

Sulfate Deficiency in Neurological Disease Following Aluminum and Glyphosate Exposure



Stephanie Seneff
June 2, 2015



***"If we all worked on the assumption
that what is accepted as true is
really true, there would be little
hope of advance."***

-- Orville Wright

Outline

- Introduction
- Sulfate
- Melatonin and the pineal gland
- Aluminum-glyphosate synergy
- Sulfate, vitamin D and autism
- Anemia and hypoxia
- Manganese dysbiosis
- Glyphosate and mitochondria
- Iron and mycoplasmas
- Sulfate and histamines (*if time!*)
- Summary

Outline

- **Introduction**
- Sulfate
- Melatonin and the pineal gland
- Aluminum-glyphosate synergy
- Sulfate, vitamin D and autism
- Anemia and hypoxia
- Manganese dysbiosis
- Glyphosate and mitochondria
- Iron and mycoplasmas
- Sulfate and histamines
- Summary

At the Cellular Level...



Neurons in the brain clear their cellular debris while we sleep, and they depend upon sulfate to do this.

- Prostate cancer cells produce cholesterol sulfate
- Breast cancer cells produce estrone sulfate → good substitute for cholesterol sulfate

Wake-Sleep Cycle*

“Circadian signals are more important than food or exercise for wellness. Wellness is about optimized circadian signal specificity and sensitivity.”

Jack Kruze, MD

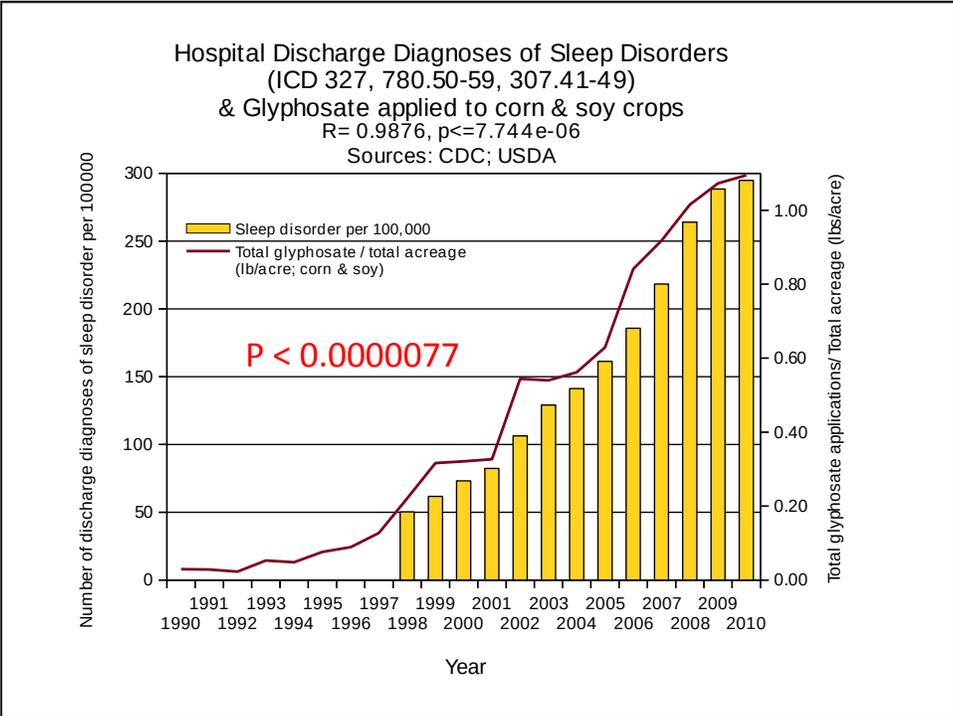
*jackkruse.com/tensegrity-4-magnetism-electrons-sleep/
(Thanks to Lienke Katz for pointing me to Jack Kruze's writings)

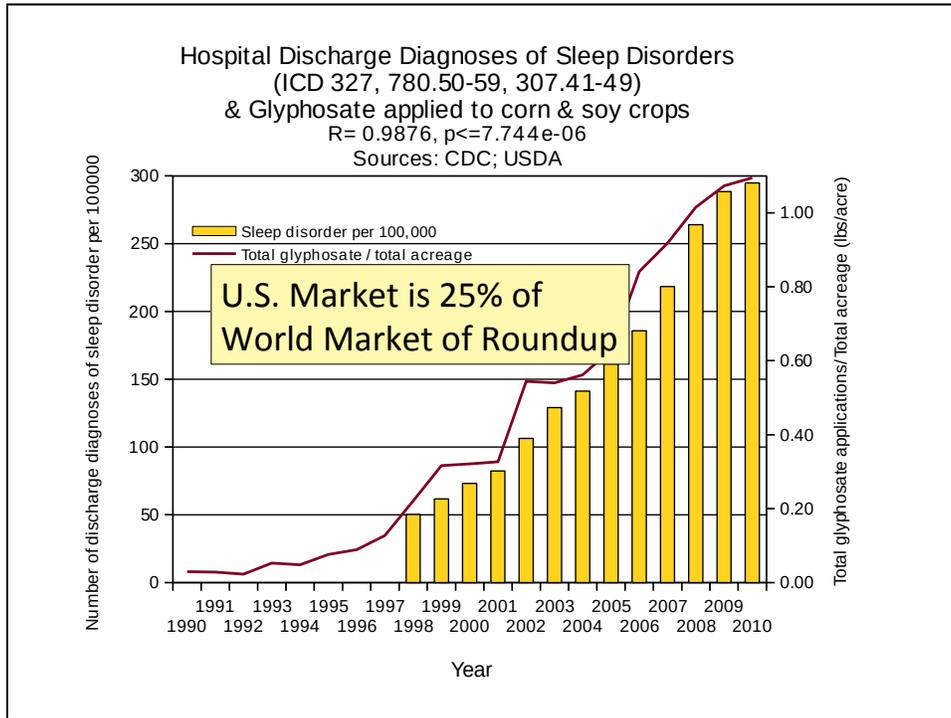
Wake-Sleep Cycle*

**Healthy circadian rhythms
depend on sulfate**

Jack Kruze, MD

*jackkruze.com/tensegrity-4-magnetism-electrons-sleep/
(Thanks to Lienke Katz for pointing me to Jack Kruze's writings)





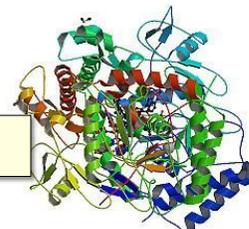
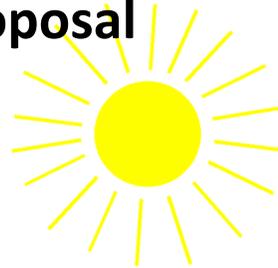
Sleep disorder is associated with depression, Alzheimer's disease, dementia, Parkinson's disease, ADHD, multiple sclerosis and autism.

Outline

- Introduction
- **Sulfate**
- Melatonin and the pineal gland
- Aluminum-glyphosate synergy
- Sulfate, vitamin D and autism
- Anemia and hypoxia
- Manganese dysbiosis
- Glyphosate and mitochondria
- Iron and mycoplasmas
- Sulfate and histamines
- Summary

A Provocative Proposal

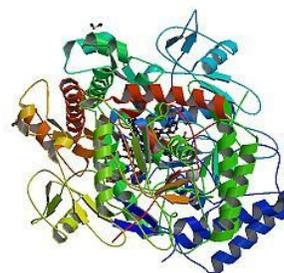
- Cholesterol sulfate supplies oxygen, sulfur, cholesterol, energy and negative charge to all the tissues
- Sulfate is synthesized from sulfide in skin and blood stream utilizing energy in sunlight
 - Protects from UV damage and keeps microbes out
- Endothelial Nitric Oxide Synthase (eNOS) performs the magic



The skin is a solar powered battery!

eNOS is Very Vulnerable*

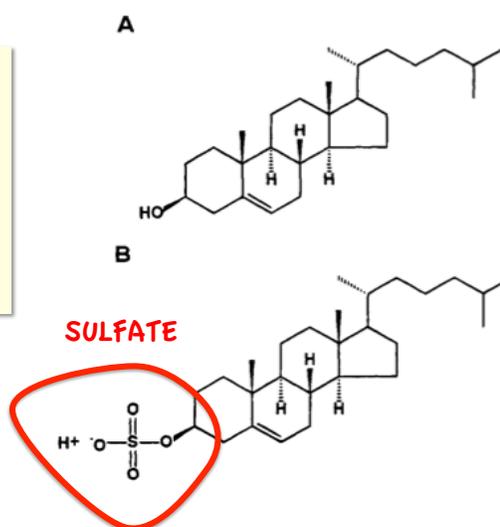
- eNOS depends on:
 - Cobalamin (vitamin B12, cobalt)
 - Heme iron, sulfur, zinc, oxygen
 - Glutathione
 - Sunlight
 - Tryptophan: converts UV to blue light; source of NAD
- eNOS is a cytochrome P450 enzyme:
 - Highly vulnerable to various environmental toxicants like mercury, aluminum, glyphosate, etc.



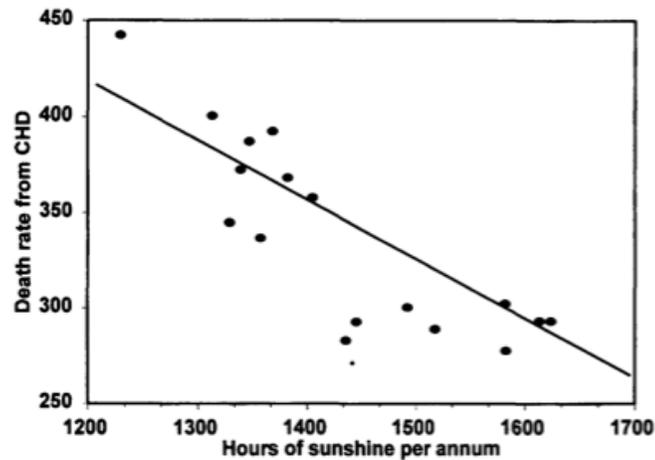
*S. Seneff et al., Entropy 2012, 14, 2492-2530.

Cholesterol and Cholesterol Sulfate

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



Heart Disease Mortality and Sunlight*



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

Swedish Population Study on Sun Exposure*

“We found that all-cause mortality was inversely related to sun exposure habits. The mortality rate amongst avoiders of sun exposure was approximately *twofold higher* compared with the highest sun exposure group”



*PG Lindqvist et al., Journal of Internal Medicine, 2014, 276; 77–86

Sulfate is Vastly Underappreciated!

- Sulfate is the 4th most abundant anion in the blood and protects it from coagulating
- Detoxifies drugs, food additives, and toxic metals
- Essential component of extracellular matrix proteins throughout the tissues and vasculature
- Cerebroside sulfate is a major constituent of myelin sheaths surrounding axons in neurons

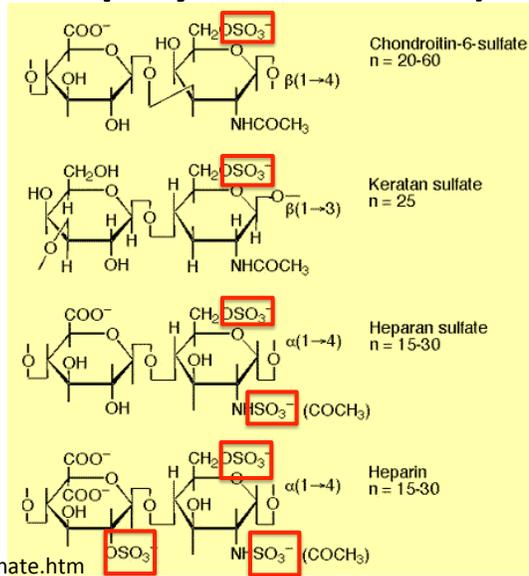
Sulfated Biomolecules*

- Sulfated mucopolysaccharides (glycosaminoglycans)
- Steroid sulfates
- Phenol sulfates
- Tyrosine sulfate
- Bilirubin sulfate
- Arylamine sulfates
- Choline sulfate in lichens, fungi and marine algae
- Sulfolipids

*IH Goldberg, The sulfolipids. *J. Lipi Res.* Apr. 1961, 2(2), 103-109.

Sulfated Glycosaminoglycans (GAGs) (also called “Mucopolysaccharides”)

- Prominent in extracellular matrix of *all cells*
- Amount of sulfate depends on availability
- Crucial for maintaining negative charge and protecting from infection



<http://www.science-autism.org/sulphate.htm>

Various Factors that Increase Sulfate*

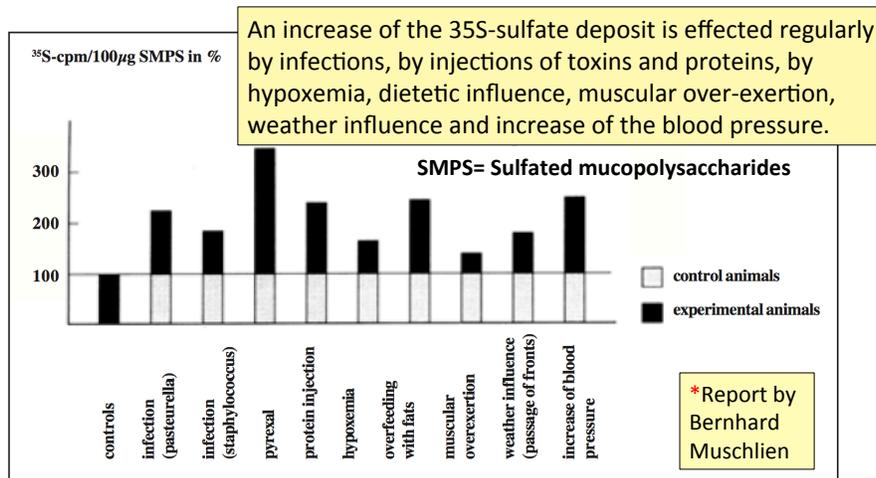


Fig. 2: Selected examples of factors that cause an increase of the SMPS synthesis, illustrated at the parameter of the ³⁵S-sulfate deposit in the connective tissue of various organs.

SMPS = Sulfated mucopolysaccharides = glycosaminoglycans

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

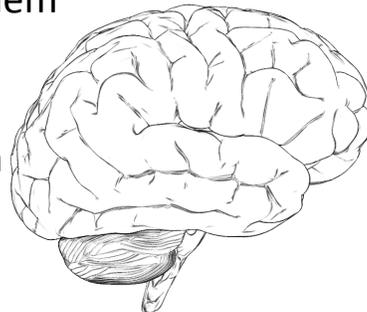
Outline

- Introduction
- Sulfate
- **Melatonin and the pineal gland**
- Aluminum-glyphosate synergy
- Sulfate, vitamin D and autism
- Anemia and hypoxia
- Manganese dysbiosis
- Glyphosate and mitochondria
- Iron and mycoplasmas
- Sulfate and histamines
- Summary

A Hypothesis

Many neurological diseases of the brain have a common origin:

- **Insufficient supply of sulfate to the brain**
- Enhanced toxic metal exposure (e.g., aluminum, mercury) due to impaired ability to detoxify and eliminate them
- Toxic metals interfere with sulfate synthesis
- This results in accumulation of cellular debris, including damaged mitochondria



In Brief...

- Heparan sulfate in the lysosomes is critical for recycling cellular debris
 - Heparan sulfate deficiency leads to autism
- Pineal gland delivers sulfate to cerebral spinal fluid via melatonin
- Aluminum and mercury disrupt pineal gland
- Sunlight deficiency is a contributing factor
- Glyphosate works synergistically with aluminum

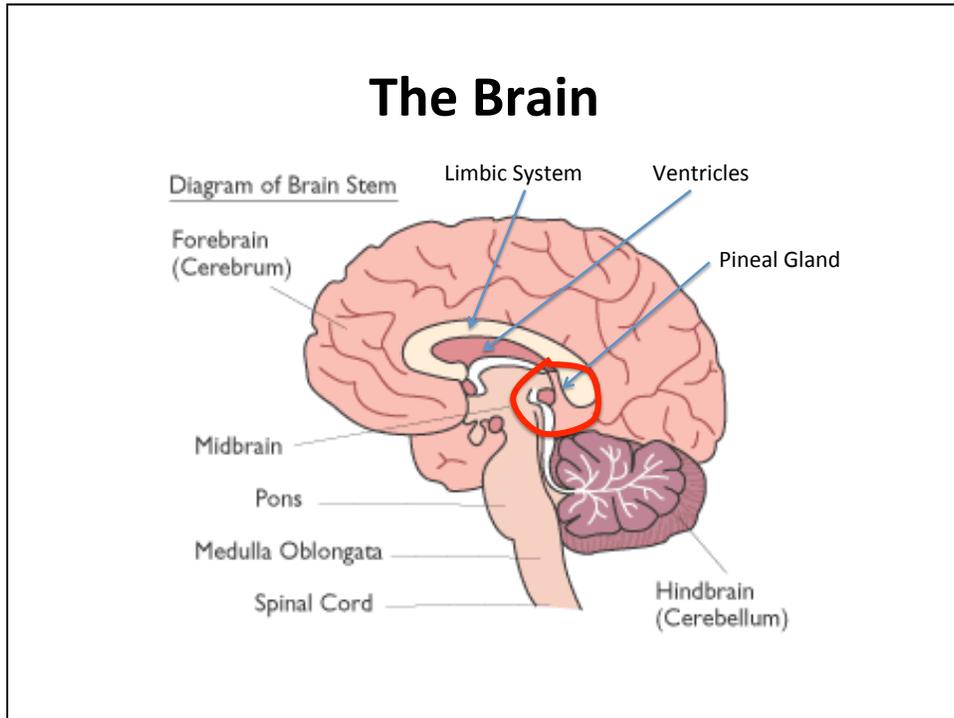
An Important Role for Sleep

- It has recently been argued that a crucial role for sleep is to clear cellular debris*
- This takes place in the lysosome, which depends upon sulfate in heparan sulfate proteoglycans to protect from free radicals**

*Sleep Drives Metabolite Clearance from the Adult Brain. L Xie et al., Science 342:373-377, 2013

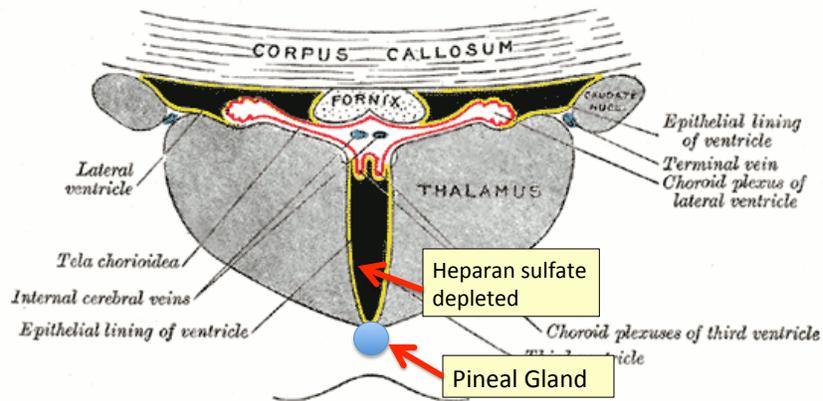
**Inhibition by heparin of Fe(II)-catalysed free-radical peroxidation of linolenic acid. M.A. Ross et al., Biochem. J. 1992, 286: 717-720.

The Brain



Third Ventricle and Pineal Gland

The third ventricle is depleted in heparan sulfate in association with autism in both humans and mice^{*,**}

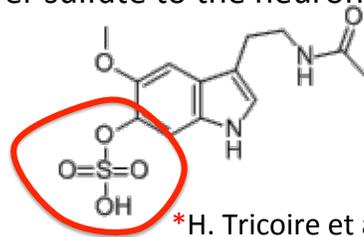


*B.L. Pearson et al., Behav Brain Res. 2013 Apr 15;243:138-45.

**F Mercie et al., Neurosci Lett 506, 2012, 208-213.

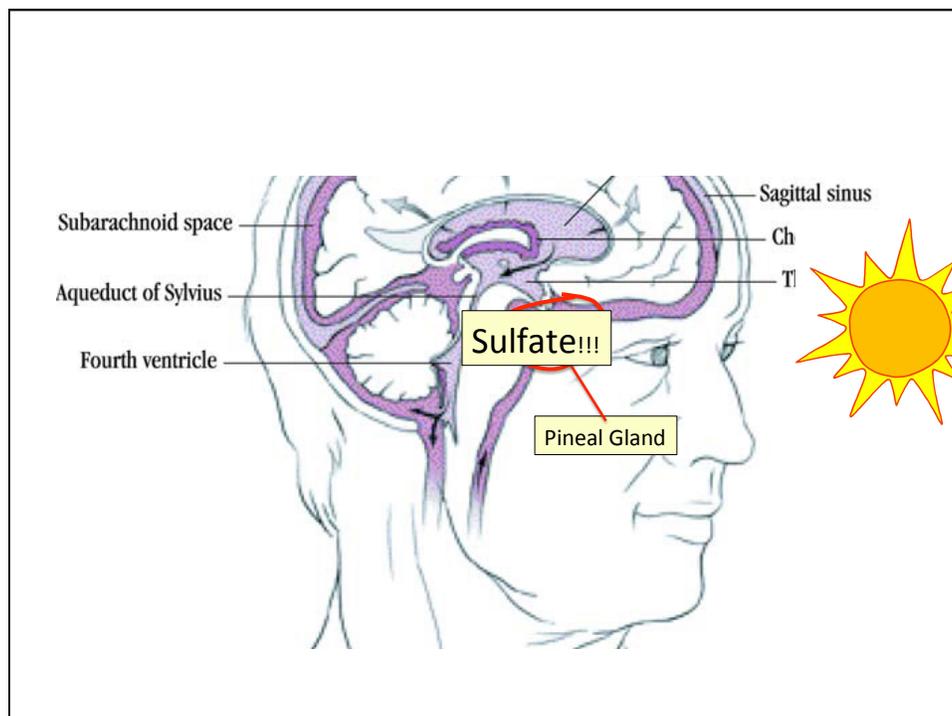
“Melatonin Enters the Cerebrospinal Fluid through the Pineal Recess”*

- The tip of the third ventricle is encased in the pineal gland
- The pineal gland delivers melatonin *sulfate* to the third ventricle and it diffuses to all the cerebrospinal fluid
- I propose that a key purpose of melatonin is to deliver sulfate to the neurons at night.



Melatonin sulfate

*H. Tricoire et al., Endocrinology 143(1):84–90



“Light-induced 3-O-Sulfotransferase Expression Alters Pineal Heparan Sulfate Fine Structure : A Surprising Link to Circadian Rhythm”*

- Pineal gland builds up heparan sulfate supplies *by day*
- Melatonin is sulfated in transport *at night*
 - Highly lipophilic molecule needs sulfate to make it water-soluble
 - This allows it to move through the cerebrospinal fluid
- When melatonin is delivered, sulfate is released!

Melatonin is a sulfate-delivery system!!

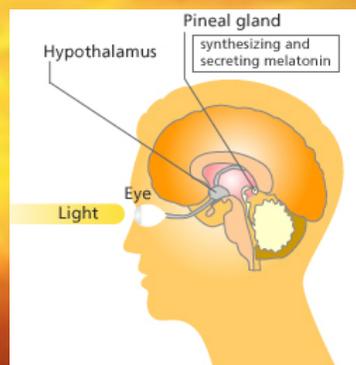
*B. Kuberan et al., J. Biol. Chem. 2004, 279:5053-5054.

A Really Bad Idea!



Pineal Gland: “Seat of the Soul”

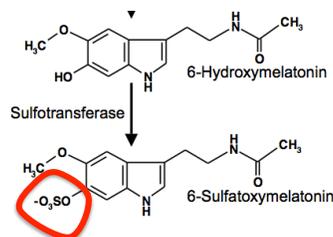
The pineal gland produces sulfate by day (responding to light) and stores it in heparan sulfate molecules



The pineal gland produces melatonin in the evening and transports it as melatonin sulfate to various parts of the brain

REM Sleep Cycle

- Melatonin Induces REM sleep
- Alzheimer’s is associated with reduced REM sleep cycle AND calcified pineal gland*



- Pineal gland calcification correlates inversely with REM sleep**
- DHEA SULFATE but not DHEA injections increase melatonin production in rats***

*R. Mahlberg et al., Neurobiol Aging. 2008 Feb;29(2):203-9

**R. Mahlberg et al., Sleep Med. 2009 Apr;10(4):439-45.

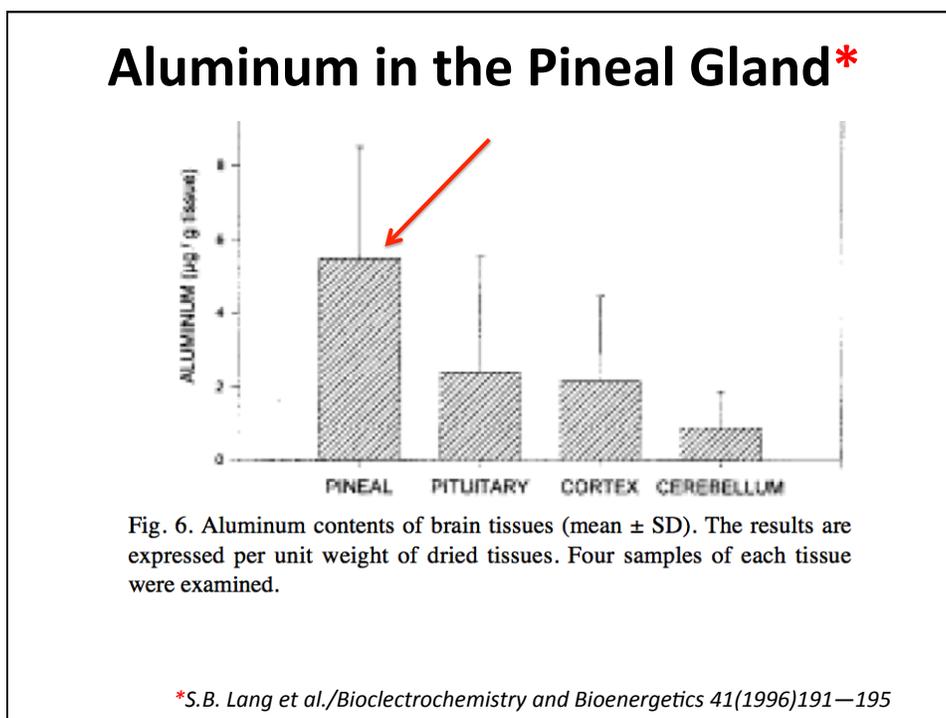
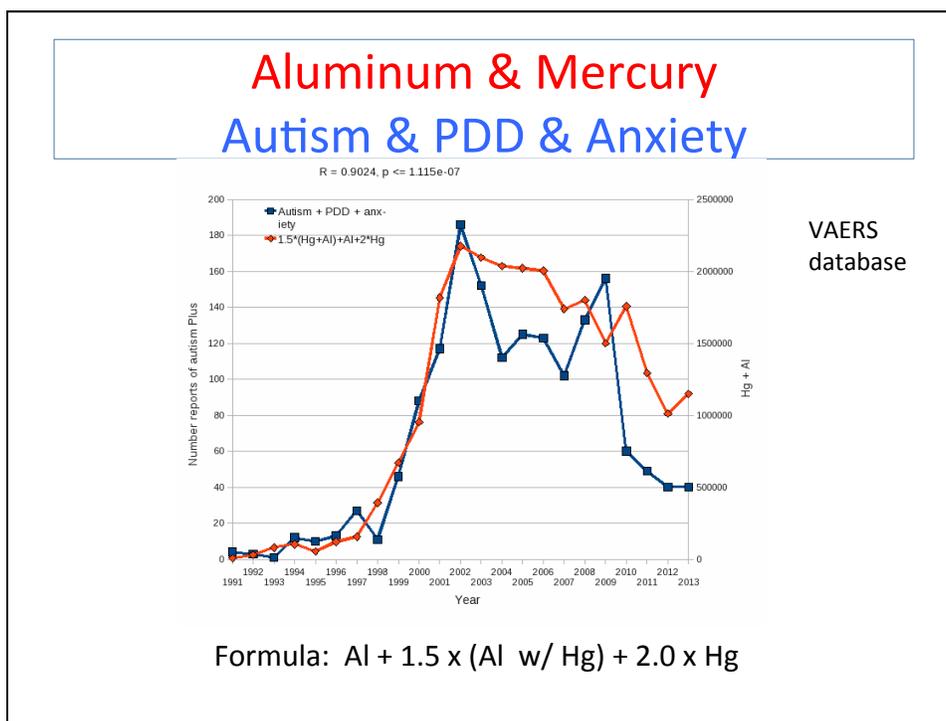
***Y. Djeridane et al., Steroids. 2004 May;69(5):343-9.

Outline

- Introduction
- Sulfate
- Melatonin and the pineal gland
- **Aluminum-glyphosate synergy**
- Sulfate, vitamin D and autism
- Anemia and hypoxia
- Manganese dysbiosis
- Glyphosate and mitochondria
- Iron and mycoplasmas
- Sulfate and histamines
- Summary

Sleep Disorder, Aluminum, and the Pineal Gland

- Sleep disorder is linked to many neurological diseases:
 - Autism, Alzheimer's, depression, schizophrenia, ALS, Parkinson's disease, etc.
- Insomnia occurs much more frequently as an adverse reaction in VAERS to vaccines containing aluminum than to those not containing aluminum ($p = 0.0025$)
- Pineal gland is heavily perfused and outside of the blood brain barrier
 - Susceptible to aluminum toxicity

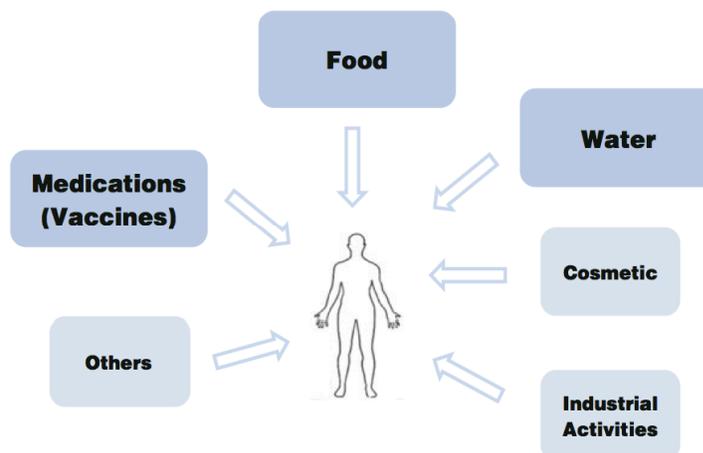


A Critical Role for Sunlight*

- Hypothesis:
 - Endothelial and neuronal nitric oxide synthase (both present in the pineal gland) produce sulfate from reduced sulfur sources catalyzed by sunlight
 - Sulfate deficiency results when this process is impaired
- Aluminum and retinoic acid, present in high SPF sunscreens, interfere with sulfate synthesis
- Aluminum accumulation in pineal gland would disrupt sulfate supplies to brain

*S. Seneff et al., Entropy 2012, 14, 2492-2530.

We live in the age of aluminum*



*C.A. Shaw and L. Tomljenovic, Immunol. Res. Epub ahead of print, 2013

We live in the age of aluminum*



*C.A. Shaw and L. Tomljenovic, Immunol. Res. Epub ahead of print, 2013

Aluminum Nanoparticles: Highly Destructive in the Brain*

- Destroyed mitochondria and severely depleted ATP
- Induced autophagy and programmed cell death
- Increased permeability of blood brain barrier
- Were persistent
- Far more damaging than larger sized aluminum particles



*L Chen et al., Nanomedicine Feb 2013; 9(2): 212–221.

Glyphosate and Aluminum: Partners in Crime

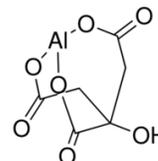


- Glyphosate induces pathogens like *C. difficile* in gut, leading to *leaky gut syndrome*
 - *C. diff* produces *p-cresol* which promotes aluminum uptake by cells
 - p-Cresol is a known biomarker for autism
 - p-Cresol is an important factor in *kidney failure* which leads to aluminum retention in tissues → dementia
- Glyphosate *cages* aluminum to promote entry
- Glyphosate promotes *calcium uptake* by voltage-activated channels
 - Aluminum gains entry as calcium mimetic
- Aluminum promotes calcium loss from bones → pineal gland calcification

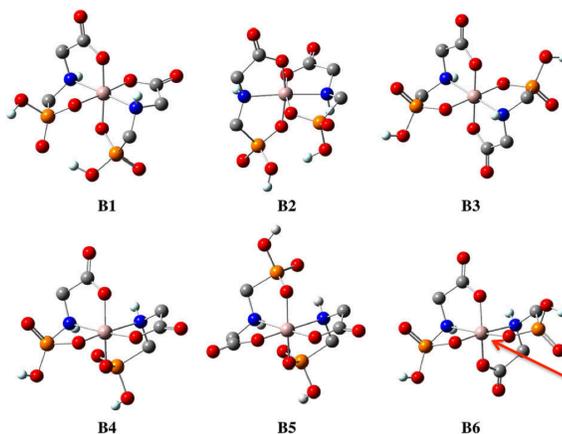
MIT Computer Science and Artificial Intelligence Laboratory

Aluminum Glyphosate*

Six different ways two glyphosate molecules can chelate aluminum



Aluminum citrate**



ALUMINA

aluminum

* M. Purgel et al., *Journal of Inorganic Biochemistry* 103 (2009) 1426–1438

** P. Sianina et al., *Clin. Chem.* 32/3, 539-541, 1986.

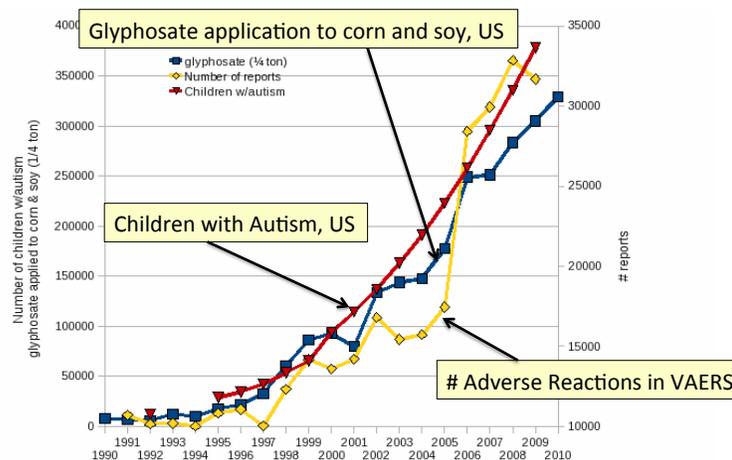
Glyphosate Suppresses Melatonin Synthesis!

- Glyphosate interferes with shikimate pathway in plants and microbes → tryptophan depletion*
- Tryptophan is sole precursor to melatonin
- Melatonin binds to aluminum, cadmium, copper, iron and lead, reducing their toxicity**

*N. de María et al., J Agric Food Chem 2006, 54, 2621-2628.

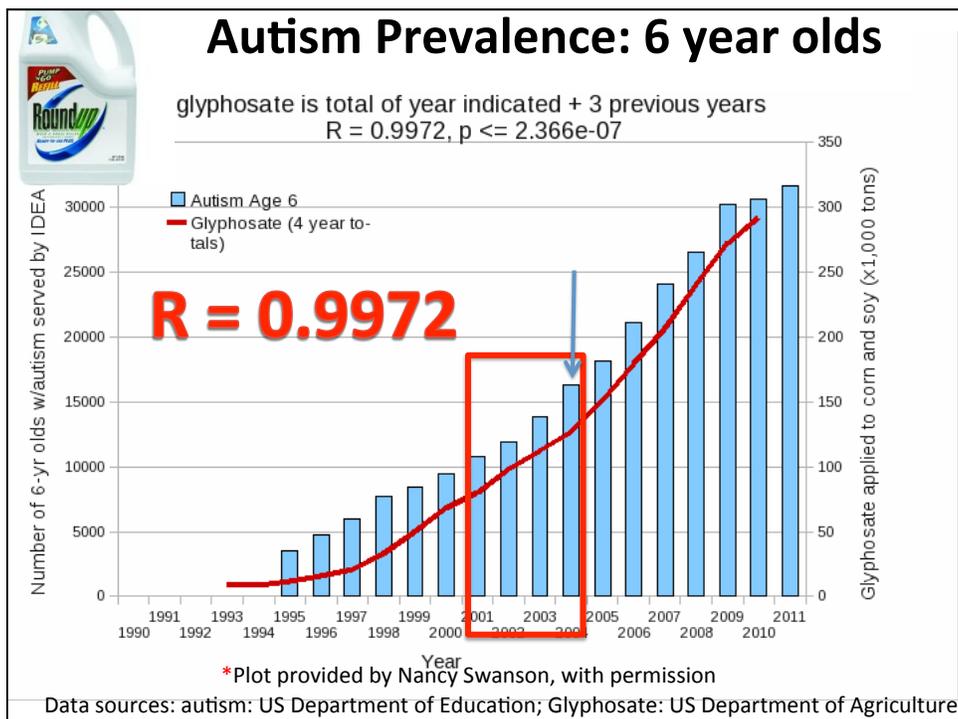
**J. Limson et al. J. Pineal Res. 1998; 24:15–21.

Autism, Glyphosate, Vaccine Reactions*



*Collaboration with Nancy Swanson

MIT Computer Science and Artificial Intelligence Laboratory



Outline

- Introduction
- Sulfate
- Melatonin and the pineal gland
- Aluminum-glyphosate synergy
- **Sulfate, vitamin D and autism**
- Anemia and hypoxia
- Manganese dysbiosis
- Glyphosate and mitochondria
- Iron and mycoplasmas
- Sulfate and histamines
- Summary

Sulfate in Fetal Development*

- Fetus depends on mother for sulfate supply
- Sulfate is essential for transporting sterols (like estrogen and DHEA) and supplying extracellular matrix proteins everywhere with sufficient negative charge
- Sulfate detoxifies xenobiotics like **acetaminophen (tylenol)** and is essential for excreting toxins like **aluminum** and **mercury**
- Sulfate is severely deficient in autistic children (1/3 the normal level of free sulfate in blood stream)

* Dawson, "Sulfate in Fetal Development," Semin Cell Dev Biol 2011

Autism-like socio-communicative deficits and stereotypies in mice lacking heparan sulfate*

- Experiment with "designer" mice: impaired heparan sulfate synthesis in brain
- Mice exhibited all the classic features of autism – both cognitive and social



* F. Irie et al., PNAS Mar. 27, 2012, 109(13), 5052-5056.

“Heparan sulfate deficiency in autistic postmortem brain tissue from the subventricular zone of the lateral ventricles”*

“Aberrant extracellular matrix glycosaminoglycan function localized to the subventricular zone of the *lateral ventricles* may be a biomarker for autism, and potentially involved in the etiology of the disorder.”

*BL Pearson et al., Behav Brain Res. 2013;243:138-45

“Heparan sulfate deficiency in autistic postmortem brain tissue from the subventricular zone of the lateral ventricles”*

“New neurons develop from stem cells in this zone through the action of “fractones” composed of heparan sulfate proteoglycans** the disorder.”

*BL Pearson et al., Behav Brain Res. 2013;243:138-45

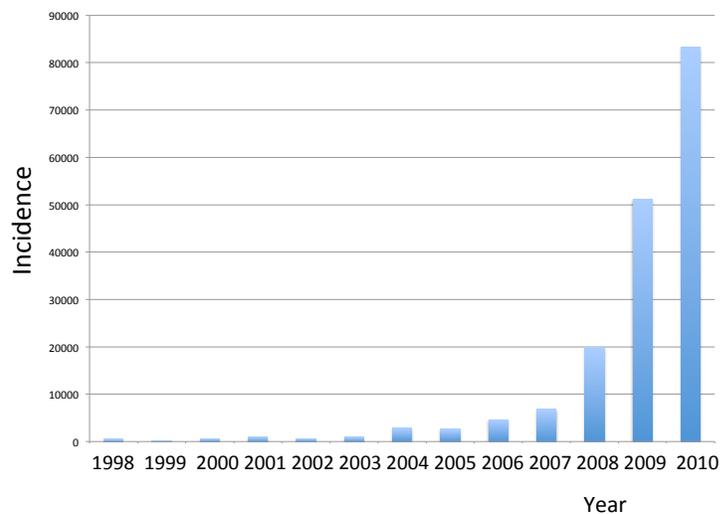
**F. Mercier et al., Neuroscience Letters 506 (2012) 208–213

Vitamin D Prevents Sulfate Wasting*

- Activated vitamin D prevents sulfate wasting from the kidney in urine
- Mice engineered to have defective vitamin D receptors or with vitamin D deficiency had significantly reduced serum sulfate levels
- This was associated with sulfate depletion in the skeleton

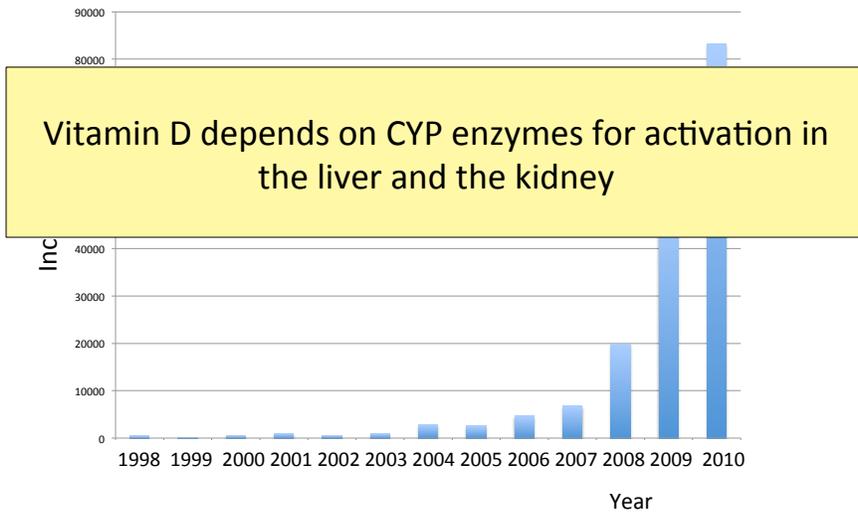
*M.J.G. Bolt et al., Am J Physiol Endocrinol Metab 287: E744 –E749, 2004.

Vitamin D Deficiency Epidemic



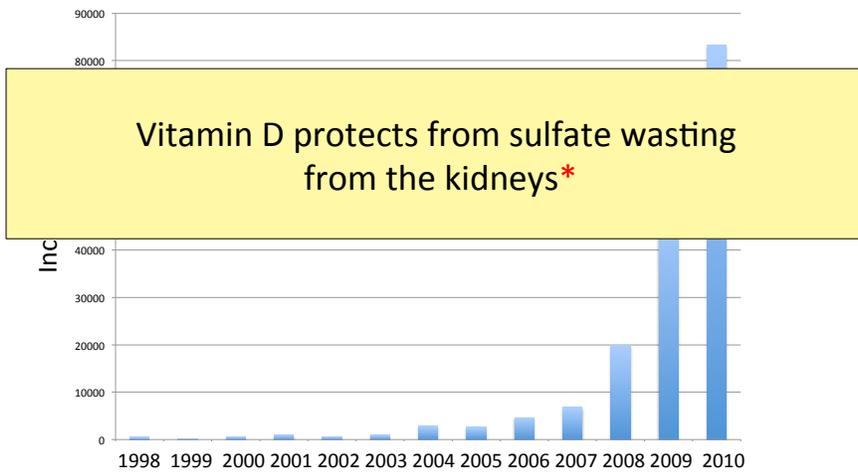
Plot derived from hospital discharge data from the CDC

Vitamin D Deficiency Epidemic



Plot derived from hospital discharge data from the CDC

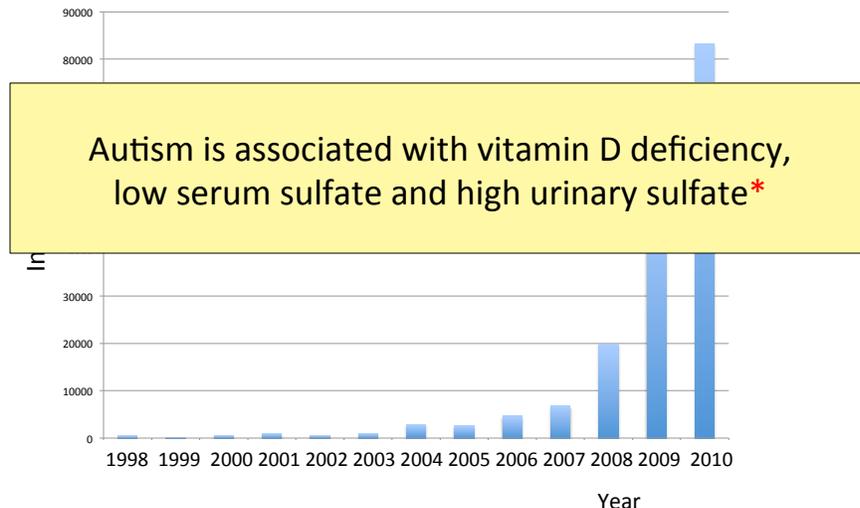
Vitamin D Deficiency Epidemic



*MJG Bolt et al., Am J Physiol - Endocrinology and Metabolism 2004;287(4):E744-E749.

Plot derived from hospital discharge data from the CDC

Vitamin D Deficiency Epidemic



Autism is associated with vitamin D deficiency, low serum sulfate and high urinary sulfate*

*RH Waring et al., Journal of Nutritional and Environmental Medicine 2000;10(1):25-32.
Plot derived from hospital discharge data from the CDC

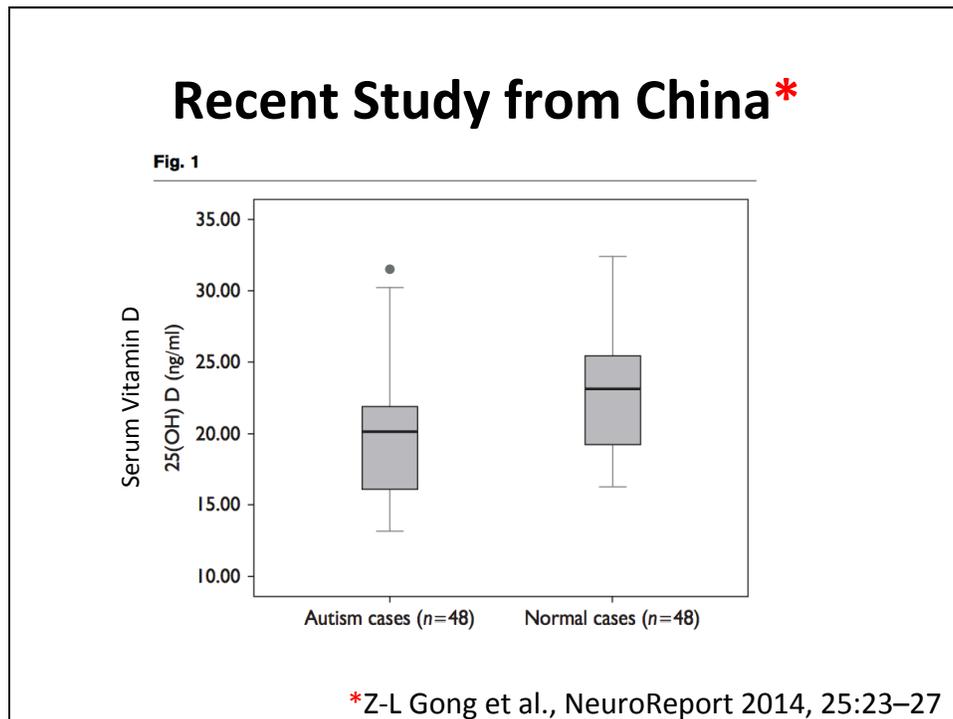
Inflammation and Vitamin D: The Infection Connection*

- The problem appears to be a bottleneck in the production of 25(OH) vitamin D in the liver

$$\text{D3} \xrightarrow{\text{Liver}} 25(\text{OH}) \text{D3} \xrightarrow{\text{Kidney}} 1,25(\text{OH})_2 \text{D3}$$
- Both steps depend on CYP enzymes
- Liver CYPs are destroyed by glyphosate and aluminum??

$$\rightarrow 1,25(\text{OH})_2 \text{D3} \gg 25(\text{OH}) \text{D3}$$

*M. Mangin et al., Inflamm Res 2014; 63:803-819.



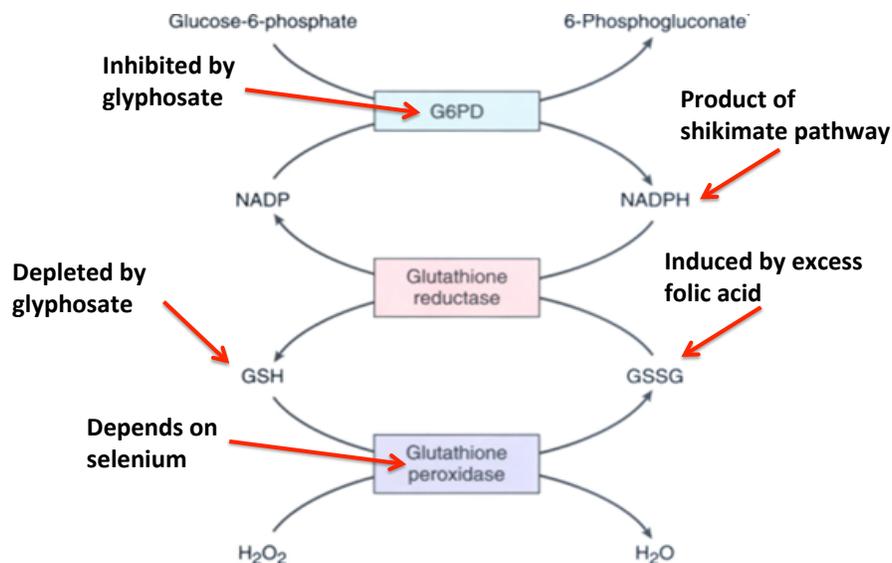
Outline

- Introduction
- Sulfate
- Melatonin and the pineal gland
- Aluminum-glyphosate synergy
- Sulfate, vitamin D and autism
- **Anemia and hypoxia**
- Manganese dysbiosis
- Glyphosate and mitochondria
- Iron and mycoplasmas
- Sulfate and histamines
- Summary

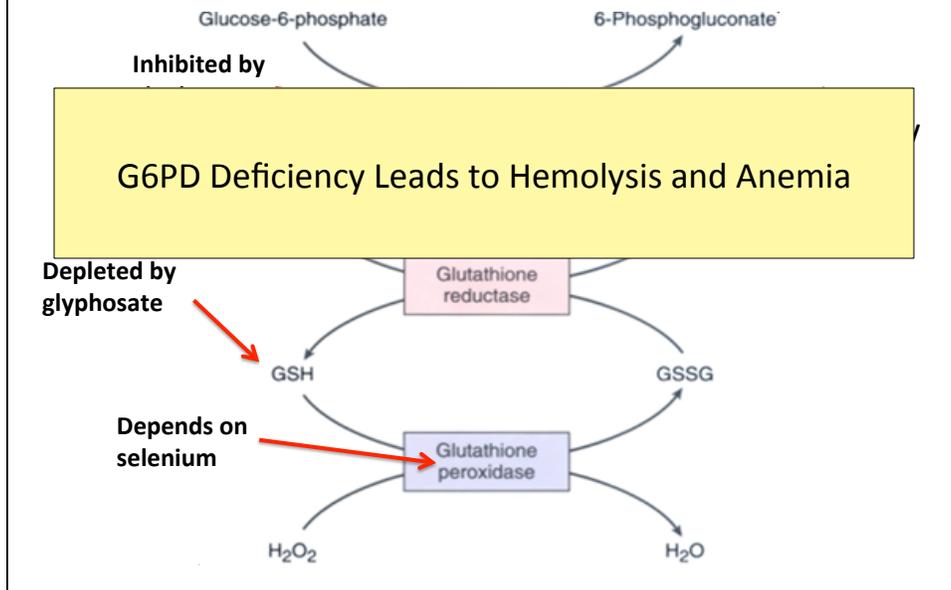
Glyphosate: The Central Mechanisms

- Glyphosate acts as an antibiotic to disrupt gut bacteria, leading to overgrowth of pathogens
- Disruption of liver CYP enzymes leads to impaired bile flow and low vitamin D
 - This disrupts sulfate synthesis and transport
 - Also impairs detoxification of other toxic chemicals
- Damage to red blood cells leads to anemia and toxicity due to free iron
 - Hypoxia ensues → low grade encephalopathy
- Manganese, aluminum and glutamate become toxic to the brain

This Detoxification Scheme is Essential in Red Blood Cells



This Detoxification Scheme is Essential in Red Blood Cells



Glyphosate also interferes with heme synthesis needed to replenish RBCs

Anemia leads to low oxygen which induces chronic low grade encephalopathy linked to autism

Entropy **2013**, *15*, 372-406; doi:10.3390/e15010372

OPEN ACCESS

entropy

ISSN 1099-4300

www.mdpi.com/journal/entropy

Review

Is Encephalopathy a Mechanism to Renew Sulfate in Autism?

Stephanie Seneff ^{1,*}, Ann Lauritzen ², Robert M. Davidson ³ and Laurie Lentz-Marino ⁴

Outline

- Introduction
- Sulfate
- Melatonin and the pineal gland
- Aluminum-glyphosate synergy
- Sulfate, vitamin D and autism
- Anemia and hypoxia
- **Manganese dysbiosis**
- Glyphosate and mitochondria
- Iron and mycoplasmas
- Sulfate and histamines
- Summary

Paper on Glyphosate and Manganese Published March 24, 2015



Surgical Neurology International

OPEN ACCESS

For entire Editorial Board visit:
<http://www.surgicalneurologyint.com>

Editor:

James I. Ausman, MD, PhD
University of California, Los
Angeles, CA, USA

Original Article

Glyphosate, pathways to modern diseases III: Manganese, neurological diseases, and associated pathologies

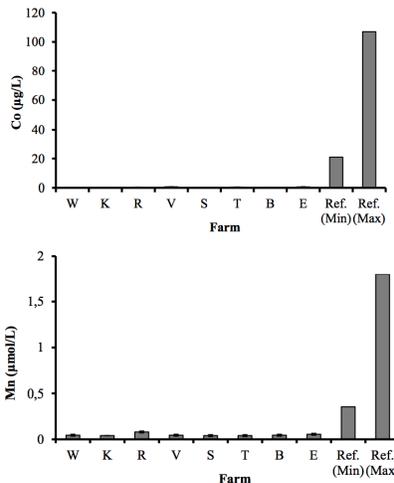
Anthony Samsel, Stephanie Seneff¹

Research Scientist and Consultant, Deerfield, NH 03037, ¹Spoken Language Systems Group, Computer Science and Artificial Intelligence Laboratory, MIT, Cambridge MA 02139, USA

E-mail: Anthony Samsel - anthony@samsel@acoustictracks.net; *Stephanie Seneff - seneff@csail.mit.edu
*Corresponding author

Received: 22 September 14 Accepted: 21 January 15 Published: 24 March 15

Severe Deficiency in Serum Manganese and Cobalt in Cows*



Eight different farms: all cows tested had glyphosate in the urine

*M. Krüger et al., J Environ Anal Toxicol 2013, 3:5

Manganese and Autism*

- Glyphosate chelates manganese
- Manganese disruption leads to:
 - Disrupted gut bacteria → anxiety
 - Impaired dopamine synthesis → thyroid disease
 - Glutamate and ammonium toxicity in the brain
 - Mitochondrial damage (impaired Mn-SOD)
 - Impaired bone development and osteoporosis
 - Impaired development of perineuronal nets
- Many of these pathologies are associated with autism

*A Samsel and S Seneff, Surg. Neurol. Int. 2015;6:45.

Low Manganese in Teeth Linked to Autism*

- Studied lead, mercury and manganese levels in tooth enamel of shed primary teeth in 84 children
- Manganese accumulated after birth was down by 60% in autistic children
- *No other result was statistically significant*



*MM Abdullah et al., *J Autism Dev Disord.* 2012 Jun;42(6):929-36.

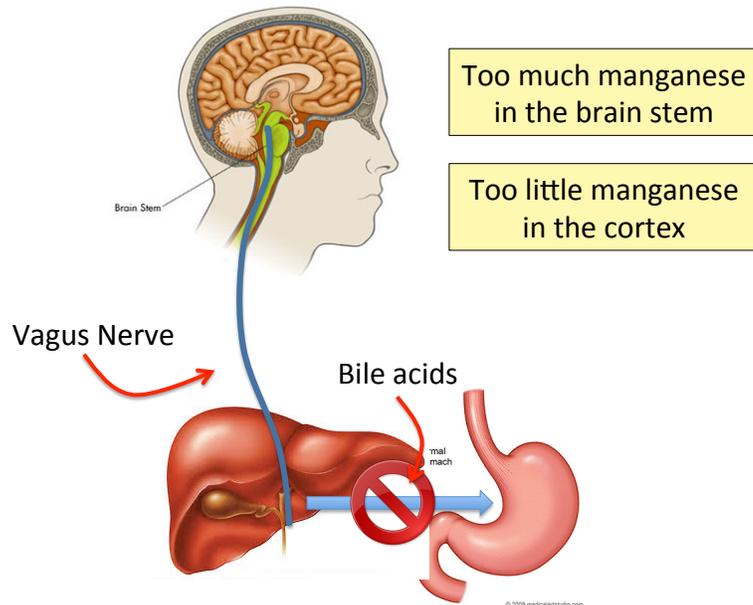
Low Manganese in Teeth Linked to Autism*

- Studied lead, mercury and manganese levels in tooth
- Other studies have shown low serum manganese and low manganese in urine samples in association with autism
- after birth was down by 60% in autistic children
- *No other result was statistically significant*



*MM Abdullah et al., *J Autism Dev Disord.* 2012 Jun;42(6):929-36.

It's not just deficiency!



Balancing the Scales



Autism

ADHD

Alzheimer's

Parkinson's

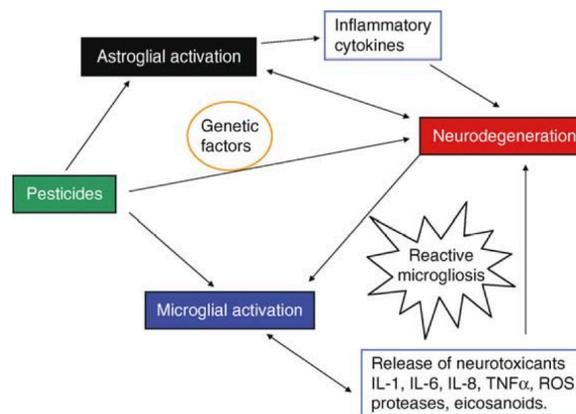
Glyphosate disrupts the body's ability to distribute the minerals safely: Everybody walks a tight rope between deficiency and toxicity

Outline

- Introduction
- Sulfate
- Melatonin and the pineal gland
- Aluminum-glyphosate synergy
- Sulfate, vitamin D and autism
- Anemia and hypoxia
- Manganese dysbiosis
- **Glyphosate and mitochondria**
- Iron and mycoplasmas
- Sulfate and histamines
- Summary

Glyphosate & Mitochondria

Pesticides and Neuroinflammatory Response*



*Figure 1, HR Dhaini, Encyclopedia of Neuroscience, Chapter 14, Springer Berlin Heidelberg., D, Hirokawa N, Windhorst U, Ed. pp.2734-2739

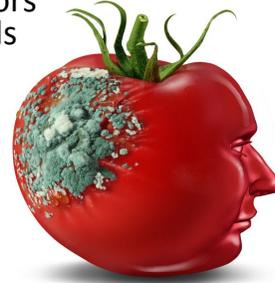
Autism and Mitochondrial Impairment*

- Mitochondrial impairment is a key feature of autism, especially in the brain
 - Impaired detox of glutamate by astrocytes (requires manganese)
 - Excess stimulation of NMDA receptors in neurons
- Glyphosate excites NMDA receptors and prevents glutamate metabolism

*Dayan Goodenowe and Elodie Pastural, Chapter 4
intechopen.com/books/autism-a-neurodevelopmental-journey-from-genes-to-behaviour/the-biochemical-basis-of-autistic-behavior-and-pathology

Glyphosate and Glutamate*

- Acute exposure activates NMDA receptors and voltage-dependent calcium channels
 - Oxidative stress and neural cell death
 - Increased glutamate released into the synaptic cleft → *excessive extracellular glutamate levels*
 - Decreased glutathione content
 - Increased peroxidation of lipids (fats)
- Chronic exposure:
 - Decreased glutamate uptake and metabolism
 - Induced calcium uptake
 - Induced oxidative stress



*<http://www.greenmedinfo.com/blog/roundup-weedkiller-brain-damaging-neurotoxin>

Mitochondria are Key!

“Damage to mitochondria is now understood to play a role in the pathogenesis of a wide range of seemingly unrelated disorders such as schizophrenia, bipolar disease, dementia, Alzheimer's disease, epilepsy, migraine headaches, strokes, neuropathic pain, Parkinson's disease, ataxia, transient ischemic attack, cardiomyopathy, coronary artery disease, chronic fatigue syndrome, fibromyalgia, retinitis pigmentosa, diabetes, hepatitis C, and primary biliary cirrhosis.”*

*J Neustadt and SR Pieczenik, Molecular Nutrition and Food Research 2008;52:780-788

Mitochondria are Key!

Many of these conditions are going up in prevalence in step with glyphosate usage on corn and soy crops

Alzheimer's disease, epilepsy, migraine headaches, strokes, neuropathic pain, Parkinson's disease,

Glyphosate makes manganese unavailable to mitochondria, and they need manganese to protect them from oxidative damage

*J Neustadt and SR Pieczenik, *Molecular Nutrition and Food Research* 2008;52:780-788

Microglia are Crucial for Synaptic Transmission*

- Microglia are the immune cells of the brain
- Microglia have their “fingers” on the pulse of synaptic transmission by neurons
- Microglial activation by toxic stimuli provokes astrocytes to release glutamate which is then metabolized by neurons in the mitochondria in place of sugar

This signals that mitochondrial complex I is sick

*C Béchade *et al.*, *Front Cell Neurosci.* 2013; 7: 32.

Microglia are Crucial for Synaptic Transmission*

- Microglia are the immune cells of the brain
- Microglia Glyphosate interferes with its pulse of synaptic transmission conversion to glutamine
- Microglial activation by toxic stimuli provokes astrocytes to release **glutamate** which is then metabolized by neurons in the mitochondria in place of sugar

Glutamate metabolism by mitochondria bypasses Complex I (unlike glucose)

*C Béchade *et al.*, *Front Cell Neurosci.* 2013; 7: 32.

Mechanisms underlying the neurotoxicity induced by glyphosate*

“Taken together, these results demonstrated that Roundup® might lead to excessive extracellular **glutamate** levels and consequently to glutamate excitotoxicity and oxidative stress in rat hippocampus. “ - quote from abstract

*D Cattani *et al.*, *Toxicology* 320 (2014) 34–45

Outline

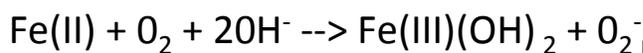
- Introduction
- Sulfate
- Melatonin and the pineal gland
- Aluminum-glyphosate synergy
- Sulfate, vitamin D and autism
- Anemia and hypoxia
- Manganese dysbiosis
- Glyphosate and mitochondria
- **Iron and mycoplasmas**
- Sulfate and histamines
- Summary

Iron is Essential but Toxic

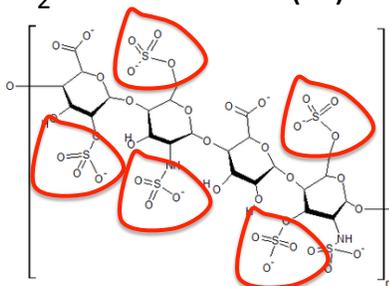
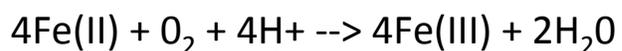
- Glyphosate interferes with heme synthesis – this greatly increases the problem of free iron in the blood
- **Fenton reaction** leads to hypersensitivity to hydrogen peroxide → damage to delicate cellular membrane fatty acids
- “ROS” = reactive oxygen species

Heparin Protects from ROS due to Iron*

Free radical production (*Fenton* reaction):



But, in the acidic environment of heparin:



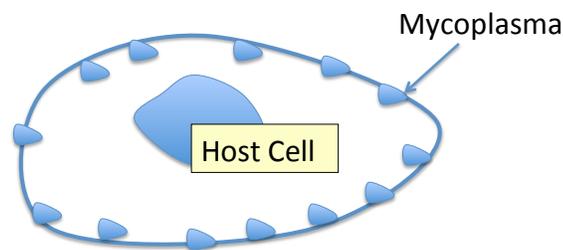
*M.A. Ross et al., Biochem. J. 1992, 286, 717-720.

“Chronic and age-related increases in ROS production will cause mitochondrial damage and dysfunction that perpetuate a catastrophic cycle of cellular injury, further ROS generation, mitochondrial decline, and cell death.”*

* S.W. Ballinger et al., Circ Res. 2000;86. P. 965

Eventually the Mitochondria Become so Impaired that they can't produce ATP

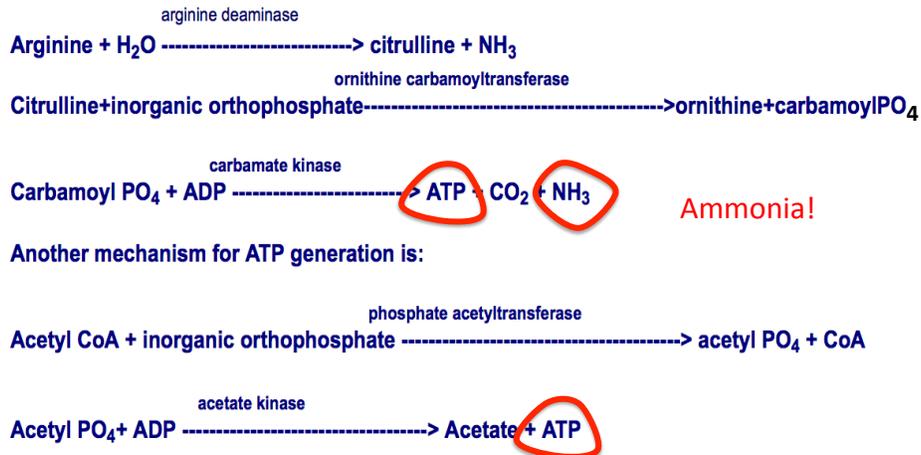
- Is this why mycoplasmas come into play??
- Mycoplasmas are tiny bacteria *without a cell wall*
- Mycoplasmas can produce ATP without CYP enzymes: a SUPER benefit when CYPs are impacted by toxic chemicals in the environment



Mycoplasmas

- Smallest bacteria yet discovered
- Can live without oxygen
- Can not live outside of a host cell
- Generate ATP from arginine
arginine → citrulline + *ammonia*
- They have no cytochromes!!! (SAFE)
- Associated with gastric cancer, lung cancer, renal cancer, prostate cancer, colon cancer
- *Hide inside immune cells and inactivate the vitamin D receptors!*

Mycoplasma: Safe Metabolism to generate ATP for the host cell!!



Outline

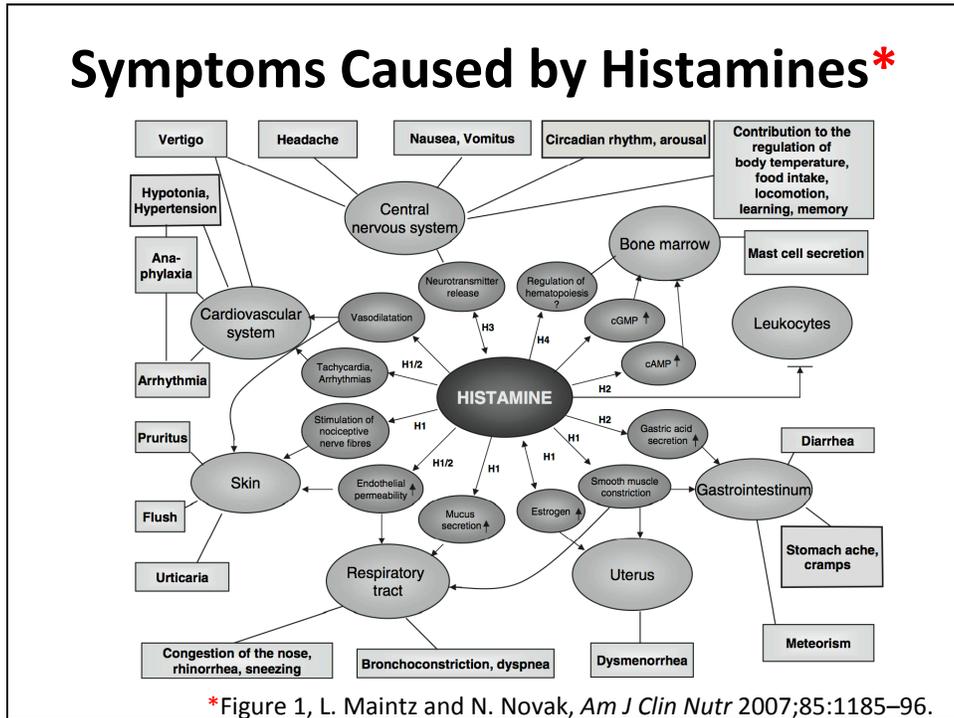
- Introduction
- Sulfate
- Melatonin and the pineal gland
- Aluminum-glyphosate synergy
- Sulfate, vitamin D and autism
- Anemia and hypoxia
- Manganese dysbiosis
- Glyphosate and mitochondria
- Iron and mycoplasmas
- Sulfate and histamines
- Summary

Sulfate and Histamines

Heparan Sulfate Promotes Histamine Breakdown*

- Intestinal diamine oxidase (DAO) is synthesized in the mature enterocytes of the villus tip and is then transported to the binding sites on the intestinal vasculature.
- Heparin and heparan sulfate induce release of the bound DAO, so that it can break down histamine
- *Conclusion: deficiencies in heparan sulfate lead to build-up of histamines!*

* L. D'Agostino et al., *Biochim Biophys Acta* 1989;993(2-3):228-32.



DAO Deficiency → Histamine Accumulation*

Adverse effects derived from DAO Deficiency	
Central nervous system	Migraine, headache, hangover, sickness
Cardiovascular system	Hypotension, hypertension and arrhythmia
Epithelial system	Urticaria, atopic skin, psoriasis
Respiratory system	Nasal congestion, asthma
Digestive system	Irritable bowel syndrome, constipation, satiety, stomachache, vomits
Muscular system	Fibromyalgia, muscular pains
Skeletal system	Bone pains

*www.deficitdao.org/dao-deficiency/#.VRWYtWZGqDc

Summary

- Autism and Alzheimer's disease have reached epidemic proportions in the Western world
 - Hypothesis: Both are caused by a severe deficiency in sulfate supplies to the brain
- Pineal gland can synthesize sulfate stimulated by sunlight and deliver it via melatonin sulfate
 - Aluminum and glyphosate work synergistically to derail this process
 - Sunlight deficiency contributes to the pathology
- Mitochondrial disorder: mycoplasmas and histamines arise from impaired sulfate supplies