Download these slides

people.csail.mit.edu/seneff/2015/ WAPF_heart.pptx

New Paper Just Released!

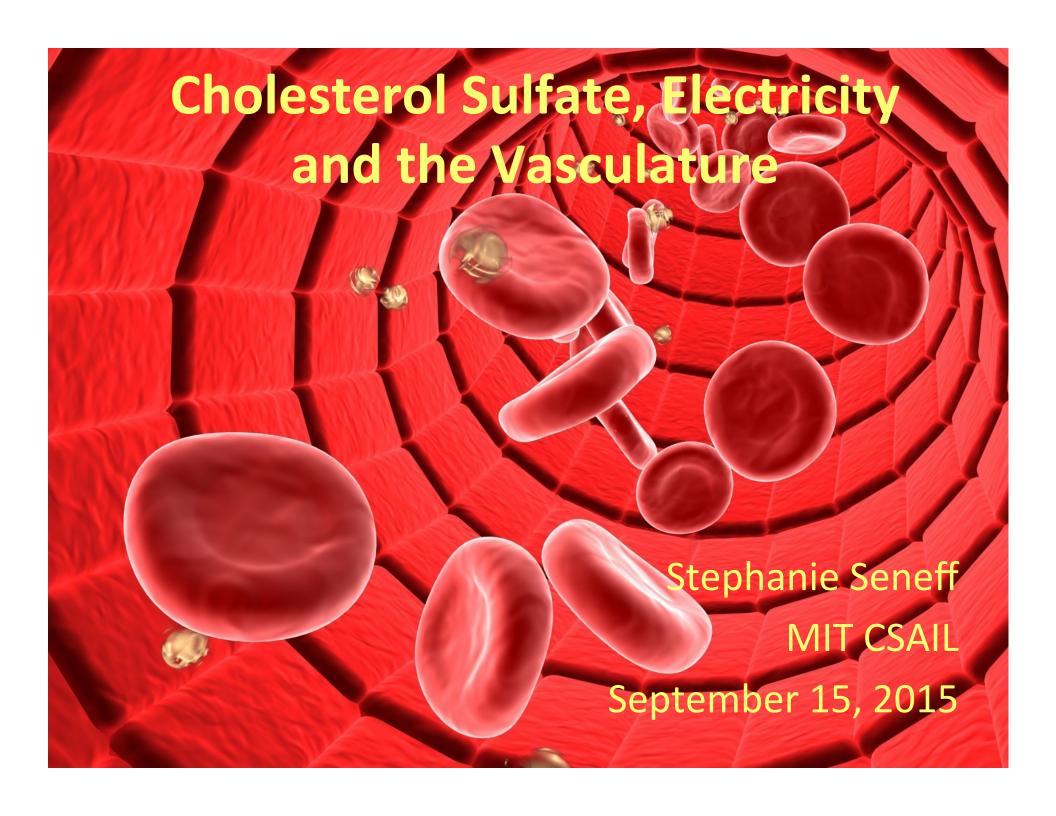
Anthony Samsel and Stephanie Seneff.

Glyphosate, pathways to modern diseases IV: cancer and related pathologies.

Journal of Biological Physics and Chemistry 15 (2015) 121–159.

Check it out here:

http://www.gmfreecymru.org/pivotal_papers/crucial61.html



The fatal tendency of mankind to leave off thinking about a thing when it is no longer doubtful, is the cause of half their errors.

- John Stuart Mill, 1859

Belief:

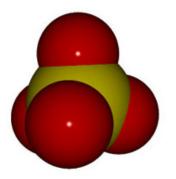
Cholesterol is a toxic substance that needs to be avoided in the diet, and statin drugs are the best way to keep cholesterol levels low

Reality:

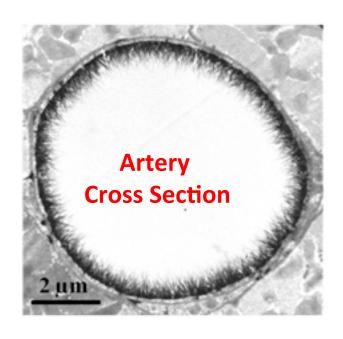
Cholesterol is essential for human life and it protects us from multiple modern diseases

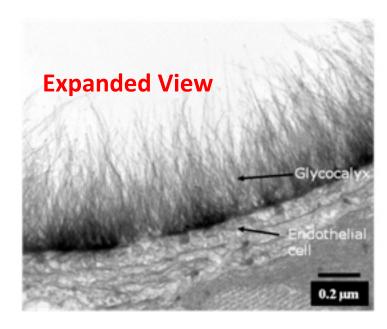
Outline

- Sulfate and the Glycocalyx
- Cholesterol Sulfate and Heart Disease
- Streaming Potential
- Roundup, StAR and Sterol Homeostasis
- Iron and GGT
- How to Stay Healthy!



Sulfate and the Glycocalyx





The Broad Picture

- Water plays a vital role in human physiology, but it needs sulfate to work properly
- Cholesterol sulfate, produced upon sun exposure, provides sulfate to the vasculature
- Toxic chemicals (especially glyphosate) disrupt sulfate synthesis and sulfate transport
 - This harms red blood cells and induces anemia
 - It also induces an inflammatory response leading to systemic cellular injury
- Sulfate deficiency is behind most modern diseases

It's All About the Blood

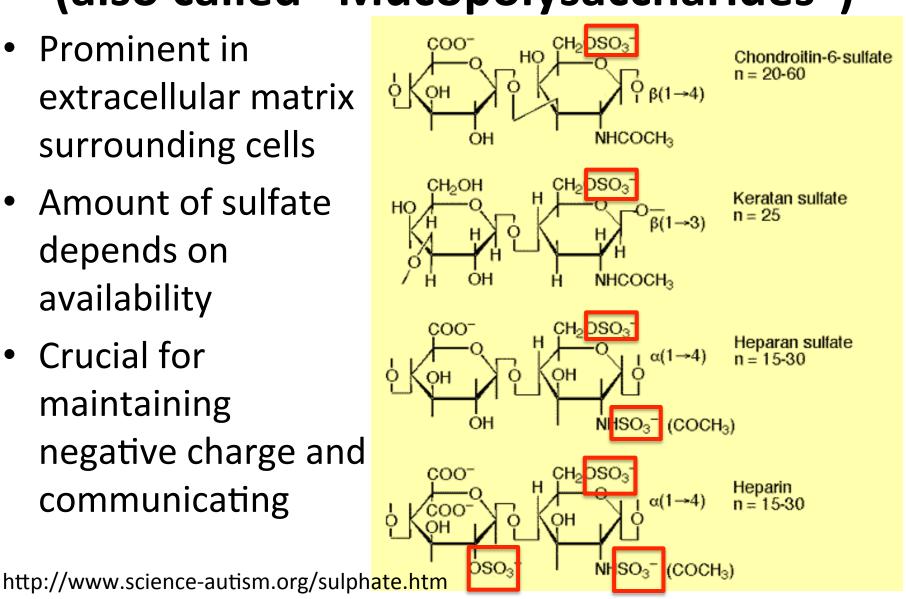
- We are 2/3 water by mass and 99% by molecule count
- Most of the water in the body is gelled
- The BIG EXCEPTION is the flowing blood!
- Blood delivers nutrients to and removes waste from all the tissues
- Gelled water lines the vessel wall and provides slick, frictionless passage of red blood cells through the capillaries
- Sulfate keeps the water gelled along the border
- Sulfate transport is problematic

Sulfate is Crucial to Maintain Structured Water

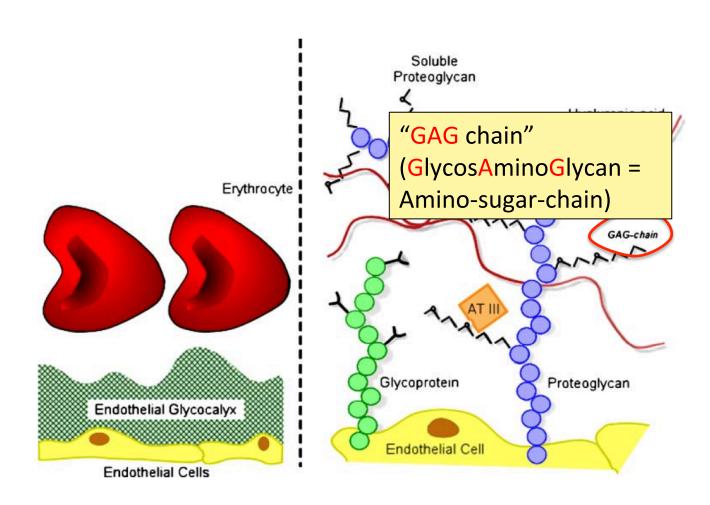
- Most cells in the body maintain an extracellular matrix that is formed from "glycosylated" proteins with complex sugar chains attached to them, and sulfate ions bound to the sugars at strategic locations in an irregular but non-random pattern
- The glycocalyx that lines the walls of all blood vessels is formed from these glycoproteins

Sulfated Glycosaminoglycans (GAGs) (also called "Mucopolysaccharides")

- Prominent in extracellular matrix surrounding cells
- Amount of sulfate depends on availability
- Crucial for maintaining negative charge and communicating



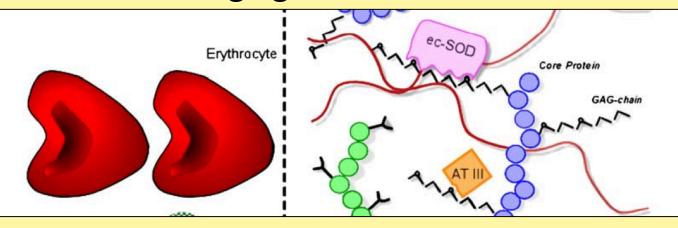
Endothelial Glycocalyx Schematic*



^{*}S Reitsma et al., Pflugers Arch - Eur J Physiol (2007) 454:345–359

Endothelial Glycocalyx Schematic*

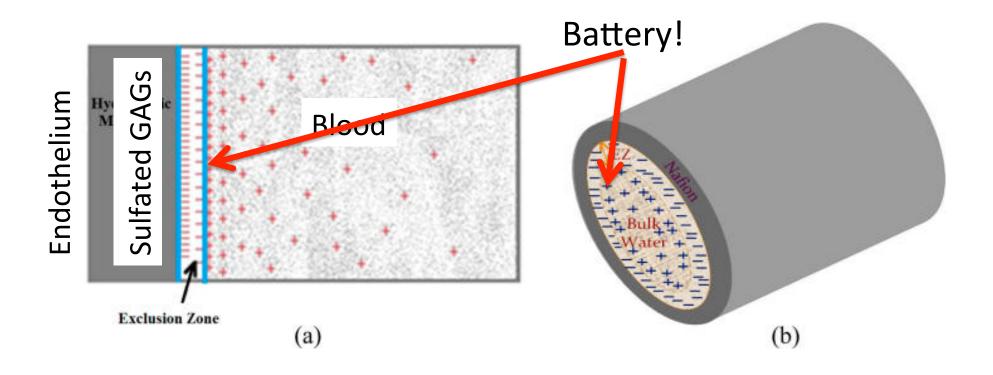
Gel layer prevents attack of vessel wall by blood sugars and oxidizing agents.



Cellular signaling mechanisms (e.g., antioxidant ec-SOD and clot-protective AT III) depend on sulfates to work.

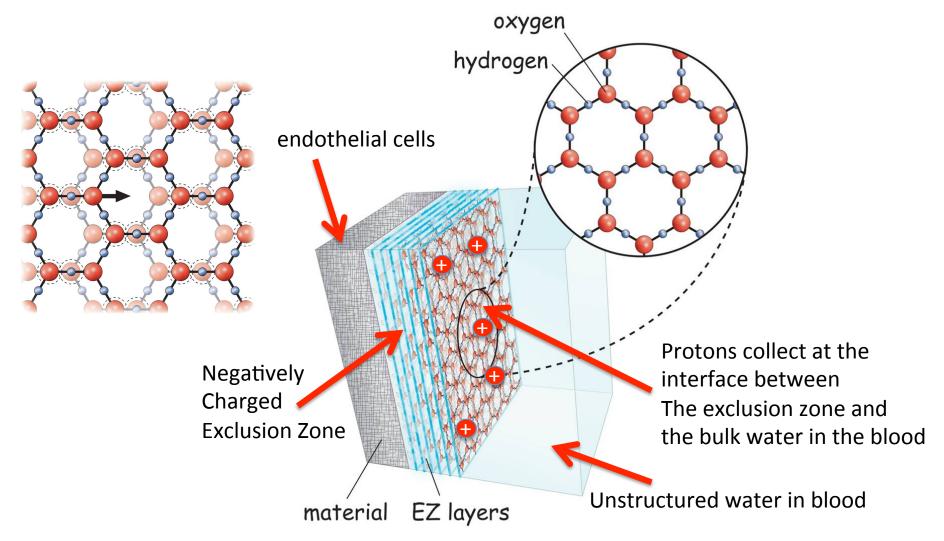
^{*}S Reitsma et al., Pflugers Arch - Eur J Physiol (2007) 454:345–359

Exclusion Zone: Model of Capillary*



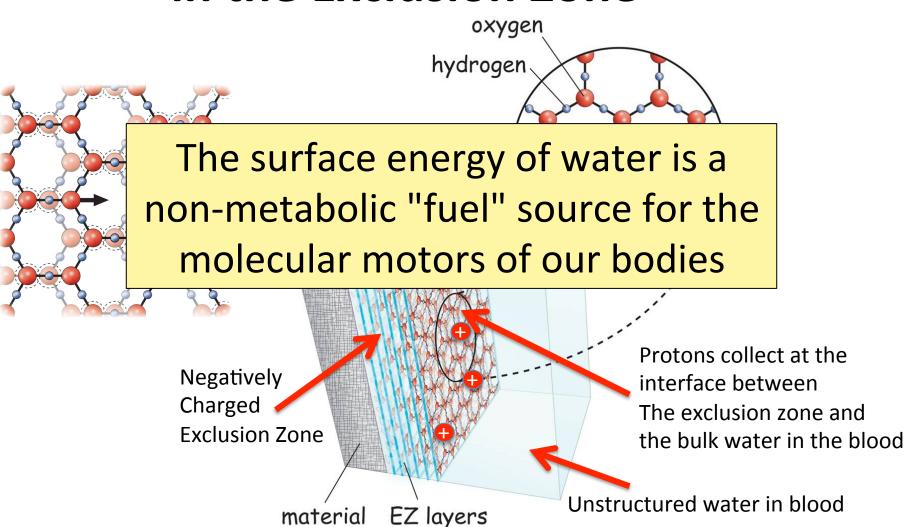
^{*}Figure 9, M. Rohani and G.H. Pollack, Langmuir 2013, 29, 6556–6561

Water Organizes Into "Crystals" in the Exclusion Zone*



^{*}http://doublehelixwater.eu/understanding-water-contents/exclusion-zone-form/

Water Organizes Into "Crystals" in the Exclusion Zone*



^{*}http://doublehelixwater.eu/understanding-water-contents/exclusion-zone-form/

Cholesterol Sulfateand Heart Disease

Cholesterol: Saint, Not Villain

- Cholesterol is to animals as chlorophyll is to plants: it gives us a brain and mobility
 - The brain makes up 5% of the body's weight and contains 25% of the body's cholesterol
- Why would cholesterol pile up in the arteries leading to the heart, if not for a good reason??

Cholesterol and Cholesterol Sulfate

Sulfation makes cholesterol water-soluble and therefore much easier to transport

Equally important is that cholesterol *carries sulfate*

A Provocative Proposal*

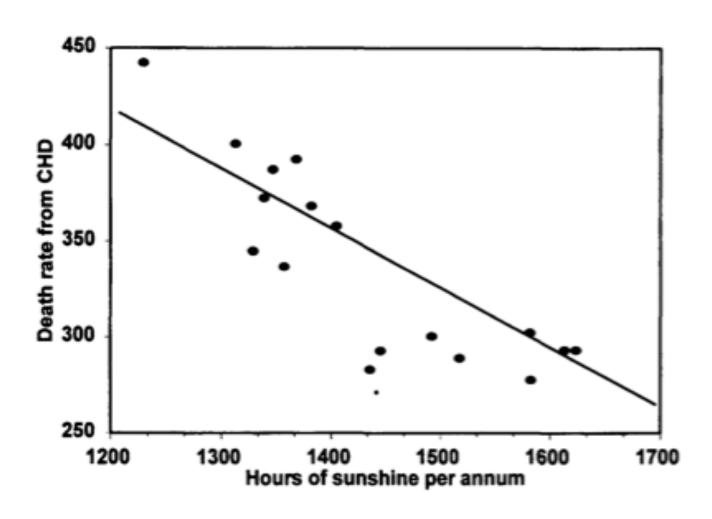
 Cholesterol sulfate supplies oxygen, sulfur, cholesterol, energy and negative charge to all the tissues



- Sulfate is synthesized from sulfide in skin and blood stream utilizing energy in sunlight
 - Protects from UV damage and keeps microbes out

^{*}S Seneff et al. Theor Biol Med Model 2015; 12:9

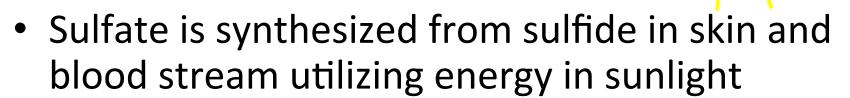
Heart Disease Mortality and Sunlight*



^{*}Grimes et al., Q. J. Med. 1996; 89:579-589

A Provocative Proposal*

 Cholesterol sulfate supplies oxygen, sulfur, cholesterol, energy and negative charge to all the tissues



- Protects from UV damage and keeps microbes out
- Endothelial Nitric Oxide Synthase (eNOS) performs the magic

The skin is a solar powered battery!

^{*}S Seneff et al. Theor Biol Med Model 2015; 12:9

A Provocative Proposal*

 Cholesterol sulfate supplies oxygen, sulfur, cholesterol,

BOLD CLAIM:

Deficiencies in cholesterol and sulfate supplies to the blood and to the tissues are the most important factor behind modern diseases

The skin is a solar powered battery!

^{*}S Seneff et al. Theor Biol Med Model 2015; 12:9

eNOS is Very Vulnerable*

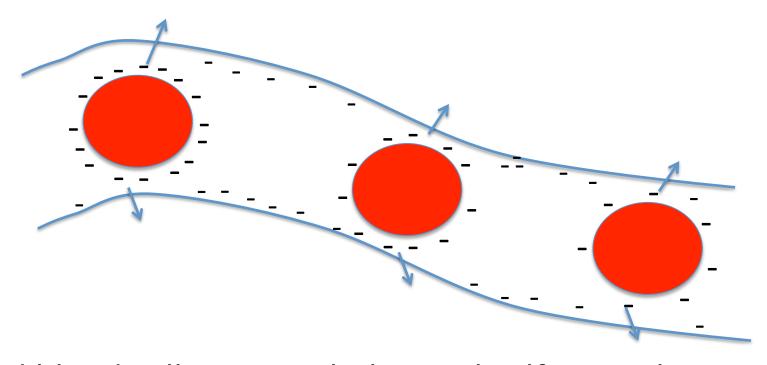
- eNOS depends on:
 - Cobalamin (vitamin B12, cobalt)
 - Heme iron, sulfur, zinc, oxygen
 - Glutathione
 - Sunlight



 Highly susceptible to damage from various environmental toxicants like mercury, aluminum, glyphosate (*Roundup herbicide*), etc.



Cholesterol sulfate provides negative charge*



Red blood cells export cholesterol sulfate to the capillary wall, supplying it with cholesterol, sulfate, and negative charge

^{*} Davidson and Seneff, Entropy 14, 1399-1442, 2012

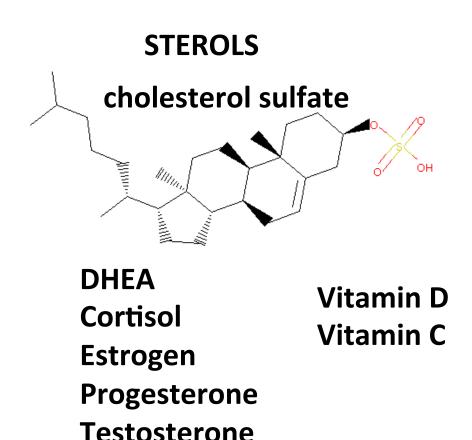
They Knew a Long Time Ago*

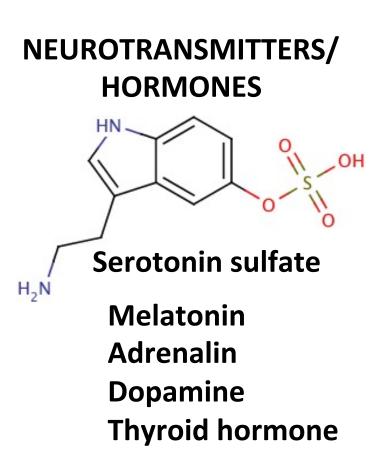
- Article published in 1960
- Fed cholesterol to monkeys
 - Induced atherosclerosis
- If sulfur-containing nutrients are added, atherosclerosis is prevented
- These nutrients provide source of sulfate to enable cholesterol transport



^{*} G.V. Mann et al., Am. J. Clin. Nutr. 8, 491-497, 1960

Sulfation as Sulfate Transport





- These are all sulfated for transport in the blood
- Is sulfate transport an important role that they play??

Various Factors that Increase Sulfate*

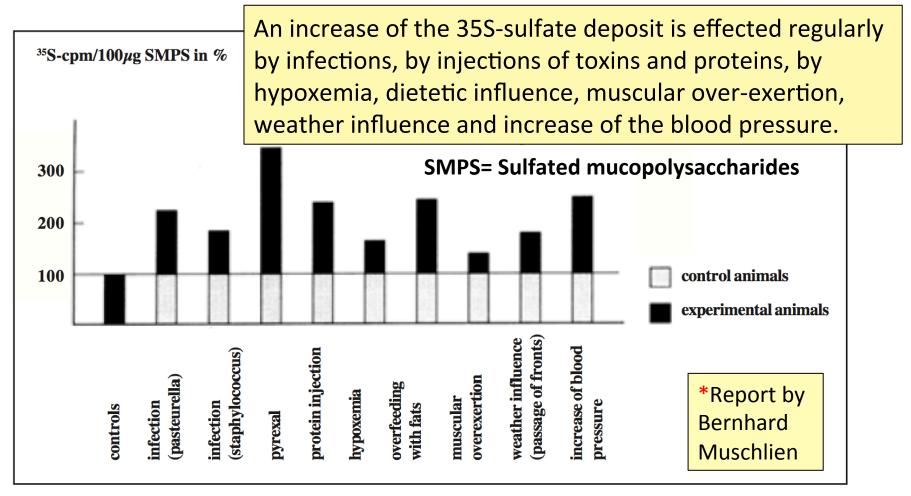
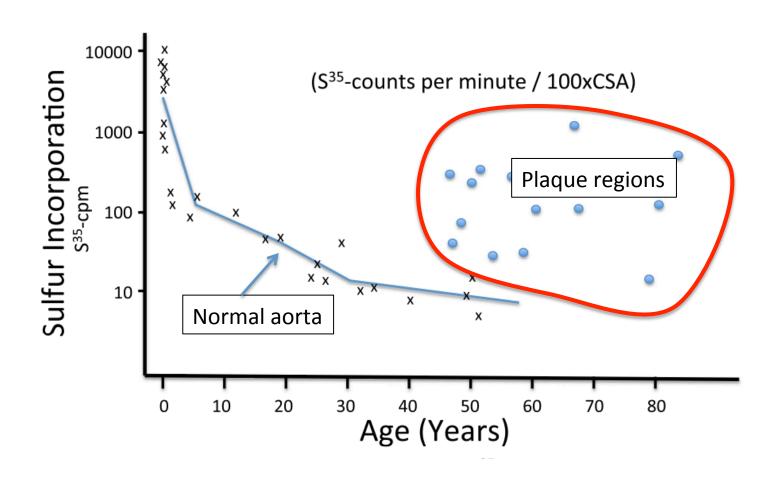


Fig. 2: Selected examples of factors that cause an increase of the SMPS synthesis, illustrated at the parameter of the ³⁵S-sulfate deposit in the connective tissue of various organs.

SMPS = Sulfated mucopolysaccharides = glycosaminoglycans

First published in the German language in the SANUM-Post magazine (17/1991)

Sulfur Incorporation into GAGs with Age*



^{*}WH Hauss et al.. J Atheroscler Res. 1962;2(1-2):50-61

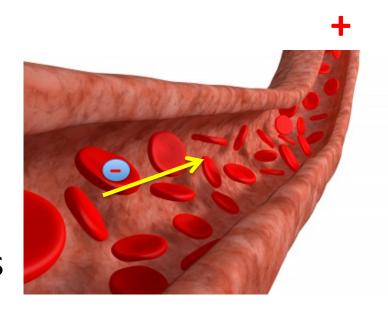
Streaming Potential

Zeta Potential

- Zeta potential (Z) is a measure of the flow rate of charged particles (e.g., red blood cells) in an electric field
- Impaired blood flow is a key problem in multiple modern diseases
 - Results from insufficient negative charge (Z) in the blood vessels, due to insufficient supply of sulfate anions (delivered as cholesterol sulfate by the red blood cells)
- The benefits of "grounding" are due to supply of negative charge from the earth

Electrokinetic Vascular Streaming Potential (EVSP)*

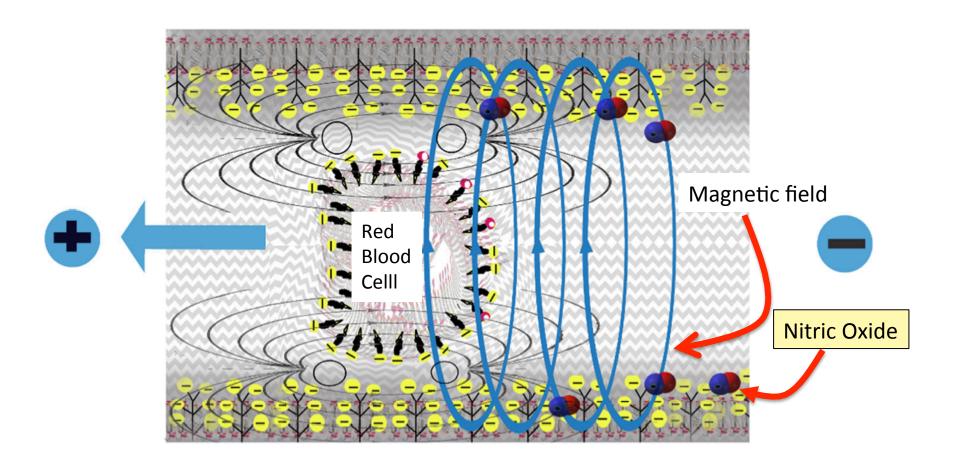
- Field strength is proportional to the zeta potential → promotes blood flow
- Contains a DC component and an AC component (very low frequency, depends on pulse rate and heart rate)



- Influences endothelial cells:
 - Enhances release of nitric oxide (vasorelaxant)
 - Increases calcium-based depolarization

^{*}D.P. Trivedi et al., Bioelectromagnetics 34:22-30, 2013

Moving RBC Creates Magnetic Field*



^{*}S Seneff et al., Theor Biol Med Model 2015; 12: 9

Various Factors that Increase Sulfate*

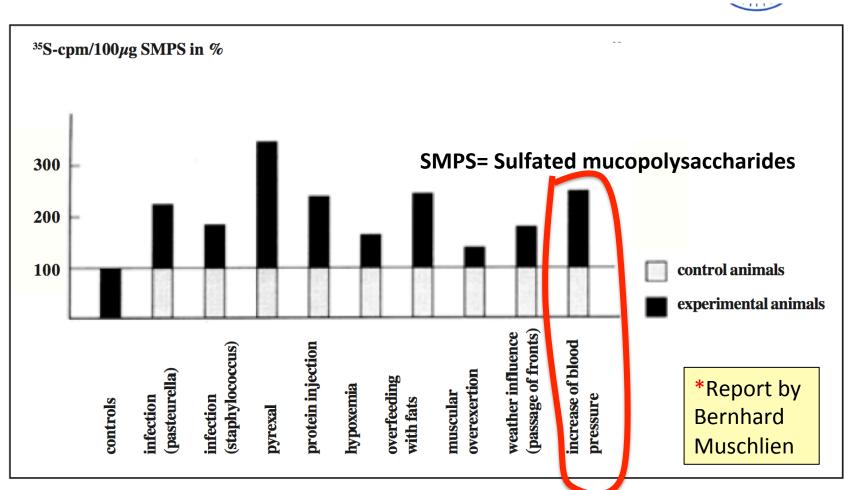


Fig. 2: Selected examples of factors that cause an increase of the SMPS synthesis, illustrated at the parameter of the ³⁵S-sulfate deposit in the connective tissue of various organs.

SMPS = Sulfated mucopolysaccharides = glycosaminoglycans

First published in the German language in the SANUM-Post magazine (17/1991)

Streaming Potential

Streaming potential

$$\downarrow
E_s = [Zee_oP/\eta k] [f(Y_a)]$$

 E_s = streaming potential (volts) Z = zeta potential (volts)

e = electrolyte dielectric constant

 $P = systolic pressure (N/m^2)$

k = conductivity (S/m)

 e_0 = permitivity of free space

 $\eta = viscosity (kg/m*s)$

 $F(Y_a)$ = correction for pulsatile flow

Streaming Potential

Contains both DC and AC component AC component controlled by heart rate

Higher heart rate induces stronger response

$$E_s = [Zee_o P/\eta k] [f(Y_a)]$$

 E_s = streaming potential (volts)

e = electrolyte dielectric constant

 $P = systolic pressure (N/m^2)$

k = conductivity (S/m)

Z = zeta potential (volts)

 e_0 = permitivity of free space

 $\eta = viscosity (kg/m*s)$

 $F(Y_a)$ = correction for pulsatile flow

Streaming Potential

Proportional to Zeta potential

$$E_s = [Zee_o P/\eta k] [f(Y_a)]$$

 E_s = streaming potential (volts)

e = electrolyte dielectric constant

 $P = systolic pressure (N/m^2)$

k = conductivity (S/m)

Z = zeta potential (volts)

 e_0 = permitivity of free space

 $\eta = viscosity (kg/m*s)$

 $F(Y_a)$ = correction for pulsatile flow

Streaming Potential

Proportional to blood pressure

$$E_s = [Zee_oP/\eta k] [f(Y_a)]$$

 E_s = streaming potential (volts) Z = zeta potential (volts)

e = electrolyte dielectric constant

 $P = systolic pressure (N/m^2)$

k = conductivity (S/m)

 e_0 = permitivity of free space

 $\eta = viscosity (kg/m*s)$

 $F(Y_a)$ = correction for pulsatile flow

Streaming Potential

Inversely proportional to viscosity

$$E_s = [Zee_oP/\eta k] [f(Y_a)]$$

 E_s = streaming potential (volts) Z = zeta potential (volts)

e = electrolyte dielectric constant

 $P = systolic pressure (N/m^2)$

k = conductivity (S/m)

 e_0 = permitivity of free space

 $\eta = viscosity (kg/m*s)$

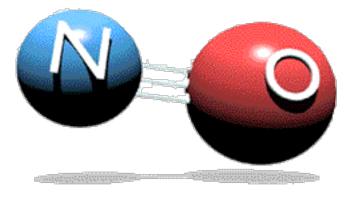
 $F(Y_a)$ = correction for pulsatile flow

Some Insights

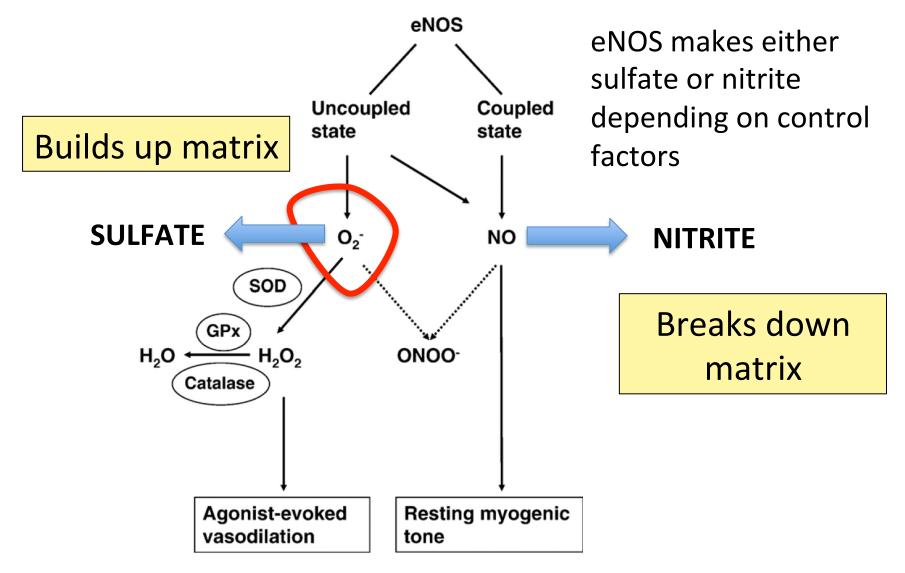
- When Z is too low (not enough bound sulfate), blood pressure must go up to compensate (high blood pressure)
- When viscosity is too high, blood pressure must go up to compensate (high blood pressure)
- Nitric oxide release is induced by the streaming potential

Why is Nitric Oxide Important?

- Nitric oxide relaxes the vessel wall and promotes increased flow & therefore oxygen
- Nitric oxide quickly converts to nitrite which can break down the glycocalyx, releasing sulfated GAGs
- These can be passed on to the capillaries to correct their deficiencies



eNOS Uncoupling*



^{*}Figure 1, M Yokoyama and K-I Hirata Cardiovascular Research 73 (2007) 8–9

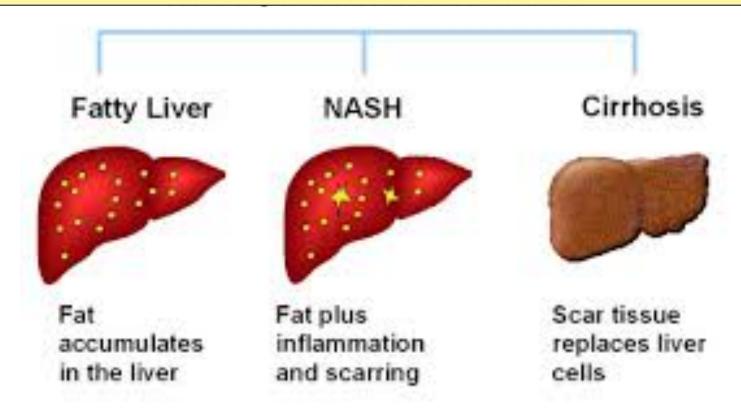
Roundup, StAR and Sterol Homeostasis





Non-alcoholic Fatty Liver Disease: An Epidemic in America

NAFLD affects almost one-quarter of the general U.S. population



An Epidemic in the Western World*

- Most common liver disorder in countries that adopt the "Western" diet
- Rate doubled between 2004 and 2010 in S. Korea
- Linked to low HDL, high LDL, and high cholesterol
- Vegetarian diet increases risk
- Insulin resistance and oxidative injury play a role

Fred Kummerow on LDL*

"LDL is not a marker of heart disease," Kummerow said. "It's a marker of ApoB." And ApoB is a marker of a lack of tryptophan.

Tryptophan is a product of the shikimate pathway, which glyphosate disrupts.



"Sulfation of 25-hydroxycholesterol regulates lipid metabolism, inflammatory responses, and cell proliferation"*

 Cholesterol and fats shipped out through bile acids

Fixes fatty liver

 Liver cells proliferate, restoring damaged liver

Suppresses inflammation

Turns on and off many enzymes

nucleus

LIVER CELL

StAR

25HC

SULT2B1b

SULFATE

25HC3S

mitochondrion

^{*}S Ren and Y Ying, Am J Physiol Endocrinol Metab 306: E123–E130, 2014

StAR is a Superstar!

- StAR protects from fatty liver disease and elevated serum LDL by promoting bile flow
- StAR is essential for synthesis of cortisol, testosterone and estrogen by the adrenal glands and by the gonads
- StAR induces export of cholesterol from cardiovascular plaque into HDL

Roundup Inhibits Steroidogenesis by Disrupting StAR Protein Expression*

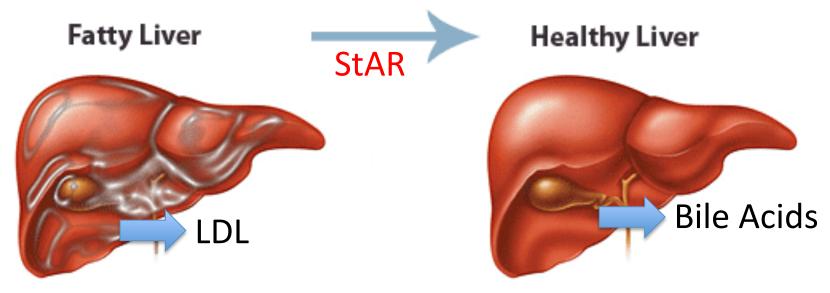
- In vitro study on testicular Leydig cells
- Roundup reduced testosterone synthesis by 94%
 - Effect due to both StAR suppression and CYP suppression



- Roundup reduced StAR protein levels by 90%
- Reduction in StAR expression in the adrenal gland disrupts synthesis of stress hormones and sex hormones

^{*}LP Walsh et al., Environ Health Perspect 2000; 108:769-776

StAR Protein, Cholesterol Sulfate, and LDL*



- 25HC3S is an important regulator of lipid biosynthesis
- Decreases liver accumulation of fat and cholesterol
- Increases bile acid production and decreases LDL export

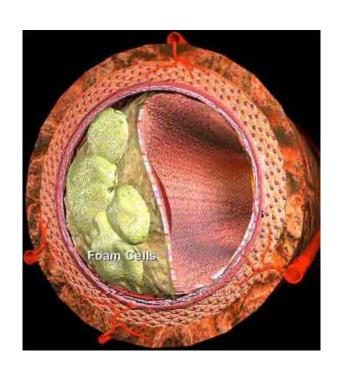
^{*}Q Bai et al., Metabolism. 2012 June ; 61(6): 836–845

Overexpression of StAR increases macrophage cholesterol efflux to HDL-AI*

Atherosclerosis:

Macrophages infiltrate the artery wall and transform to foam cells, storing fat and cholesterol

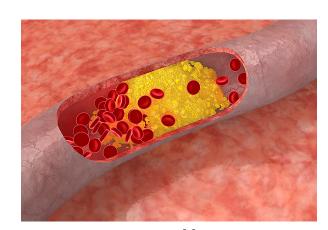
- Macrophages export their cholesterol to HDL-A1, the so-called "good cholesterol"
- Overexpression of StAR in macrophages promotes cholesterol export



^{*}JMW Taylor et al., Cardiovascular Research (2010) 86, 526–534

Why Does Cholesterol Accumulate in the Arteries Supplying the Heart?

- The heart is arguably the most important organ in the body
- It needs abundant cholesterol and sulfate to stay healthy



- When there are deficiencies, the artery wall stockpiles cholesterol waiting to become cholesterol sulfate
- Inflammation induces superoxide which oxidizes sulfur to sulfate (e.g. in homocysteine)
- Sulfate conjugation is needed for cholesterol export/delivery

Statins Make You Grow Older Faster*















*J Liu and S Seneff, Proc. IMMM, Barcelona, Spain, Oct. 2011.

Evidence that Statins Make You Grow Older Faster*

Statins

- Reduce the overall growth rate of Mesenchymal Stem Cells (MSCs)
- Inhibit their potential to differentiate into macrophages, osteoblasts and chondrocytes
- Impair DNA repair capabilities
- Increase cell senescence and apoptosis



^{*} R Izadpanah et al. Am J Physiol Cell Physiol. 2015 Jul 29:ajpcell.00406.2014 [Epub ahead of print]

Statins CAUSE Atherosclerosis and Heart Failure!*

- Inhibit vitamin K2 synthesis
 - Increase risk of hardening of the arteries (calcification)
- Function as mitochondrial toxins
 - Deplete Coenzyme Q10 and heme A → reduced ATP supply
 - Inhibit selenoprotein synthesis → oxidative stress
- Increase chances for heart failure
 - Enlarged left ventricle associated with selenium deficiency

^{*} H Okuyama et al. Expert Review of Clinical Pharmacology 2015: 8:2; 189-199

Paul's Story (anecdotal)

Lipid Measure	March	April	August	
Cholesterol	149	213	168	
Cholesterol/HDL	4.4	5.5	3.4	
HDL	34	39	49	
LDL	68	134	97	
Triglycerides	235	198	110	

- Stopped statin drug in March
- Switched to organic diet high in sulfur and cholesterol
- Spent considerable time every day outside in the sunlight, starting in April; practiced "grounding"
- Vitamin D: 44 (March), 77 (May), 112 (June)
- Lost weight and felt much more energetic

Iron and GGT

What's the Problem With Iron?

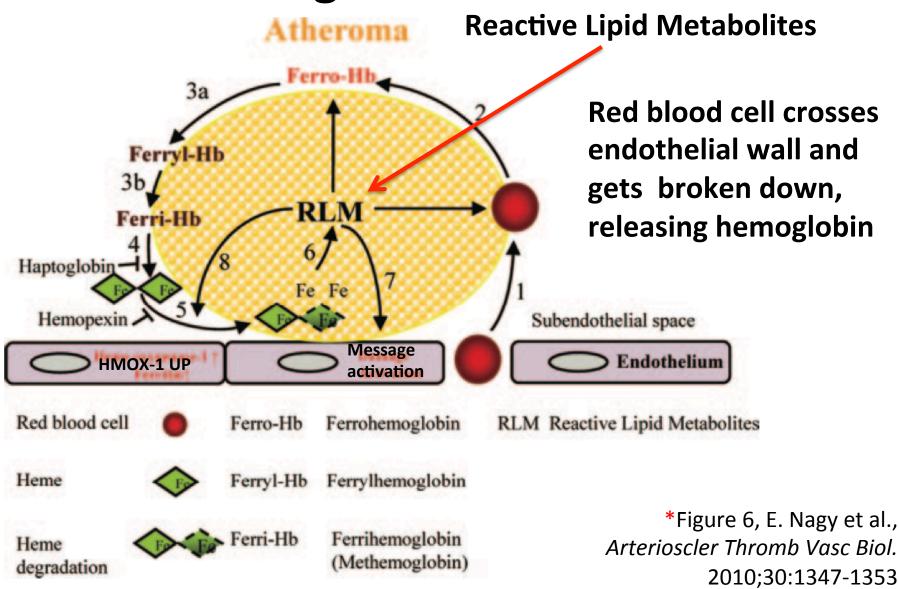


The iron paradox: iron is both vital & lethal

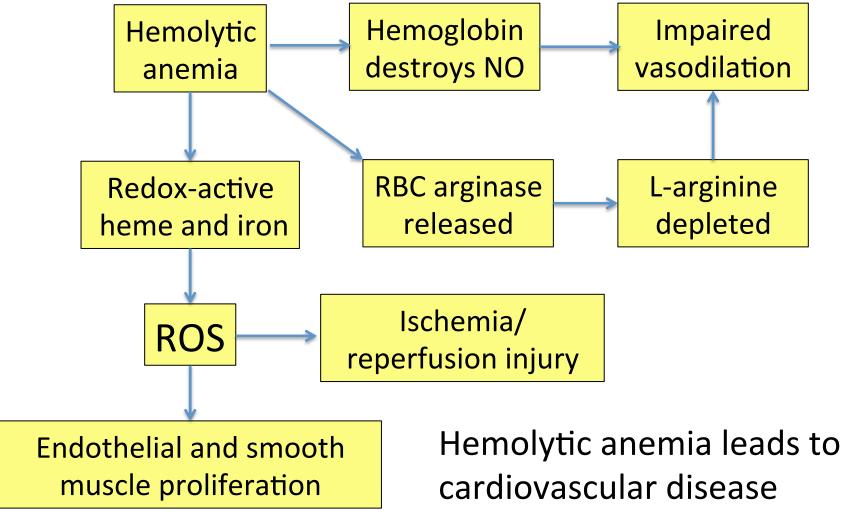
- Vital & harmful effects result from same reactions:
 - redox chemistry, interactions with O₂
- Results of iron excess:
 - Reduction of O_2 (ROS) + iron \rightarrow OH•
 - Oxidative stress damages cell membranes, DNA, protein
- Anti-oxidant defenses are overcome

 iron toxicity

Hemoglobin: Source of Iron Overload Causing LDL Oxidation*

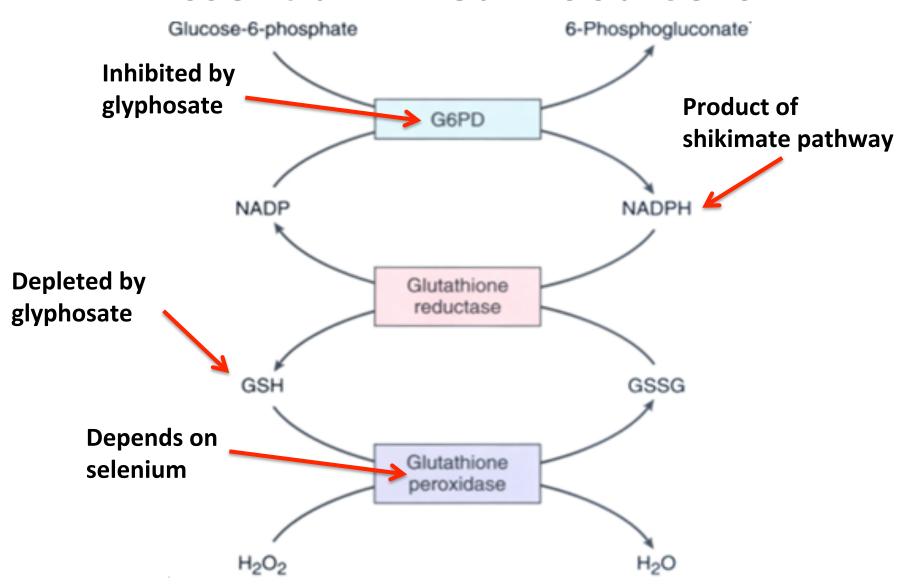


Hemolytic Anemia*



^{*}RF Machado et al., AMA, July 19, 2006 296(3), 310-318.

This Detoxification Scheme is Essential in Red Blood Cells

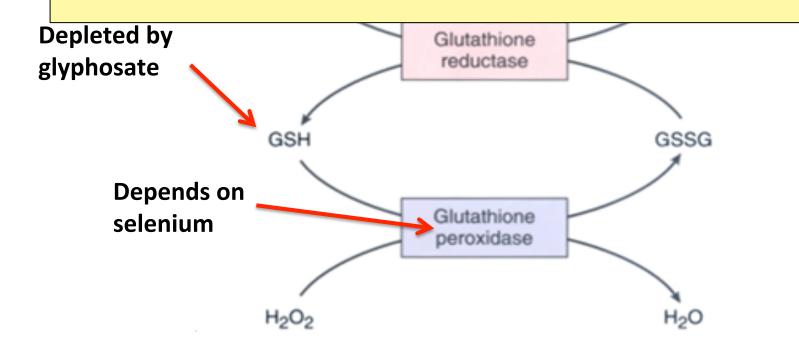


This Detoxification Scheme is Essential in Red Blood Cells

Glucose-6-phosphate 6-Phosphogluconate

Inhibited by

G6PD Deficiency Leads to Hemolysis and Anemia

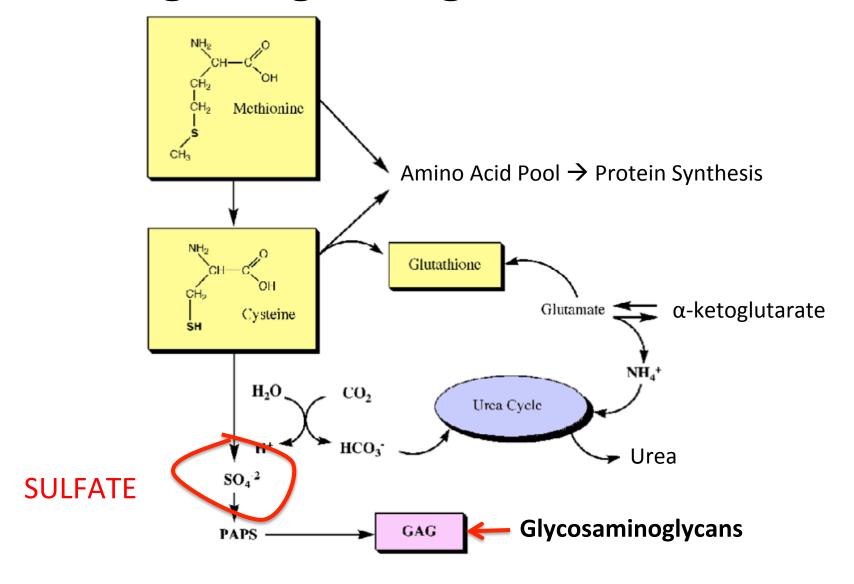


Gamma Glutamyl Transferase (GGT)*

- GGT is an enzyme that breaks down glutathione into its component amino acids
- Elevated serum GGT is a sign of liver and biliary diseases
- It's also associated with cardiovascular disease, metabolic syndrome and diabetes
- GGT accumulates in atherosclerotic plaque
- High GGT is associated with iron overload

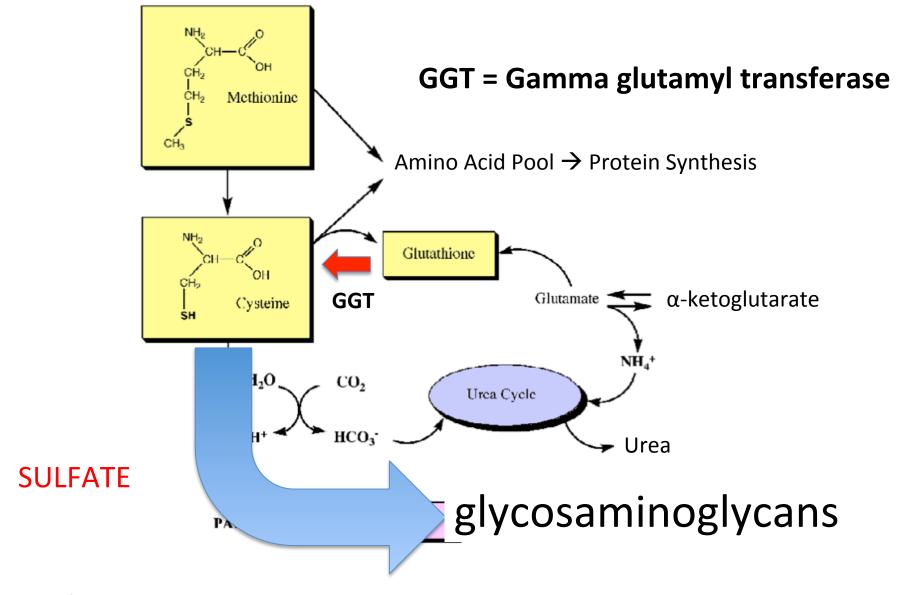
^{*}G. Koenig and S. Seneff. Disease Markers Volume 2015 (2015), Article ID 818570.

Are we getting enough sulfur in our diet?*



^{*}Figure 1, ME Nimni et al., Nutrition & Metabolism 2007, 4:24

Are we getting enough sulfur in our diet?*

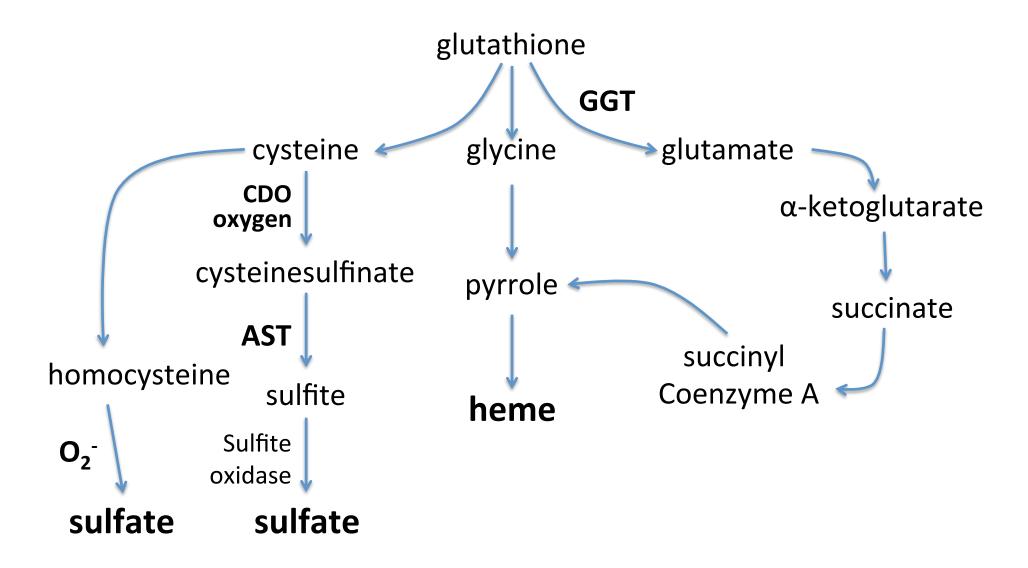


^{*}Figure 1, ME Nimni et al., Nutrition & Metabolism 2007, 4:24

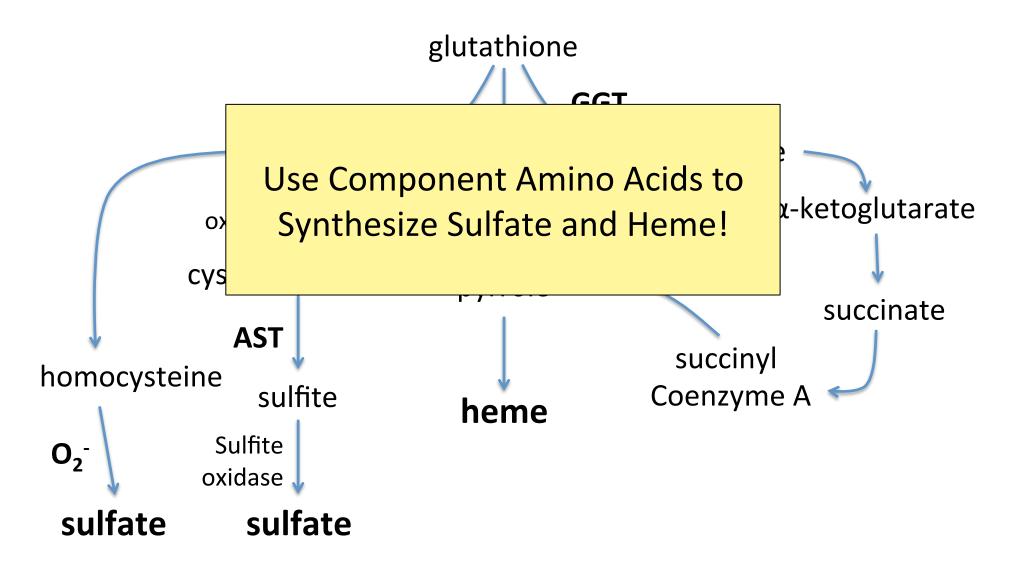
GGT Cycle* cysteine glycine DP protein cysteinylglycine glutamate γ-glutamyl amino acid ► GSH cysteine 5-oxoproline amino acid γ-glutamyl amino acid **GSH** glutathione

*Figure 4 in SC Lu et al., *Mol Aspects Med*. 2009; 30(1-2): 42–59.

The Real Reason for GGT?



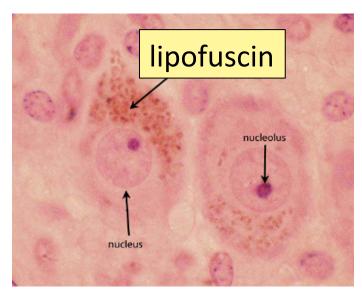
The Real Reason for GGT?



Ferrous Iron in Lysosomes: Key Role in Cardiovascular Disease*

- Lysosomes in macrophages recycle iron in hemoglobin in atherosclerotic plaque
- Fe(II)
 superoxide via

 Fenton reaction



- Superoxide damages cellular proteins and DNA
- Result: lipofuscin accumulation
 - Lipofuscin accumulation reflects biological rather than chronological age

^{*}T Kurz et al., The International Journal of Biochemistry & Cell Biology 43 (2011) 1686–1697

Heparin Protects from ROS due to Iron*

Free radical production (Fenton reaction):

$$Fe(II) + O_2 + 20H^- --> Fe(III)(OH)_2 + O_2^-$$

But, in the acid environment of heparin:

$$4Fe(II) + O_2 + 4H + --> 4Fe(III) + 2H_2O$$

*M.A. Ross et al., Biochem. J. 1992, 286: 717-720.

superoxide

water

Heparin Protects from ROS due to Iron*

Free radical production (*Fenton* reaction): /

Fe(II)
$$+ 0_2 + 20H^- --> Fe(III)(OH)_2 + 0_2^-$$

But, in the 4Fe(II

Heparin taken up by lysosomes allows them to safely handle iron

*M.A. Ross et al., Biochem. J. 1992, 286: 717-720.

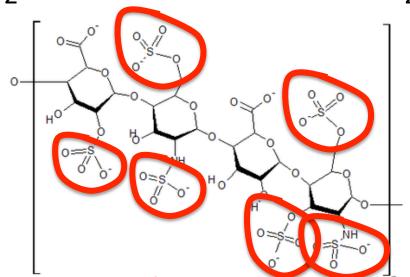
water

Heparin Protects from ROS due to Iron*

Free radical production (Fenton reaction):

$$Fe(II) + O_2 + 20H^- --> Fe(III)(OH)_2 + O_2^-$$

But Heparin is loaded with sulfates!!



*M.A. Ross et al., Biochem. J. 1992, 286: 717-720.

superoxide

GGT induces Inflammatory Response

- GGT releases iron from chelators (such as glyphosate!)
- Free iron induces Fenton reaction (damages cellular proteins and membrane fatty acids)
- GGT is needed to break glutathione into its component amino acids to produce heme and sulfate
- Glyphosate disrupts both pathways

GGT induces Inflammatory Response

GGT releases iron from chelators (such as

• 5.4-fold increased expression of GGT in livers of rats exposed to Roundup over their lifetime (Seralini's study)

• Grypnosate disrupts both pathways

GGT & Chronic Obstructive Pulmonary Disease (COPD)*

"We found that in adults aged 40 years and older, representative of the Korean population, elevated GGT levels are associated with decreased pulmonary function (in both genders) and an increased prevalence of COPD in men."

GGT & Chronic Obstructive Pulmonary Disease (COPD)*

"We found that in adults aged 40 years and

older, eleva decre and a

COPD is associated with excessive mucus production in the lungs which I believe provides sulfate for the vasculature**

ion,

ders)

^{*}HW Kim et al., Lung, 2014 Jul 11. [Epub ahead of print]

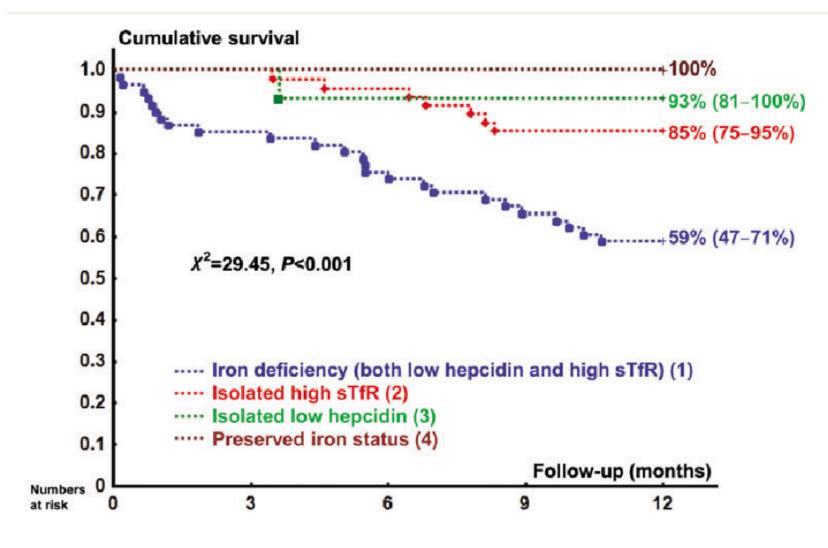
^{**}DT Wright et al., Am J Physiol 271(5 Pt 1):L854–L861

"Iron deficiency: an emerging therapeutic target in heart failure"*

"In patients with heart failure, iron deficiency is frequent but overlooked, with a prevalence of 30%–50%. ... Recent European guidelines recommend the monitoring of iron parameters (ie, serum ferritin, transferrin saturation) for all patients with heart failure. Ongoing clinical trials will explore the benefits of iron deficiency correction on various heart failure parameters."

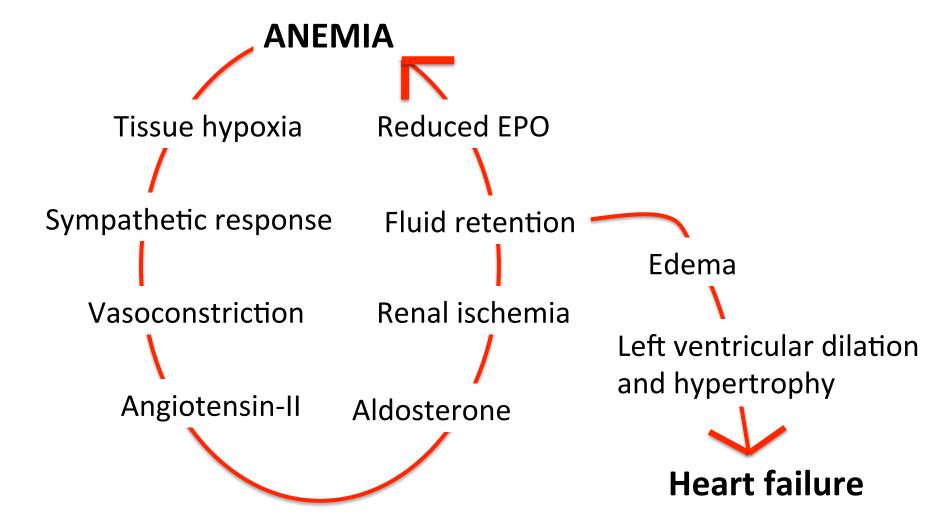
^{*}A Cohen-Solal et al., Heart 2014 [Epub ahead of print]

Low Iron Linked to Heart Failure*



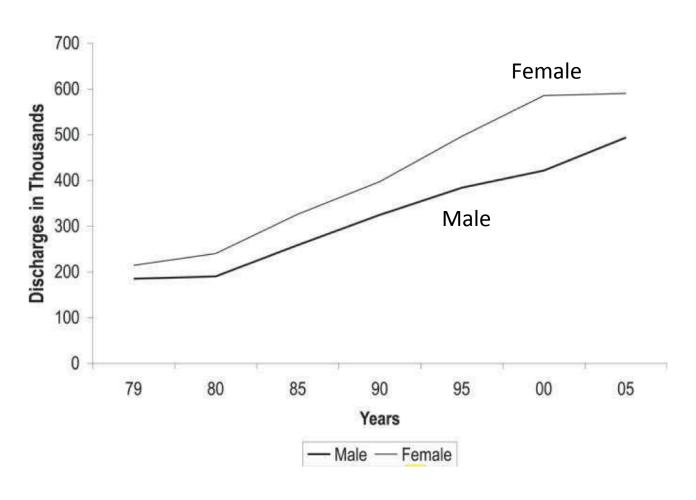
^{*}EA Jankowska et al., European Heart Journal Advanced Access, June 13, 2014

"The long term effects of all these factors on the heart can be disastrous"*



^{*}DS Silverberg et al., The European Journal of Heart Failure 4 (2002) 681–686

Heart Failure Rate Is Increasing*



*Chart 7-3, Circulation Jan 29, 2008, p. e89

How to Stay Healthy!

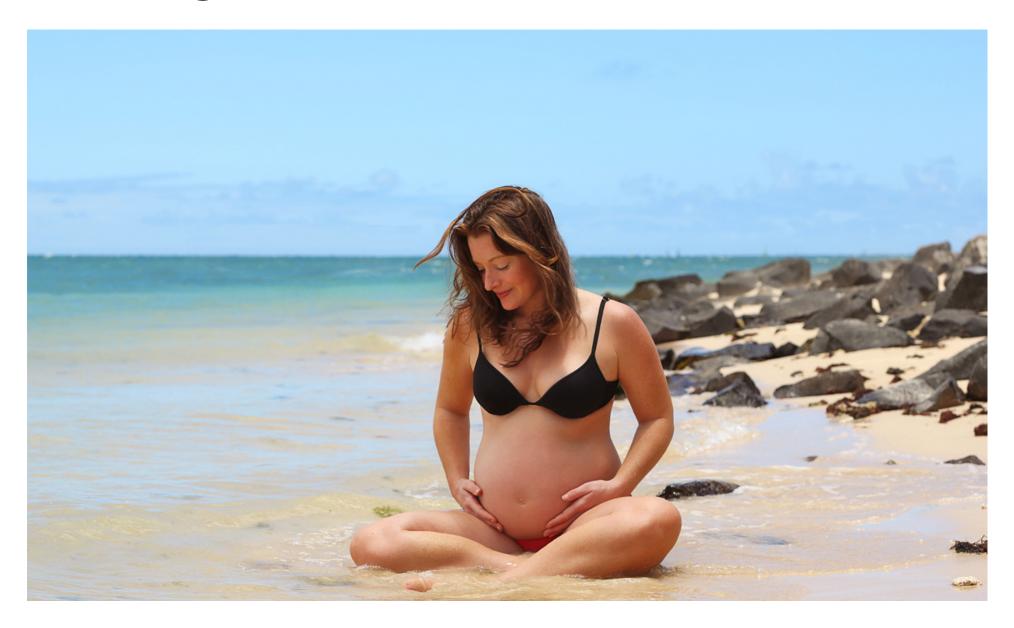
How to Stay Healthy

- Plenty of dietary sulfur
- Plenty of dietary cholesterol
- Plenty of flavonoids
- Plenty of sun exposure

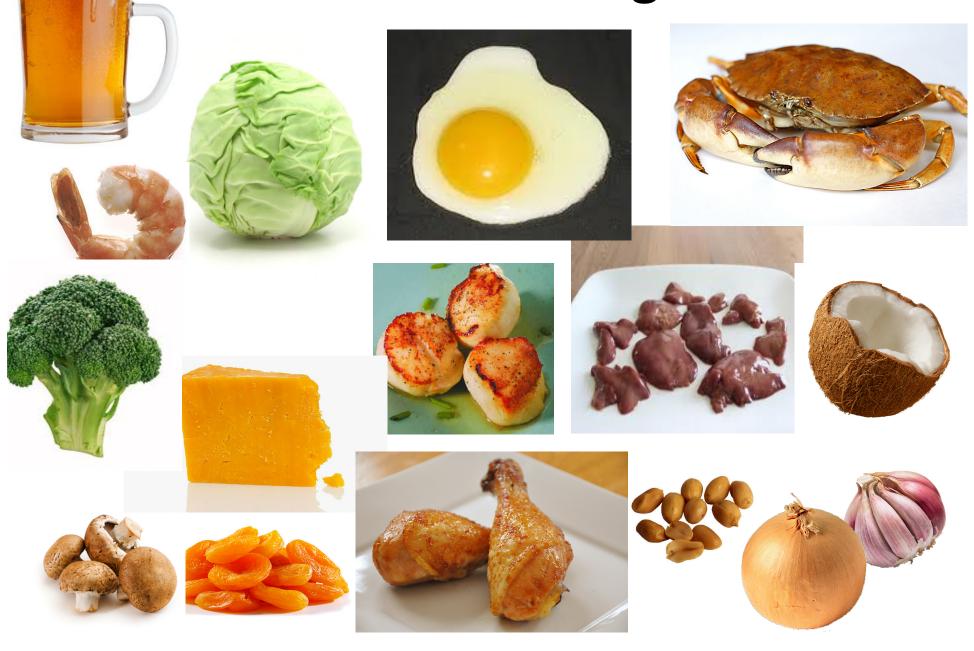




Hang Out in the Water at the Seashore



Eat Foods Containing Sulfur!



Supplemental Sources of Sulfur*

- glucosamine sulfate
- chondroitin sulfate
- glutathione
- N-acetylcysteine
- alpha lipoic acid
- taurine
- DMSO, MSM

My personal favorite is Epsom salt baths:

These can have many beneficial

effects and are nearly nontoxic

Magnesium sulfate uptake through the skin

- S-adenosylmethionine (SAMe)
- Epsom salts (Mg-sulfate)

^{*}S Parcell, Alternative Medicine Review 7(1), 2002, 22-44



AND Flavonoids and Polyphenols!











Flavonoids Transport Sulfate!

- Flavonoids are found in fruits, vegetables, nuts, seeds, herbs, spices, stems, flowers, tea and red wine.
- Flavonoids suppress nitric oxide synthesis in macrophages (inflammatory response)
- In plants, they generally occur as glycosylated and sulfated derivatives

Summary

- Cholesterol sulfate is vitally important to health
 - It is produced in the skin upon sunlight exposure
 - Roundup and other toxic exposures disrupt its supply
 - Sulfate deficiency is behind most modern diseases
- The blood depends on sulfate to maintain flow
 - Zeta potential drives blood flow from artery to vein
 - Heart disease and fatty liver disease reflect cholesterol buffering waiting for sulfate supplies
- StAR is a superstar but it's vulnerable to Roundup
 - StAR deficiency leads to fatty liver, heart disease, adrenal insufficiency and low testosterone
- Roundup induces GGT which causes inflammation but recovers hemoglobin and sulfate for RBCs

Thanks to Many People

- Robert Davidson
- Gerry Koenig
- Ann Lauritzen
- Jerry Pollack
- Anthony Samsel
- Nancy Swanson
- Glyn Wainwright
- And many others