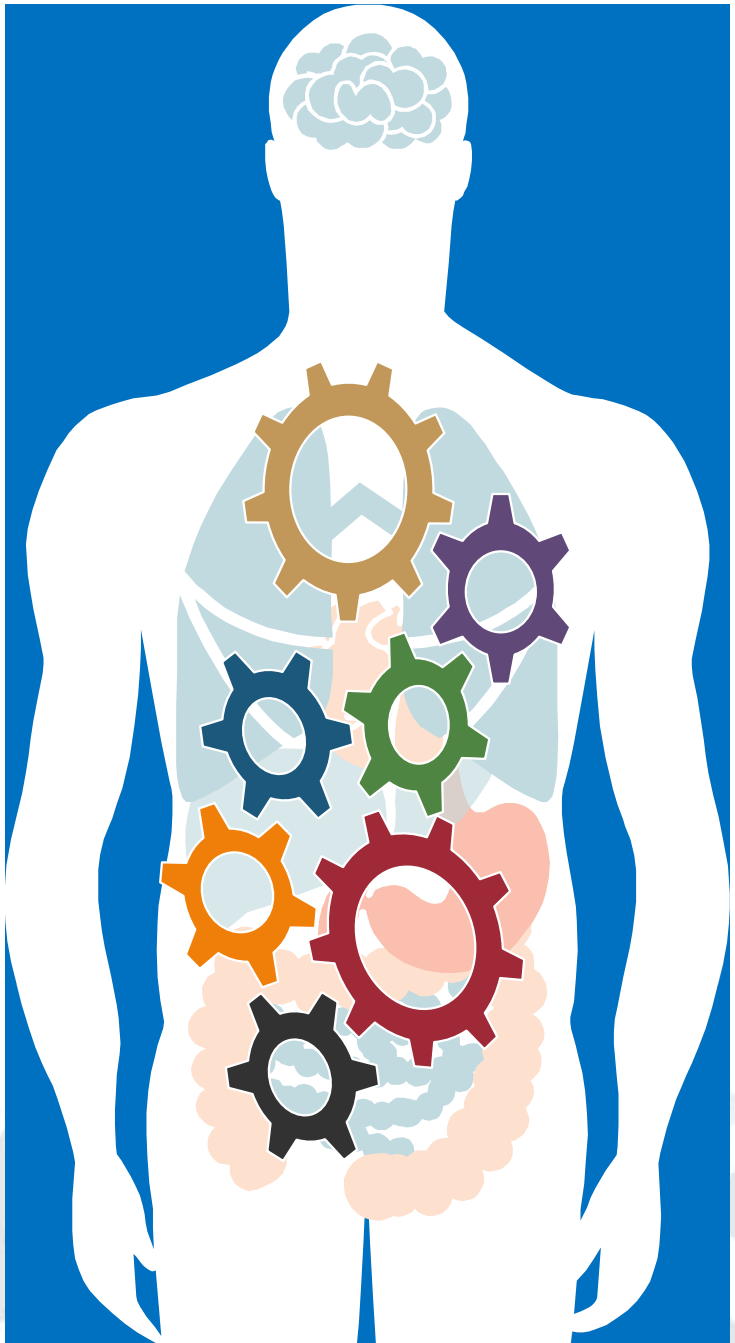
Ear Lobe

Rhonda

Cholesterol 290

Cholesterol 190

7 SYSTEMS PLAN



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6. Defense
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7 SYSTEMS PLAN

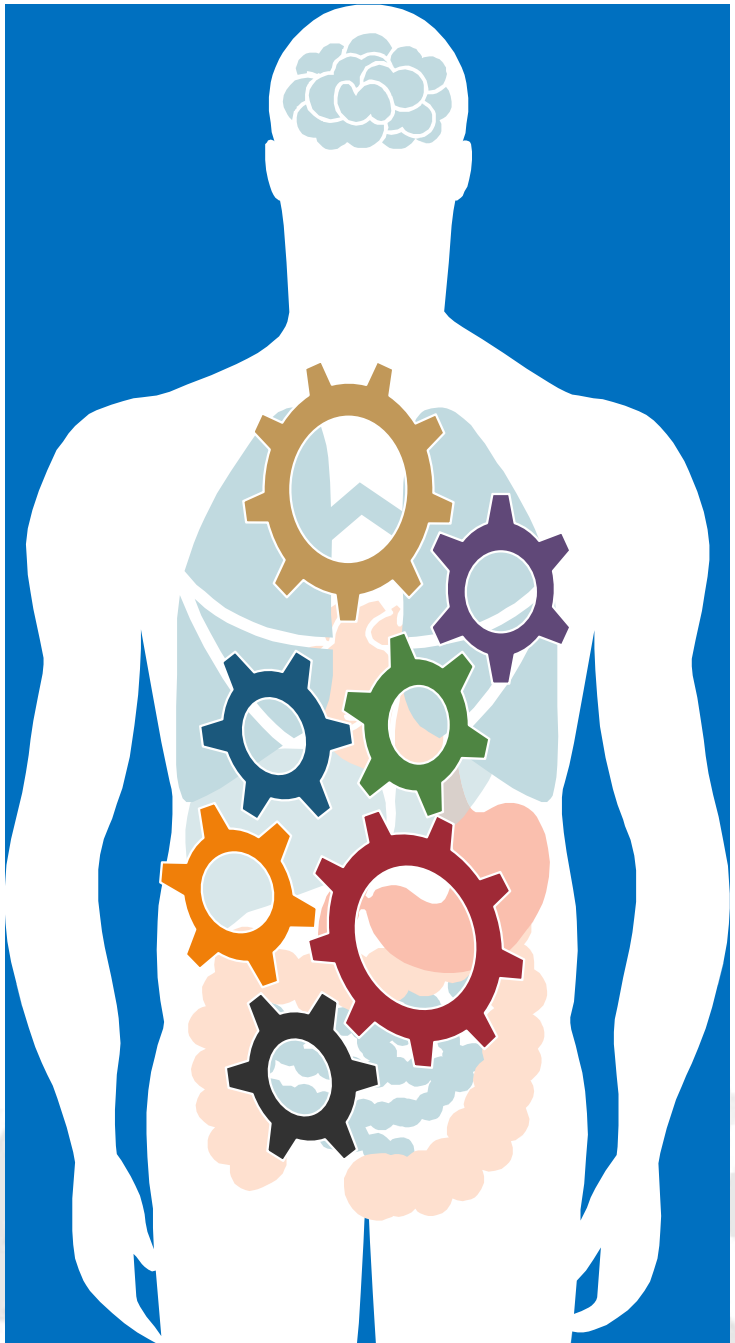
Energy System

- Mitochondria

SYSTEMS PLAN

Cindy

7 SYSTEMS PLAN



1. Structure
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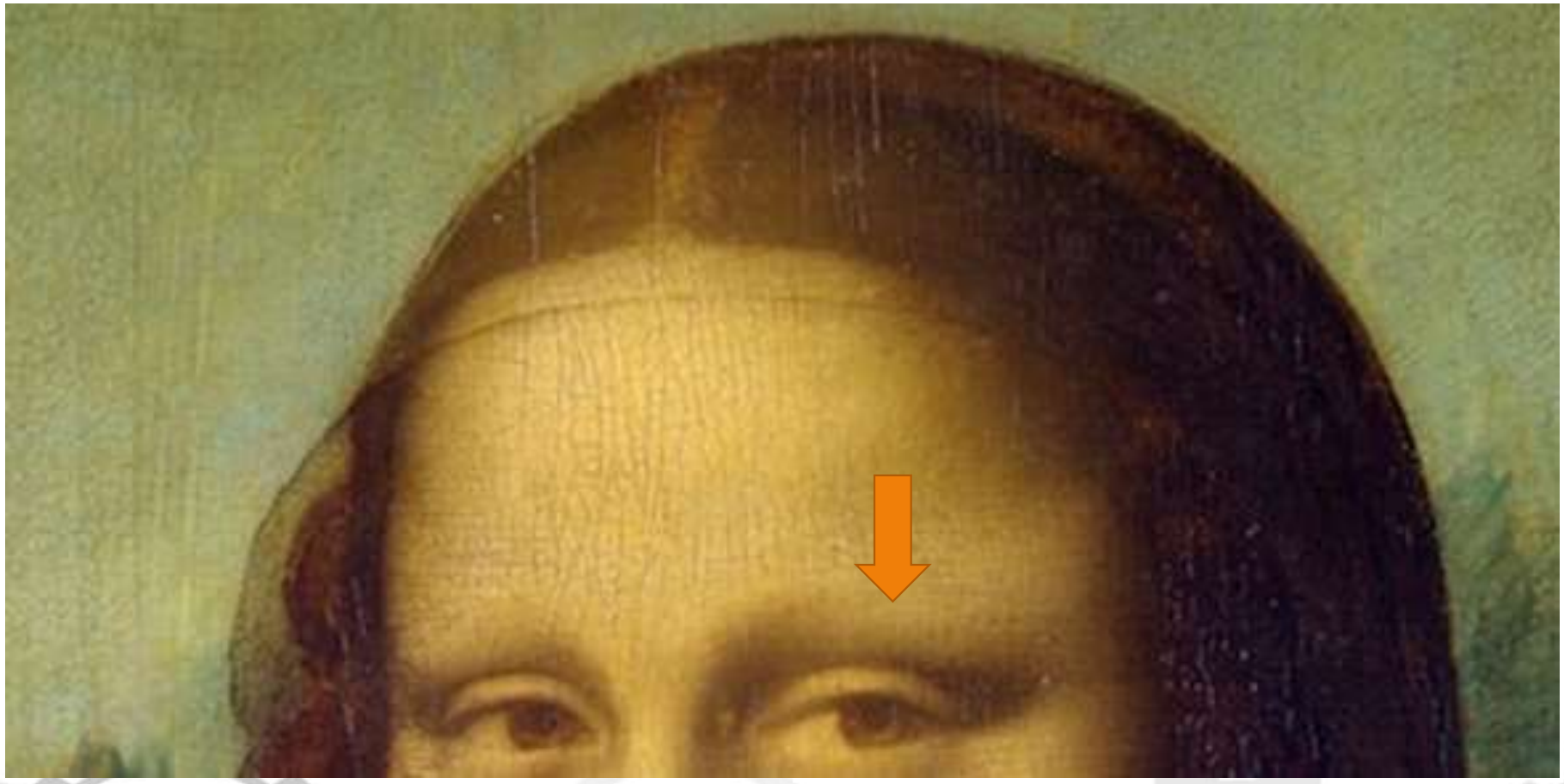
7 SYSTEMS PLAN

Communication System

Communication System

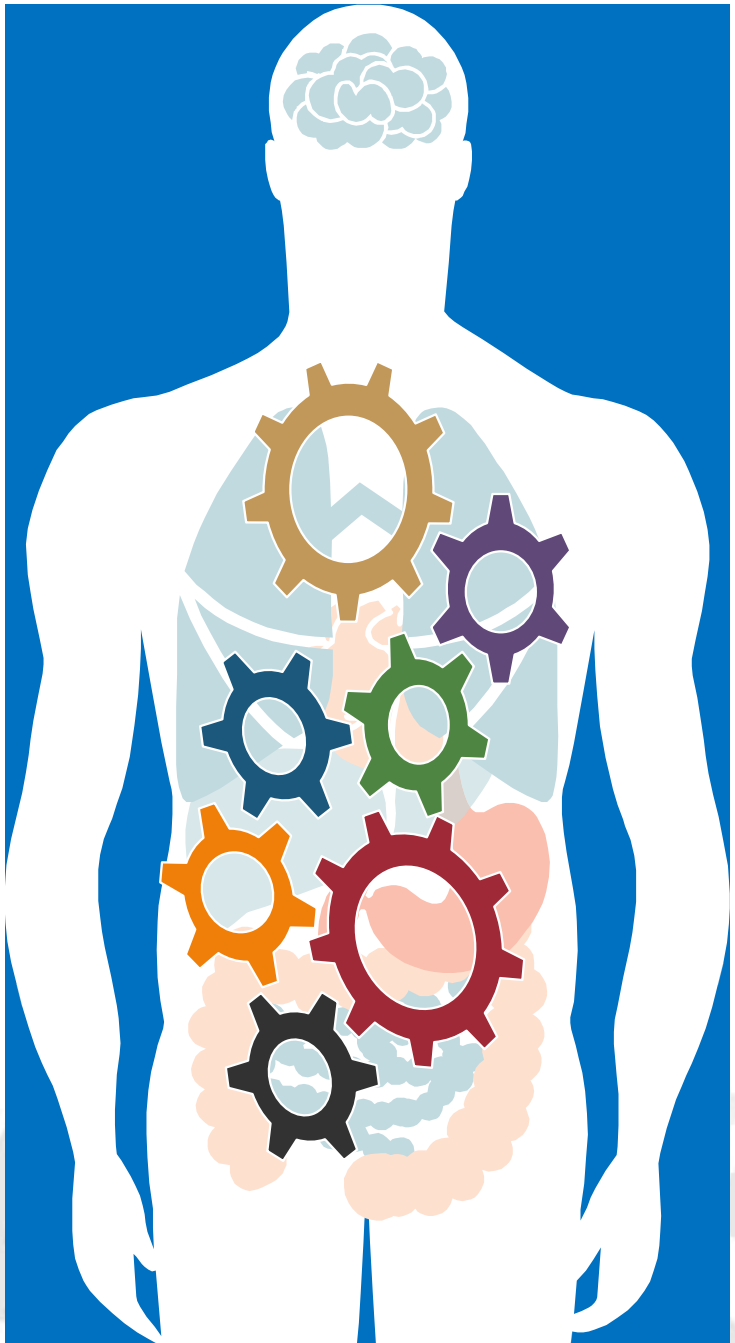


Jo Dee

Communication System

7 SYSTEMS PLAN

7 SYSTEMS PLAN



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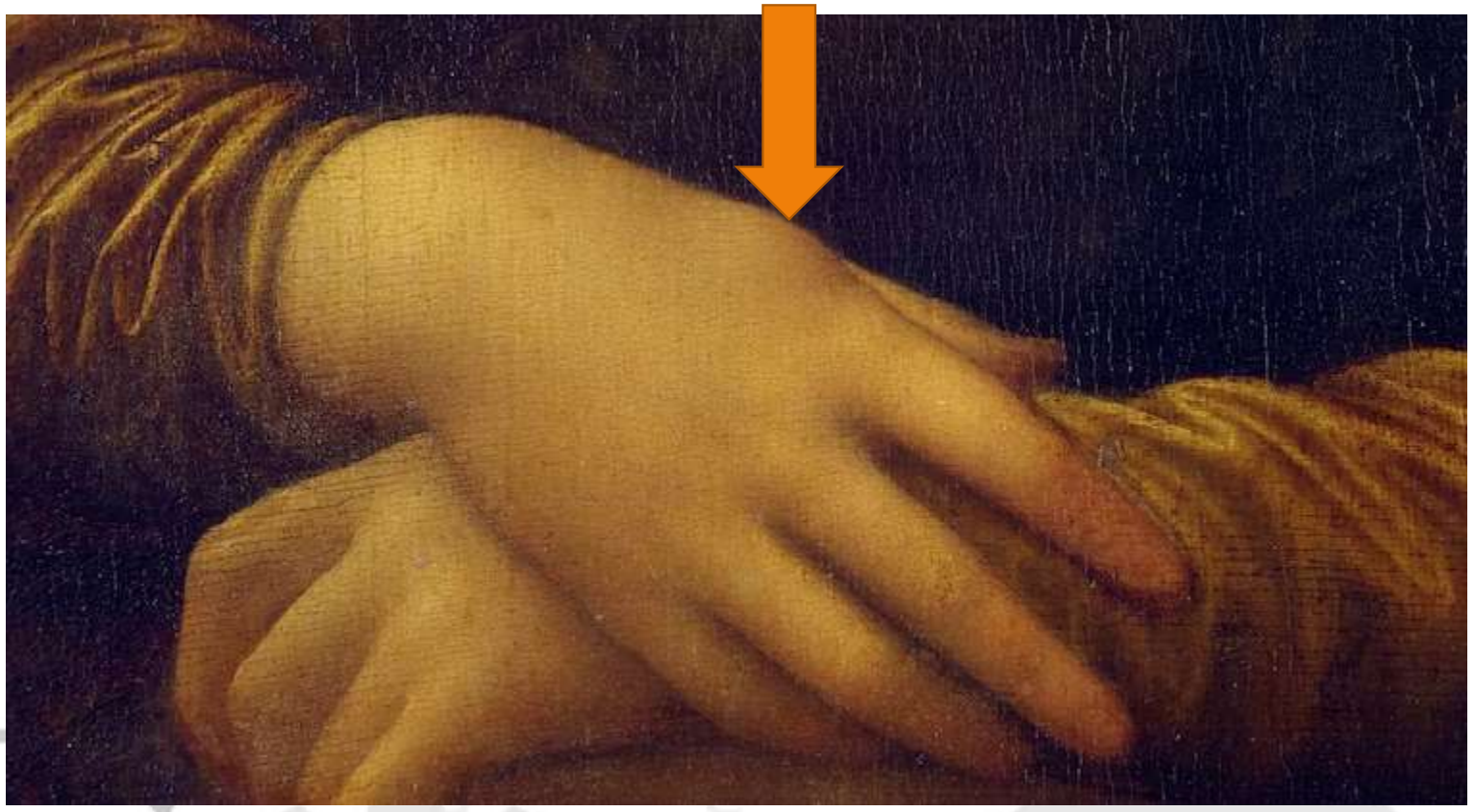
7 SYSTEMS PLAN

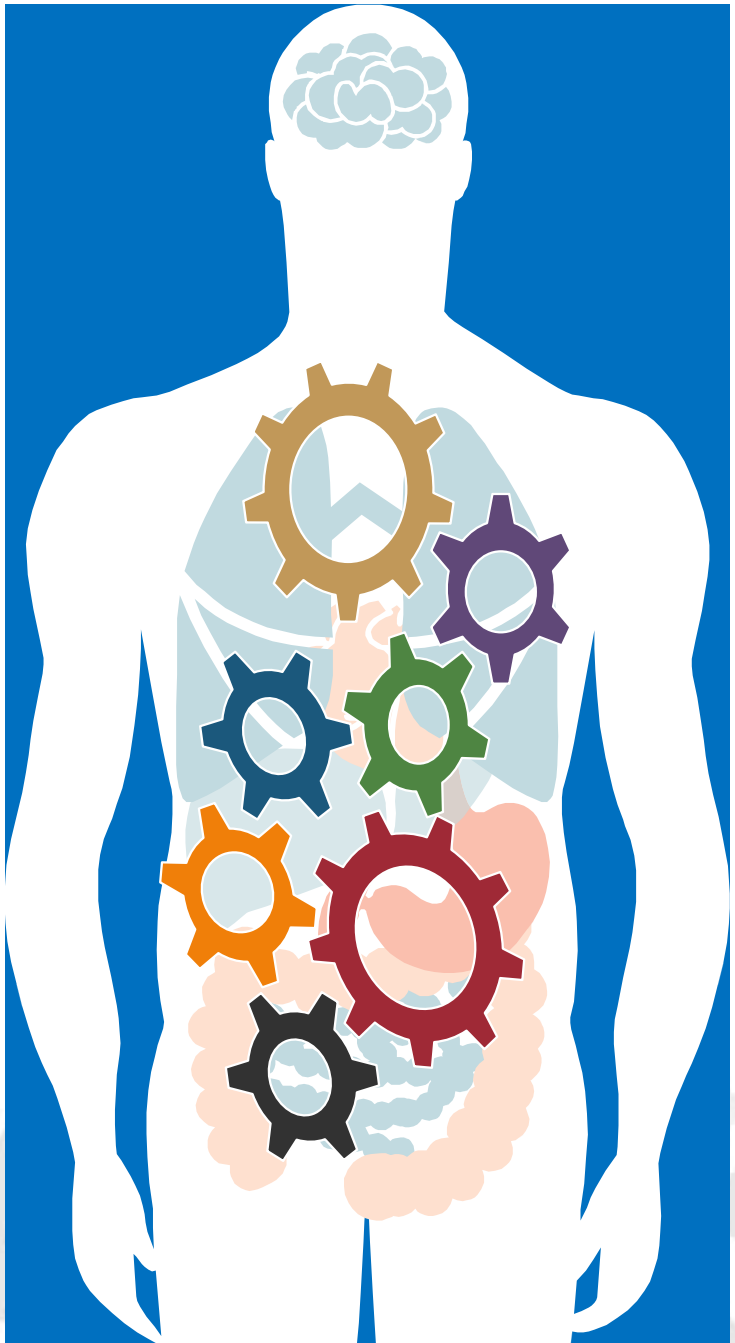
Defense System



Defense System

Marla- Fibromyalgia

7 SYSTEMS PLAN



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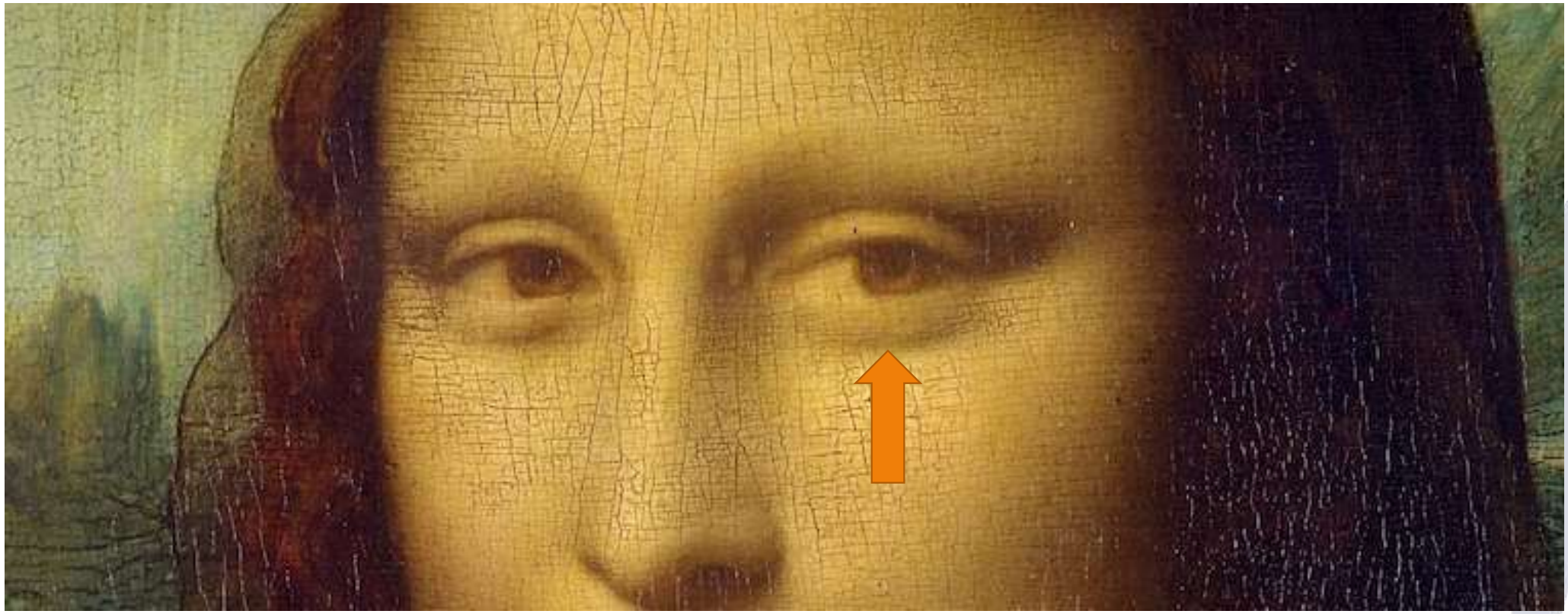
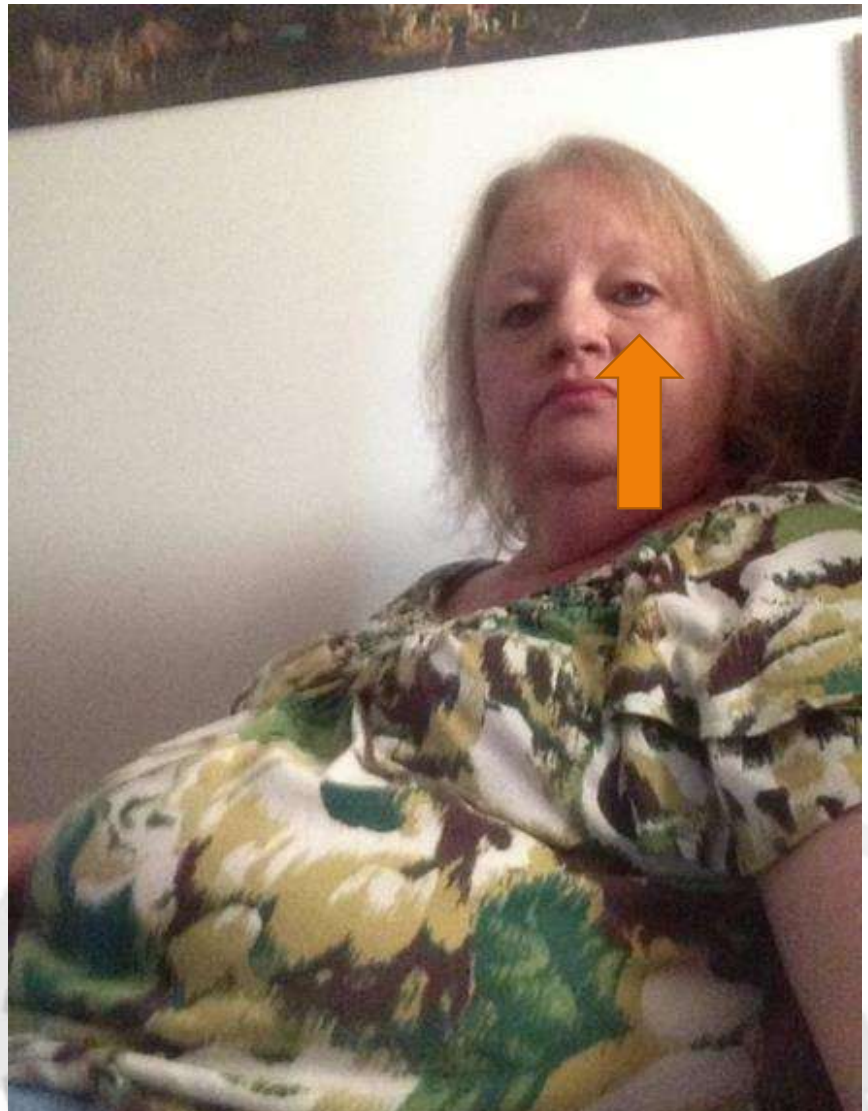
7 SYSTEMS PLAN

Detox System



Sheila



Brandy Age 30

Age 40

SYSTEMS PLAN

Thank you!

patlusedc@gmail.com
DrPatLuse.com
712-898-4844

Scan code

Recommended Food List

Foods listed in green are recommended. You want to avoid the foods listed in red.

FOODS TO EAT

**FOODS TO BE CAREFUL WITH

Vegetables Low GI	Vegetables Medium GI	Fruit	Oils	Concentrated Proteins	Nuts & Seeds	**Legumes	Grains	Dairy	Beverages	Functional Foods
Cruciferous: broccoli, brussels sprouts, cabbages, cauliflower Greens: leaf greens, bok choy, collard greens, escarole, kale, mustard greens, Swiss chard, watercress, spinach Lettuce/Mixed greens Mushrooms Salsa (sugar-free) Sprouts: alfalfa, broccoli or radish sprouts, bamboo shoots, etc. Squash: spaghetti, summer, yellow, zucchini Other vegetables: artichokes, asparagus, organic celery, chives, cucumbers, dill pickles, eggplants, garlic, green beans, hot peppers, leeks, lentils, mixed vegetable juices, okra, onions, organic sweet bell peppers, radishes, snow peas, organic tomatoes, water chestnuts	Beets Carrots Pumpkins Rutabagas Sweet potatoes or yams Tomatoes Winter squash Organic Yukon Gold Potatoes	Berries: blackberries, blueberries, raspberries, and organic strawberries Organic apples Apricots Cantaloupe Organic cherries Clementine Fresh Figs Organic grapes Honeydew melon Kiwifruits Mango Organic nectarines Oranges Organic peaches Organic pears Plums Tangerines Watermelon Bananas Dried fruit Fruit juices Pineapples	Best: Avocados and Guacamole Olives Good: Extra virgin coconut oil Cold pressed extra virgin olive oil Flaxseed oil Walnut oil Avocado oil Mayonnaise (made with avocado oil) Vegetable and Processed oils Canola oil Hydrogenated oil Margarine Peanut oil Sunflower oil Safflower oil Trans fats Vegetable shortening	Best: Low GI vegetables Tofu Tempeh Soy or veggie burger (read ingredients) Fish (wild caught) Beef (grass-fed) Lamb (grass-fed) Chicken (free-range) Good: Beef-lean Eggs (free-range) Cottage cheese Ricotta Mozzarella Parmesan Processed meat Deli Meat Hot Dogs Pork Sausage Salami Tuna	Note: Walnut Almonds Brazil nuts Macadamia Pecan Pistachios Hazelnuts Seeds: Sunflower Pumpkin Sesame seeds Nut butter: Almond butter Not as good: Peanuts Cashews Peanut butter (no sugar) Nuts with sugar or chocolate Nut butter that contains trans fats or sugar	Beans: black, butter, cannellini, garbanzo, chickpeas, great northern, pinto, kidney, lima, navy, mung, fat free refried, green soy Hummus Bean Soup Lentils: beluga, French, and red variety Peas: split green or yellow peas Baked beans Peanuts Soybean oil	Amaranth, teff, or quinoa Rice: Barley, buckwheat groats, millet Bulgur Popcorn Whole oats: Whole wheat, spelt, or kamut berries Pasta: 100% whole wheat, spelt, kamut, or black bean Crackers Breads: mixed whole-grain or 100% whole-rye Tortillas: Pita whole-wheat or low-carb Flour tortilla Wheat bread White bread Pasta	Butter or ghee Buttermilk Yogurt (plain) Dairy Substitutes: Almond milk (no sugar) Hemp milk (no sugar) Coconut milk (no sugar) All conventional dairy products including milk Processed cheese	Water Coffee Herbal or Green tea Sparkling or Mineral water Alcohol Soda Sugary beverages Fruit juices Enhanced or flavored water Diet/Artificially sweetened drinks	Dynamic Daily Meal Dynamic GI Restore Dynamic Cardio-Metabolic Dynamic Inflam Ease Dynamic GI Integrity Dynamic Detox

**Avoid these foods if you have GI issues, inflammation, auto-immune disease, or diabetes.

6 min