

Download these slides from:  
[people.csail.mit.edu/seneff](http://people.csail.mit.edu/seneff)

## Most Popular Herbicide Glyphosate Causes Autism

Stephanie Seneff

MIT CSAIL

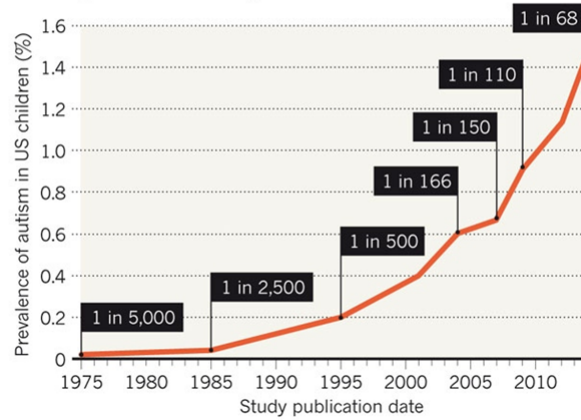
April 28, 2014



## A Frightening Trend\*

### AUTISM DIAGNOSES RISING

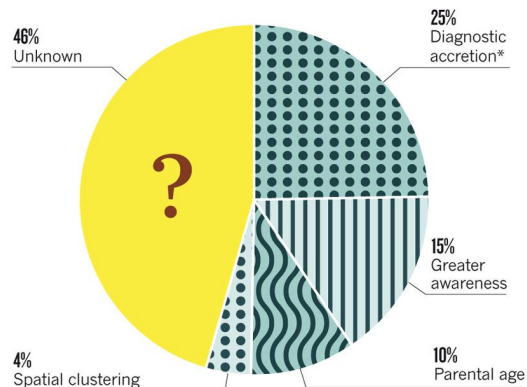
Almost 1.5% of US children are now diagnosed with autism, according to data from 11 regions in the United States.



\*K. Weintraub, Nature 479, Nov. 3 2011, 22-24.

***“If it is an environmental cause contributing to an increase, we certainly want to find it.”\****

**Reasons: unclear**



\*Children who formerly would have been diagnosed solely with mental retardation

\*K. Weintraub, Nature 479, Nov. 3 2011, 22-24.

“Autism **No!** condition”

“Autism is a *single*-factorial condition”



## Outline

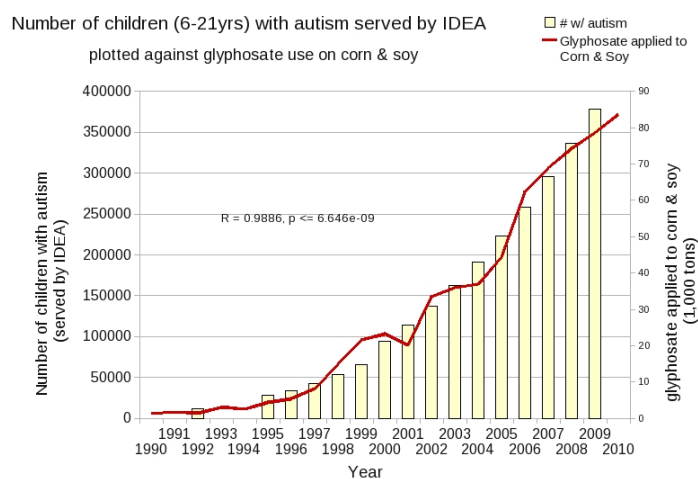
- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- Glyphosate and aluminum
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary



## Outline

- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- Glyphosate and aluminum
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary

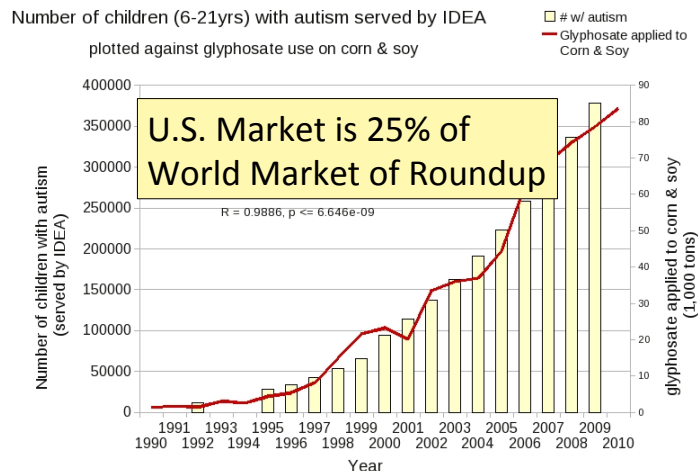
## Glyphosate and Autism\*



**Pearson Correlation Coefficient = 0.99**

\*Nancy Swanson, <http://www.examiner.com/article/data-show-correlations-between-increase-neurological-diseases-and-gmos>

## Glyphosate and Autism\*



**Pearson Correlation Coefficient = 0.99**

\*Nancy Swanson, <http://www.examiner.com/article/data-show-correlations-between-increase-neurological-diseases-and-gmos>

## Is Glyphosate Nontoxic?

- Monsanto has argued that glyphosate is harmless to humans because our cells don't have the shikimate pathway, which it inhibits
- However, our gut bacteria DO have this pathway
  - We depend upon them to supply us with essential amino acids (among many other things)
- Other ingredients in Roundup greatly increase glyphosate's toxic effects
- Insidious effects of glyphosate accumulate over time
  - Most studies are too short to detect damage

## Main Toxic Effects of Glyphosate\*

- Kills beneficial gut bacteria and allows pathogens to overgrow
- Interferes with function of cytochrome P450 (CYP) enzymes
- Chelates important minerals (iron, cobalt, manganese, etc.)
- Interferes with synthesis of aromatic amino acids and methionine
  - Leads to shortages in critical neurotransmitters and folate
- Disrupts sulfate synthesis and sulfate transport

*\*Samsel and Seneff, Entropy 2013, 15, 1416-1463*

## The Enhancing Effect of Adjuvants\*

“Adjuvants in pesticides are generally declared as inerts, and for this reason they are not tested in long-term regulatory experiments. It is thus very surprising that they amplify *up to 1000 times* the toxicity of their APs [Active Principles] in 100% of the cases where they are indicated to be present by the manufacturer.”

*\*R. Mesnage et al. BioMed Research International 2014; Article ID:179691.*

## Some Biomarkers for Autism

- Disrupted gut bacteria; inflammatory bowel
- Low serum sulfate
- Methionine deficiency
- Serotonin and melatonin deficiency
- Defective aromatase
- Zinc and iron deficiency
- Urinary p-cresol
- Mitochondrial disorder
- Glutamate toxicity in the brain

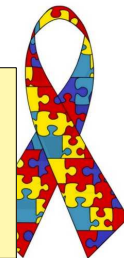


## Some Biomarkers for Autism

- Disrupted gut bacteria; inflammatory bowel
- Low serum sulfate

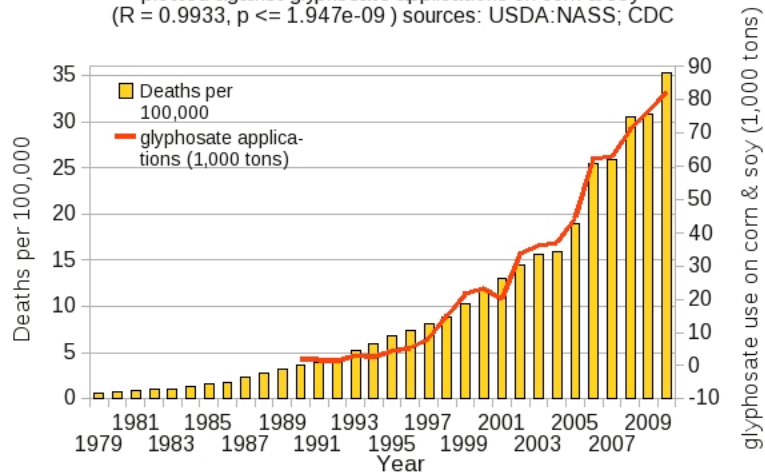
These can all be explained as potential effects of glyphosate on biological systems

- Zinc and iron deficiency
- Urinary p-cresol
- Mitochondrial disorder
- Glutamate toxicity in the brain



## Dementia and Autism Have Much in Common

Deaths from Senile Dementia (ICD F01, F03 & 290)  
plotted against glyphosate applications on corn & soy  
( $R = 0.9933$ ,  $p \leq 1.947e-09$ ) sources: USDA:NASS; CDC



Plot kindly provided by Nancy Swanson

## Outline

- Autism and glyphosate: Introduction
- **Glyphosate is TOXIC to humans**
- My earlier papers reexamined
- Glyphosate and aluminum
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary

## Roundup Safety Claims Disputed\*

“It is commonly believed that Roundup is among the safest pesticides. ... Despite its reputation, *Roundup was by far the most toxic among the herbicides and insecticides tested.* This inconsistency between scientific fact and industrial claim may be attributed to huge economic interests, which have been found to falsify health risk assessments and *delay health policy decisions.*”

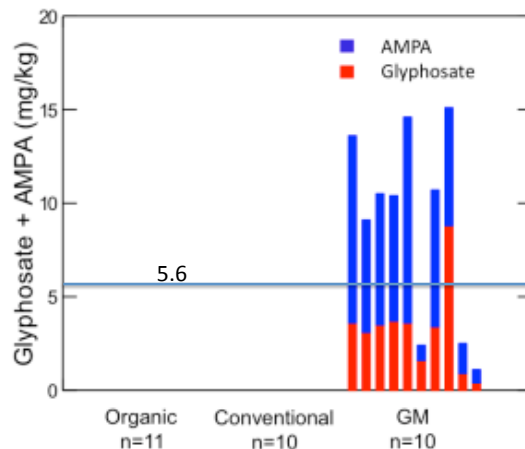
\*R. Mesnage et al., Biomed Research International, Volume 2014 (2014), Article ID 179691

## Glyphosate Test Report: Findings in American Mother's Breast milk, urine and water\*

- Moms Across America initiative!
- Breast milk levels ranging from 76 ug/l to 166 ug/l are 760 to 1600 times higher than the European Drinking Water Directive allows
- Urine testing shows glyphosate levels over 10 times higher than in Europe
- Monsanto is wrong regarding bioaccumulation

\*Posted on Apr 6 2014 - 4:19am by Sustainable Pulse

“Another claim of Monsanto's has been that residue levels of up to **5.6 mg/kg** in GM-soy represent “...*extreme levels*, and far higher than those typically found” (Monsanto 1999).”



\*Figure 1, T. Bohn et al. Food Chemistry 153, 15 June 2014, 207-215.  
[www.greenmedinfo.com/blog/how-extreme-levels-roundup-food-became-industry-normal](http://www.greenmedinfo.com/blog/how-extreme-levels-roundup-food-became-industry-normal)

## Soy Formula Linked to Seizures in Autism\*

*"There was a 2.6-fold higher rate of febrile seizures, a 2.1-fold higher rate of epilepsy comorbidity and a 4-fold higher rate of simple partial seizures in the autistic children fed soy-based formula"*



\*CJ Westmark, PLOSOne March 12, 2014, DOI: 10.1371/journal.pone.0080488.

## Outline

- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- **My earlier papers reexamined**
- Glyphosate and aluminum
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary

## Two Papers

*Entropy* **2012**, *14*, 2265-2290; doi:10.3390/e14112265

OPEN ACCESS

**entropy**

ISSN 1099-4300

www.mdpi.com/journal/entropy

Review

**Is Cholesterol Sulfate Deficiency a Common Factor in Preeclampsia, Autism, and Pernicious Anemia?**

Stephanie Seneff <sup>1\*</sup>, Robert M. Davidson <sup>2</sup> and Jingjing Liu <sup>1</sup>

*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 <sup>1\*</sup>, Ann Lauritzen <sup>2</sup>, Robert M. Davidson <sup>3</sup> and Laurie Lentz-Marino <sup>4</sup>



## The First Paper

- This paper used the US CDC VAERS database to link together preeclampsia, autism and pernicious anemia
- Pernicious anemia is due to cobalamin (B12) deficiency
- Preeclampsia is a strong risk factor for autism
- The symptoms in adverse reactions linked to anemia recapitulate preeclampsia

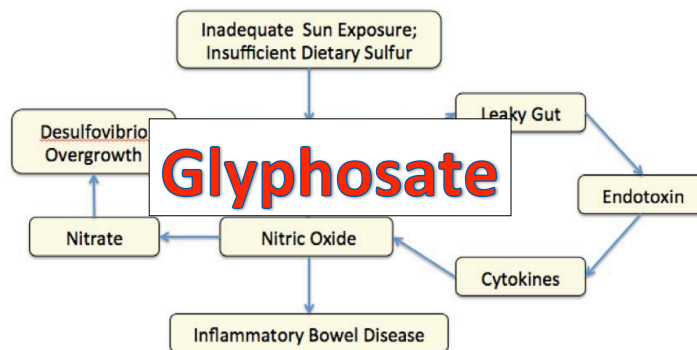
## The First Paper

- This paper used the US CDC VAERS database to link together preeclampsia, autism and pernicious anemia
- Pernicious anemia is due to cobalamin (B12) deficiency
- Preeclampsia is a strong risk factor for autism
- The symptoms in adverse reactions linked to anemia recapitulate preeclampsia

Glyphosate chelates cobalt which prevents gut bacteria from producing cobalamin

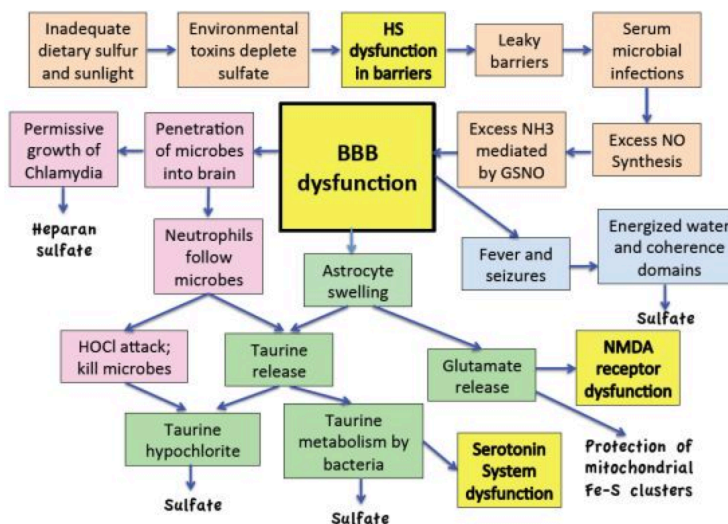
## Figure from Our First Paper\*

**Figure 1.** Feedback loop leading to excess production of nitric oxide and *Desulfovibrio* overgrowth in the gut in autism, resulting in inflammatory bowel disease.



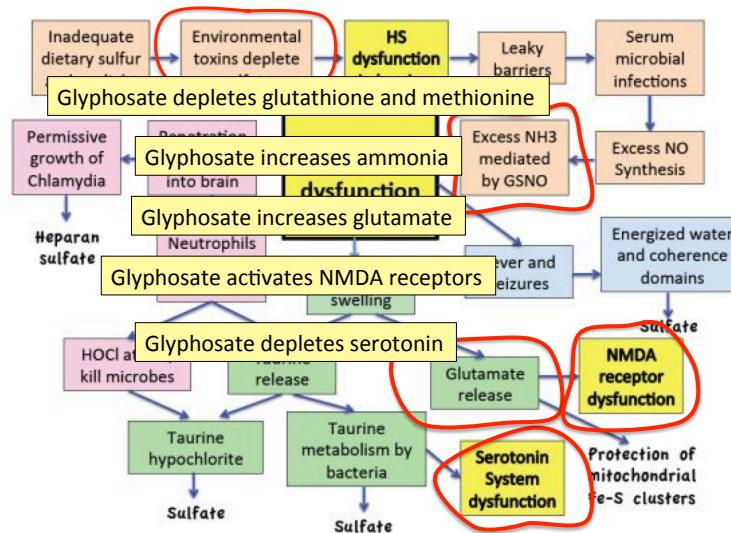
\*S. Seneff et al., Entropy 2012, 14, 2265-2290.

## Figure from Our Second Paper\*



\*S. Seneff et al. Entropy 2013, 15(1), 372-406.

## Figure from Our Second Paper\*

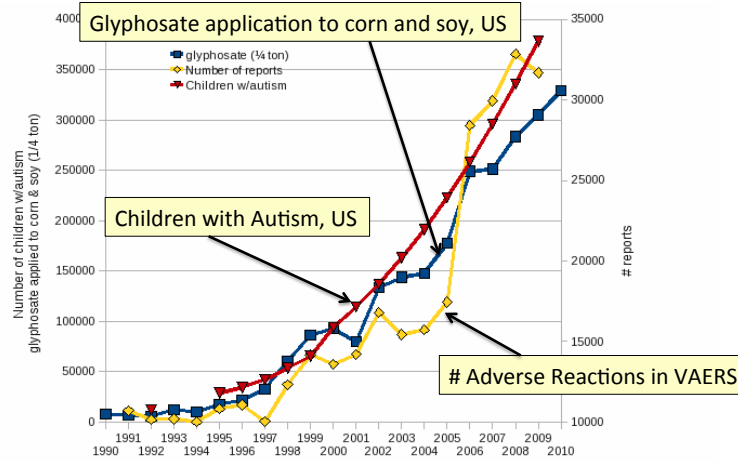


\*S. Seneff et al. Entropy 2013, 15(1), 372-406.

## Outline

- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- **Glyphosate and aluminum**
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary

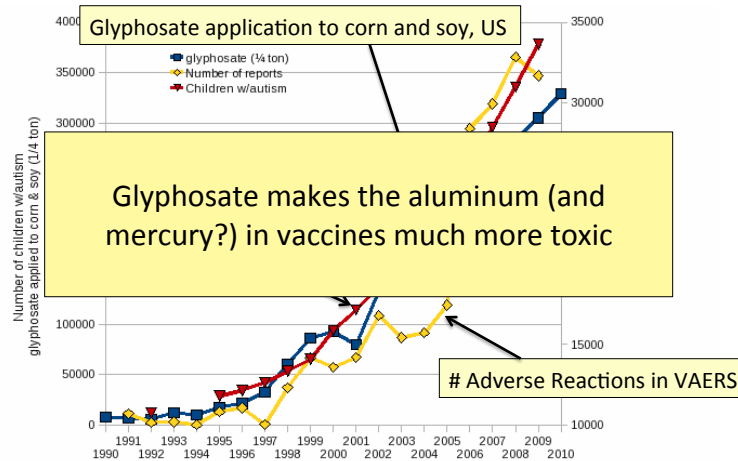
## Autism, Glyphosate, Vaccine Reactions\*



\*Collaboration with Nancy Swanson

MIT Computer Science and Artificial Intelligence Laboratory

## Autism, Glyphosate, Vaccine Reactions\*



\*Collaboration with Nancy Swanson

MIT Computer Science and Artificial Intelligence Laboratory

## Glyphosate enhances aluminum toxicity

### Glyphosate interferes with acetaminophen metabolism

*Entropy* **2012**, *14*, 2227-2253; doi:10.3390/e14112227

OPEN ACCESS

*entropy*

ISSN 1099-4300

www.mdpi.com/journal/entropy

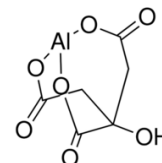
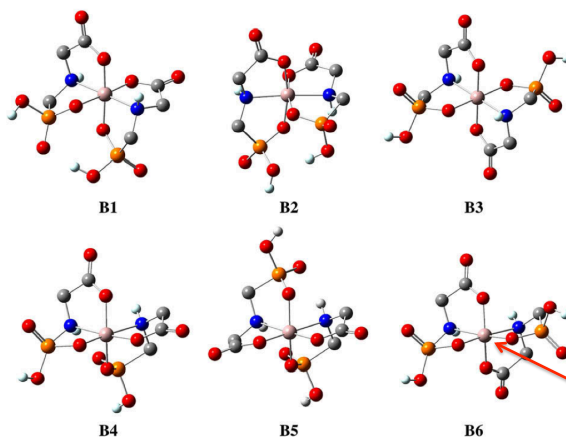
Review

### Empirical Data Confirm Autism Symptoms Related to Aluminum and Acetaminophen Exposure

Stephanie Seneff <sup>1,\*</sup>, Robert M. Davidson <sup>2</sup> and Jingjing Liu <sup>1</sup>

## Aluminum Glyphosate\*

Six different ways two glyphosate molecules can chelate aluminum



Aluminum citrate\*\*



ALUMINA

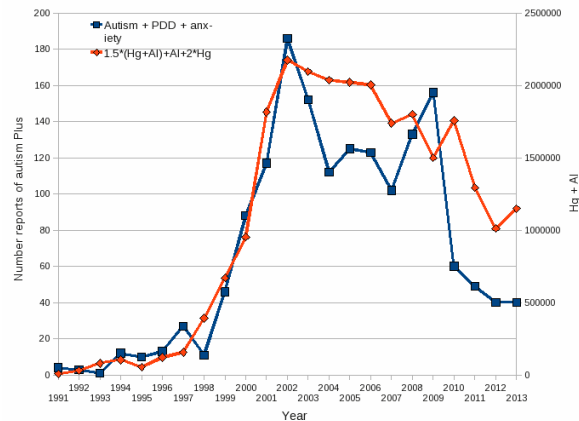
aluminum

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

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

## Aluminum & Mercury Autism & PDD & Anxiety

R = 0.9024, p <= 1.115e-07



VAERS  
database

Formula:  $Al + 1.5 \times (Al \text{ w/ Hg}) + 2.0 \times Hg$

## Outline

- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- Glyphosate and aluminum
- **Glyphosate and arsenic**
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary

Glyphosate chelates many metal cations:  
I suspect many adverse health effects from chelation  
of aluminum, arsenic, manganese, and cobalt

Glyphosate chelates many metal cations:  
I suspect many adverse health effects from chelation  
of aluminum, *arsenic*, manganese, and cobalt

*Int. J. Environ. Res. Public Health* **2014**, *11*, 2125-2147; doi:10.3390/ijerph110202125

**OPEN ACCESS**

Sri Lanka is the first  
Country to Ban Glyphosate

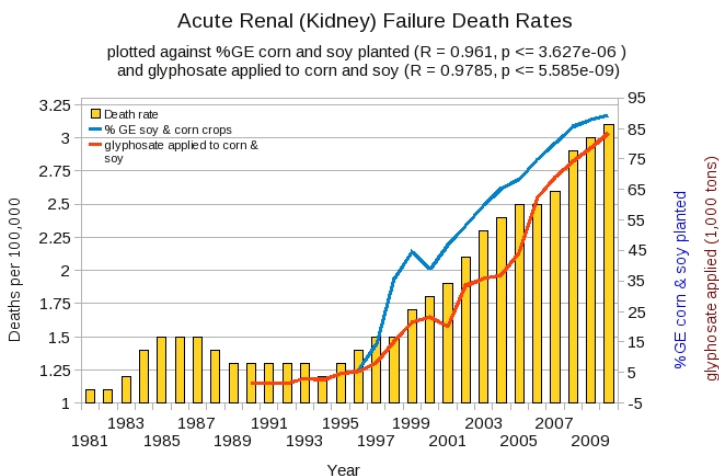
International Journal of  
**Environmental Research and  
Public Health**  
ISSN 1660-4601  
www.mdpi.com/journal/ijerph

*Hypothesis*

**Glyphosate, Hard Water and Nephrotoxic Metals: Are They the  
Culprits Behind the Epidemic of Chronic Kidney Disease of  
Unknown Etiology in Sri Lanka?** **arsenic**

This problem did not exist in Sri Lanka prior to the 1990s.

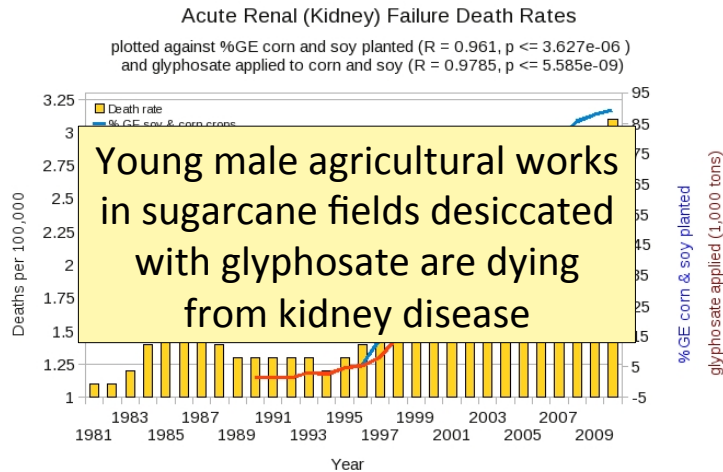
**Acute Kidney Disease Death Rate  
Plotted Against Glyphosate and GMOs\***



\*Plot prepared by Nancy Swanson from available data online



## Acute Kidney Disease Death Rate Plotted Against Glyphosate and GMOs\*



\*Plot prepared by Nancy Swanson from available data online

## Outline

- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- Glyphosate and aluminum
- Glyphosate and arsenic
- **Glyphosate and manganese**
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary

# Manganese!

“The mechanism by which glyphosate disrupts the EPSPS enzyme in plants and microorganism is by chelating the *manganese* metal co-factor of this enzyme. In other words it steals the ‘ignition key’ of the enzyme.”

Dr. Arden Andersen, D.O.,  
Food Plague Primer: Glyphosate and Genetically Engineered Crops

“Fundamentally **the herbicidal effect of glyphosate is ultimately due to soil pathogens** gaining access to the “weed” thanks to glyphosate’s weakening of the plant and killing of beneficial microbes *by the chelation of manganese* and other trace elements.”

Dr. Arden Andersen, D.O.,  
Food Plague Primer: Glyphosate and Genetically Engineered Crops

“Fu  
is u  
to t  
the  
*che*

This is analogous to glyphosate’s effect on gut bacteria: killing the beneficial bacteria and allowing the pathogens to overgrow

Dr. Arden Andersen, D.O.,  
Food Plague Primer: Glyphosate and Genetically Engineered Crops

## Glyphosate Depletes Iron, Manganese and Zinc in Plants\*

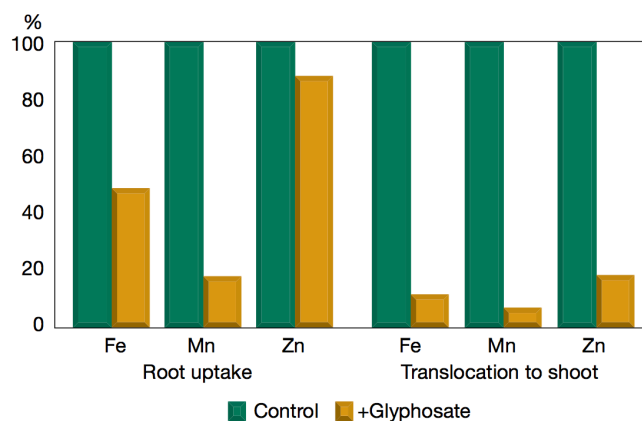
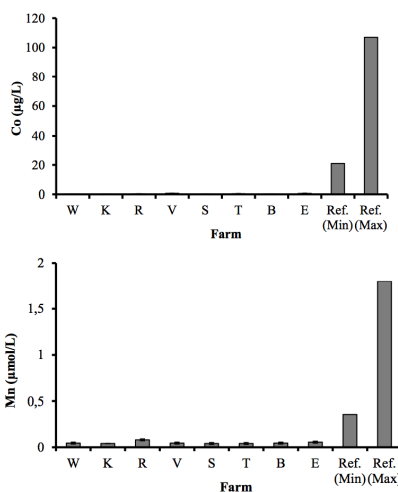


Figure 1. Effect of glyphosate\* on nutrient uptake and translocation by "non-target" plants, Eker, et al. 2006. (\* 2.5% of recommended herbicidal rate of glyphosate.)

\*D Huber, *What About Glyphosate-Induced Manganese Deficiency?* Fluid Journal, 20-22.

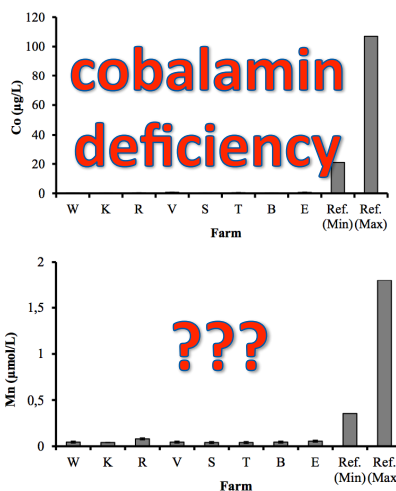
## Severe Deficiency in Serum Manganese and Cobalt in Cows\*



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

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

## 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

## Outline

- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- Glyphosate and aluminum
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary

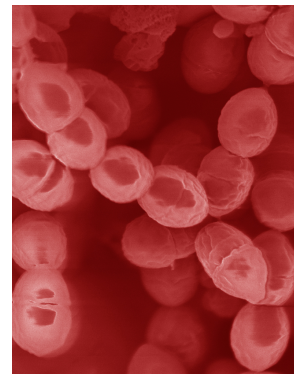
## Glyphosate Kills Beneficial Bacteria\*

- Examined effect of glyphosate and Roundup on three food microorganisms widely used as starters in dairy technologies
  - Two are species of *Lactobacillus*
- Roundup is always more potent than glyphosate, and in all cases, toxic from levels 10–100 times below the lowest agricultural uses (10,000 ppm).
- Unpredictable consequences of Roundup on soil microorganisms have to be considered

\*E Clair et al. Curr Microbiol (2012) 64:486–491

## Lactobacillus Depends on Manganese!\*

- Many lactic acid bacteria contain very high intracellular manganese levels
  - Scavenges toxic oxygen species, particularly superoxide
- Manganese deprivation suppresses growth



\* FS Archibald and M-N Duong. Journal of Bacteriology Apr 1084, 1-8.

## Lactobacillus Depends on Manganese!\*

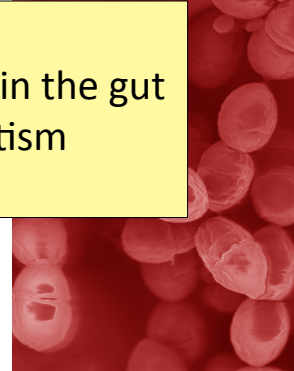
- Many lactic acid bacteria contain very high intracellular manganese

level

– Sci  
pa

Lactobacillus levels are low in the gut  
in association with autism

- Man  
suppresses growth



\* FS Archibald and M-N Duong. Journal of Bacteriology Apr 1084, 1-8.

## Lactobacillus Alleviate Anxiety\*

- Patients suffered from chronic fatigue syndrome and associated anxiety
- Patients were treated with probiotic strain of Lactobacillus (control group got a placebo)
- Significant rise in both Lactobacillus and Bifidobacteria in gut
- Significant decrease in anxiety symptoms (p = 0.01)
- Supports concept of gut-brain axis (communicate with brain via vagal nerve)

\* R Av et al. Gut Pathog. 2009 Mar 19;1(1):6. doi: 10.1186/1757-4749-1-6.

## Lactobacillus Alleviate Anxiety\*

- Patients suffered from chronic fatigue syndrome and associated anxiety
- **Increased anxiety is a comorbidity of autism**
- Significant decrease in anxiety symptoms ( $p = 0.01$ )
- Supports concept of gut-brain axis (communicate with brain via vagal nerve)

\*R Av et al. Gut Pathog. 2009 Mar 19;1(1):6. doi: 10.1186/1757-4749-1-6.

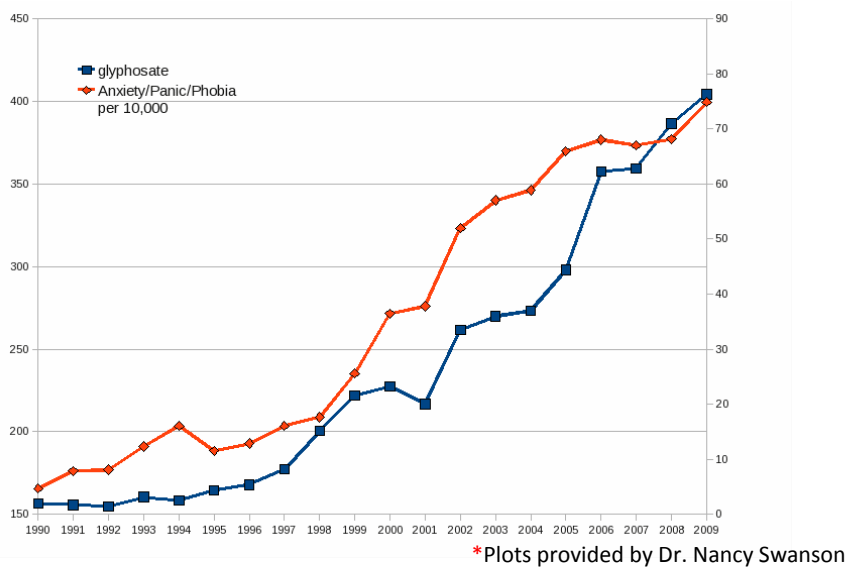
## Anxiety and Autism\*

- Specific Phobia: 30%
- Obsessive-Compulsive Disorder: 17%
- Social Anxiety Disorder/Agoraphobia: 17%
- Generalized Anxiety Disorder: 15%
- Separation Anxiety Disorder: 9 %
- Panic Disorder: 2%

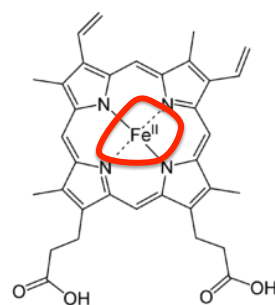
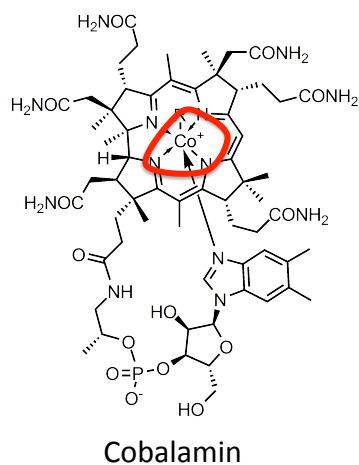
\*Van Steensel, F.J.A., Bogels, S.M., & Perrin, S. (2011). Anxiety disorders in children and adolescents with autistic spectrum disorders: A meta-analysis. *Clinical Child and Family Psychology Review*, 14, 302-317.



## Glyphosate Application on Corn and Soy Plotted against Anxiety, Panic Disorder and Phobias\*

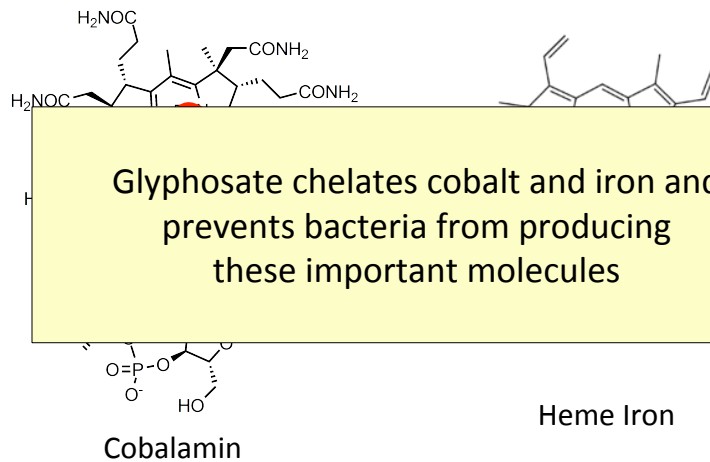


## Bacteria Incorporate Cobalt and Iron into Cobalamin and Heme



Heme Iron

## Bacteria Incorporate Cobalt and Iron into Cobalamin and Heme



## The First Paper

- This paper used the US CDC VAERS database to link together preeclampsia, autism and pernicious anemia
- Pernicious anemia is due to cobalamin (B12) deficiency
- Preeclampsia is a strong risk factor for autism
- The symptoms in adverse reactions linked to anemia recapitulate preeclampsia

## The First Paper

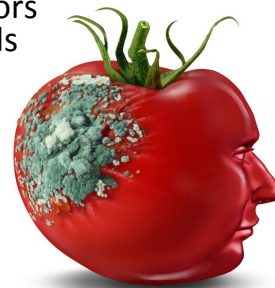
- This paper used the US CDC VAERS database to link together preeclampsia, autism and pernicious anemia
- **Pernicious anemia is due to cobalamin (B12) deficiency**
- Preeclampsia is a strong risk factor for autism
- The symptoms in adverse reactions linked to anemia recapitulate preeclampsia

## Outline

- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- Glyphosate and aluminum
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - **Glutamate and ammonia**
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary

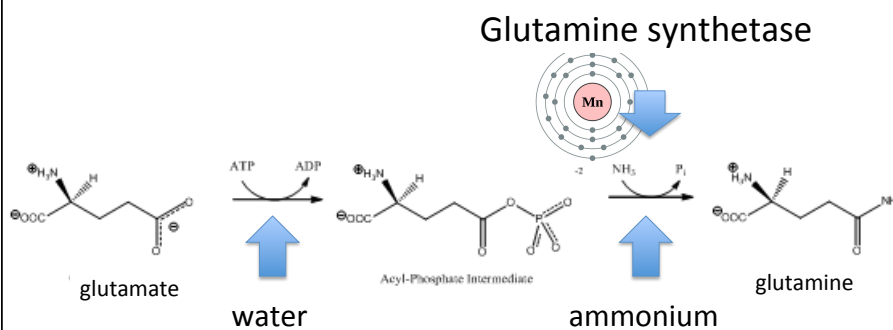
## Glyphosate and Glutamate\*

- 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



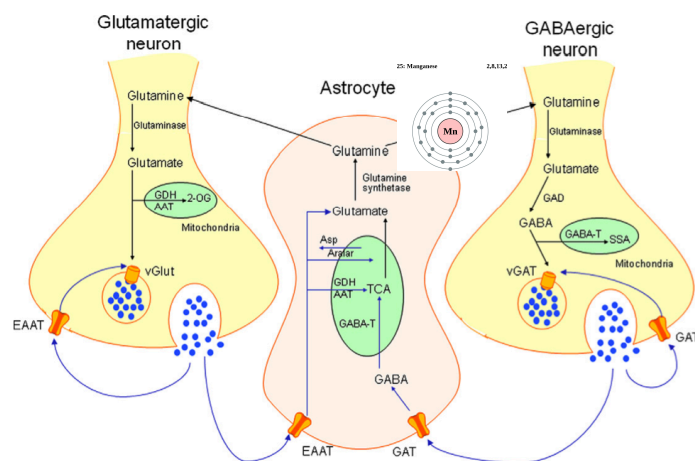
\*<http://www.greenmedinfo.com/blog/roundup-weedkiller-brain-damaging-neurotoxin>

## Glutamine Synthesis Depends on Manganese!



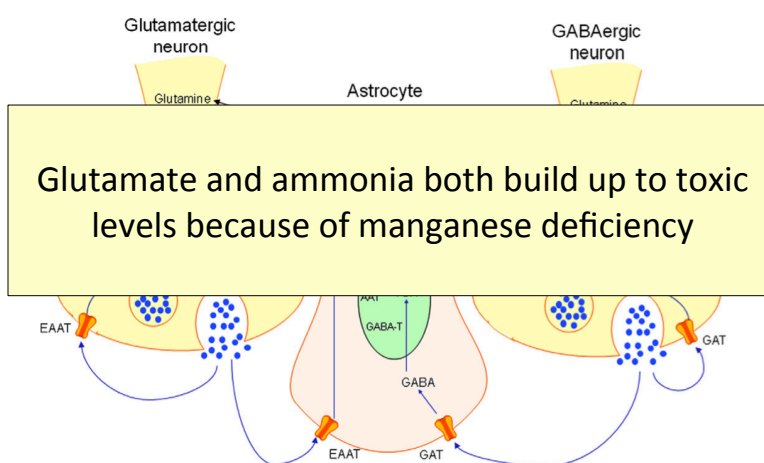
Ammonium and glutamate toxicity in the brain can arise because of insufficient manganese

## Glutamate and GABA\*



\*NM Rowley et al. Neurochemistry International 61 (2012) 546–558.

## Glutamate and GABA\*



\*NM Rowley et al. Neurochemistry International 61 (2012) 546–558.

## “Alteration of Plasma Glutamate and Glutamine Levels in Children with High-Functioning Autism”\*

Amino acid	Control	HFA	p-value
Alanine	326.1±61.6	300.3±55.0	0.145
α-Aminobutyric acid	18.8±3.8	18.7±5.4	0.971
Arginine	89.1±19.0	95.3±18.5	0.279
Asparagine	40.8±8.3	43.1±7.0	0.311

Glutamate	20.9±4.5	27.9±7.4	<0.002*
Glutamine	513.1±48.5	445.8±50.6	<0.0004**

Isoleucine	53.6±11.5	62.2±14.5	0.033
Leucine	99.0±16.1	106.4±22.4	0.210
Lysine	155.3±28.5	164.2±32.5	0.332
Methionine	23.7±5.1	25.8±5.6	0.203
Ornithine	43.9±11.3	51.9±10.8	0.021
Phenylalanine	51.7±6.8	55.1±8.4	0.146
Proline	153.7±56.4	131.7±47.6	0.165
Serine	105.4±15.6	115.8±14.7	0.027
Taurine	33.4±5.5	37.8±7.9	0.036
Threonine	100.8±19.7	112.0±24.3	0.097
Tryptophan	44.8±5.6	47.3±6.4	0.167
Tyrosine	60.9±10.5	58.4±10.1	0.425
Urea	3976.3±818.7	3759.9±773.3	0.367
Valine	200.2±29.4	217.1±29.7	0.062

\*C. Shimmura et al.  
PLoSone October  
2011 6(1):e25340

## Journal of Personal Science: One Child’s Autism Eliminated by Removal of Glutamate From Her Diet\* By Katherine Reid

First Round:

- Kale, cucumber, cilantro, nuts, seeds, fruits
- Magnesium B-complex, vitamin D3, omega 3 fats (EPA, DHA)
- Probiotics
- Gluten free and casein free (no wheat, no milk)

*Child improved significantly but still had autistic behaviors*

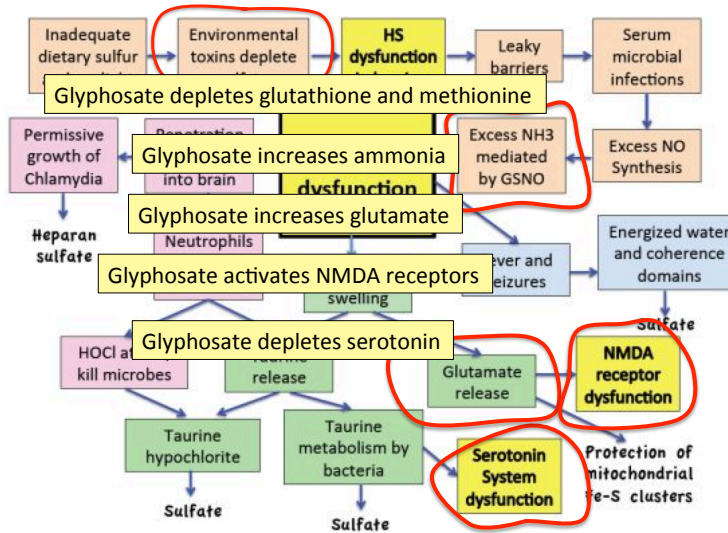
Second Round:

- ADD: ELIMINATE FREE GLUTAMATE

*Child lost the "autism" label!*

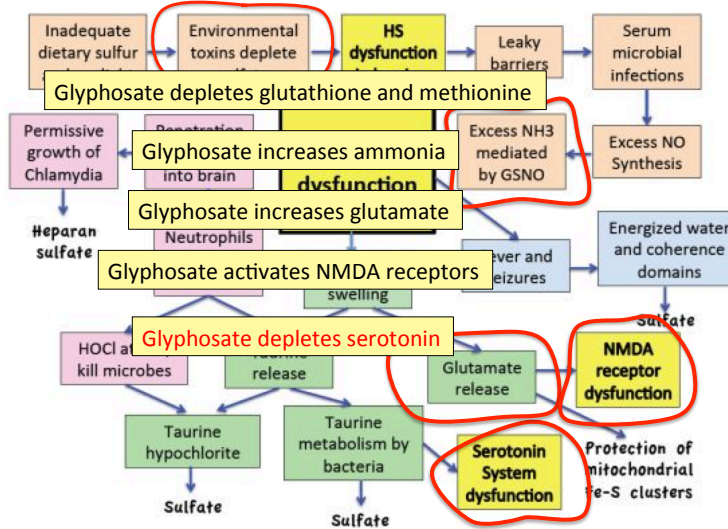
\*[blog.sethroberts.net/2013/05/17/journal-of-personal-science-one-childs-autism-eliminated-by-removal-of-glutamate-from-her-diet](http://blog.sethroberts.net/2013/05/17/journal-of-personal-science-one-childs-autism-eliminated-by-removal-of-glutamate-from-her-diet)

## Figure from Our Second Paper\*



\*S. Seneff et al. Entropy 2013, 15(1), 372-406.

## Figure from Our Second Paper\*



\*S. Seneff et al. Entropy 2013, 15(1), 372-406.

*The FASEB Journal* • Review

Adapted from the FASEB J page proofs, 02/18/14

Estimated embargo date is February 26, 2014

Actual embargo date is the date it will appear on the FASEB J website.

Here is link of where the article will appear: <http://www.fasebj.org/content/early/recent>

## Vitamin D hormone regulates serotonin synthesis.

### Part 1: relevance for autism

Rhonda P. Patrick<sup>1</sup> and Bruce N. Ames<sup>1</sup>

Glyphosate suppresses tryptophan synthesis by plants and gut bacteria

Oakland,

ver

- Autism is associated with low activated vitamin D and low brain serotonin
  - Vitamin D activates serotonin receptors in the brain
- Estrogen rescues females by boosting serotonin levels in brain
- Recommendation is supplements in both vitamin D and tryptophan (*precursor to serotonin*)

## Outline

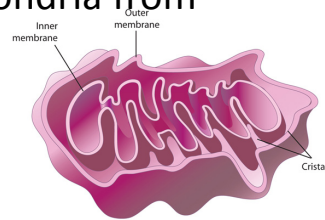
- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- Glyphosate and aluminum
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - **Mitochondrial disorder**
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary



## Autism and Mitochondrial Disorder\*

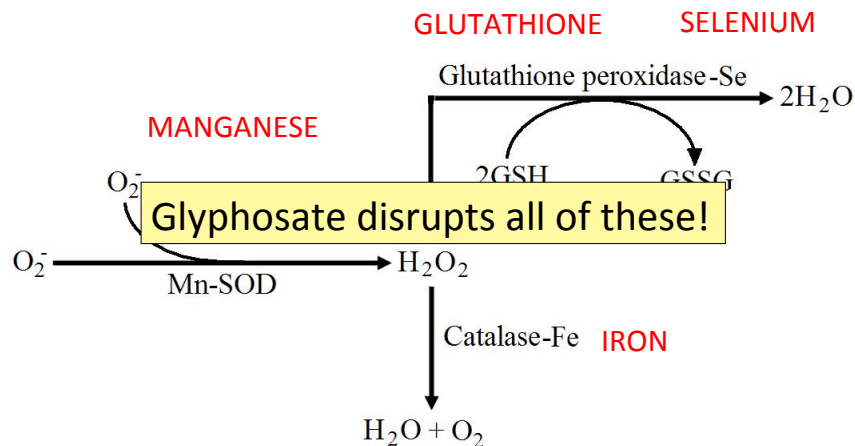
“Five of 11 patients studied were classified with definite mitochondrial respiratory chain disorder, suggesting that this might be one of the most common disorders associated with autism”

**Manganese** superoxide dismutase plays a critical role in protecting mitochondria from oxidative damage

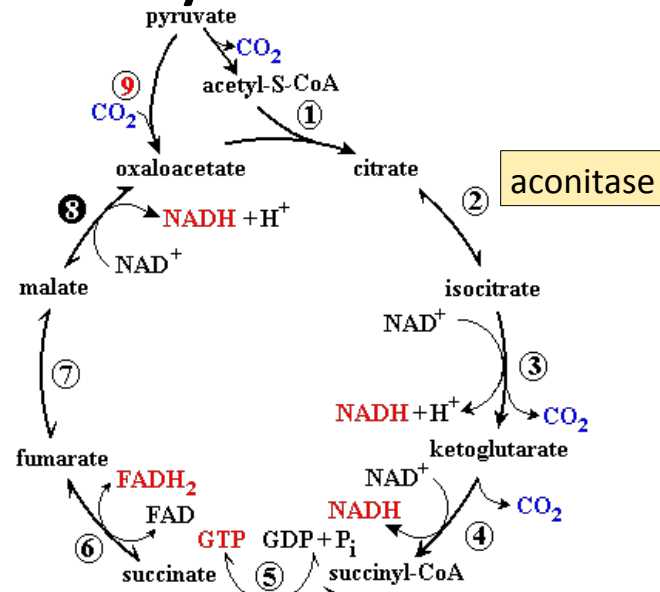


\*G Oliveira et al. Developmental Medicine & Child Neurology 47(3), 185-189, 2005.

## Detoxification of Superoxide ( $O_2^-$ )

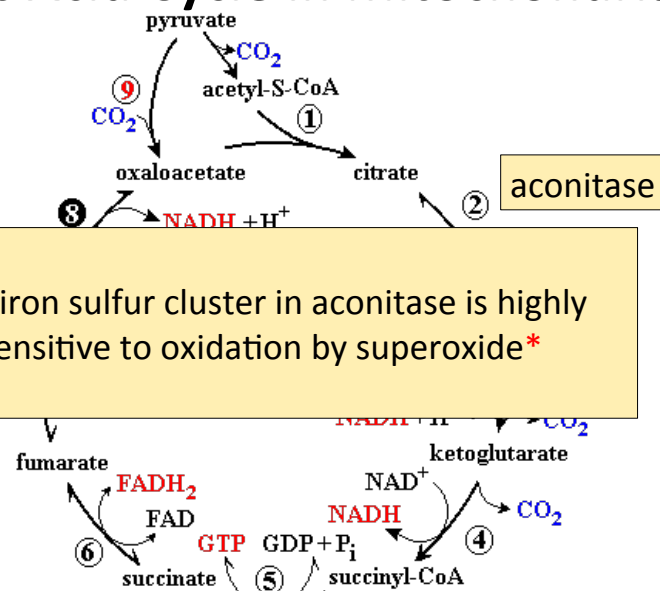


## Citric Acid Cycle in Mitochondria



\*PR Gardner. Methods in Enzymology 349:9–23.

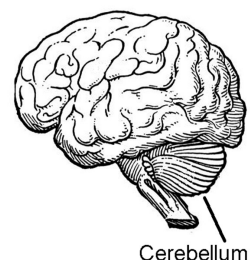
## Citric Acid Cycle in Mitochondria



\*PR Gardner. Methods in Enzymology 349:9–23.

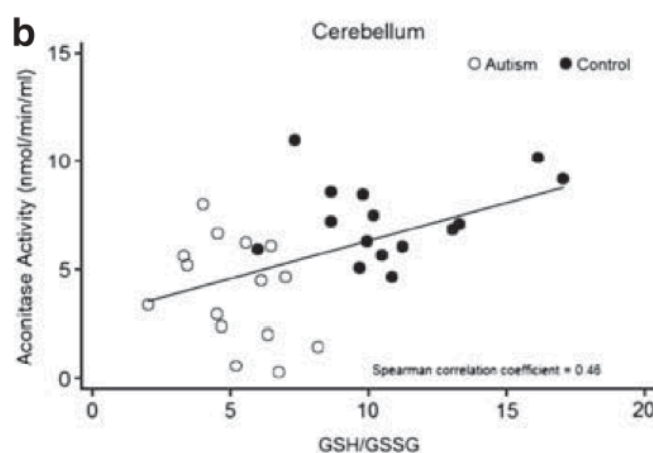
## Aconitase Dysfunction and Brain Inflammation in Autism\*

- Frozen samples of post-mortem tissues from cerebellum and temporal cortex of autism patients compared with controls.
- Compared to controls:
  - Aconitase activity was significantly reduced in the cerebellum and correlated with low glutathione levels
  - Biomarkers of inflammation were increased



\*S. Rose et al. Transl Psychiatry (2012) 2:e134.

## Aconitase & Glutathione in Cerebellum in Autism\*



\* S Rose et al. Transl Psychiatry (2012) 2:e134.

## Outline

- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- Glyphosate and aluminum
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - **Thyroid hormone**
  - Impaired bone development
- Recommendations and Summary

## Maternal Low Thyroid and Autism\*

“Severe maternal hypothyroxinemia early in gestation increased the likelihood of having an autistic child by almost 4-fold.”

Thyroid hormone is derived from tyrosine, one of the three aromatic amino acids produced via the shikimate pathway

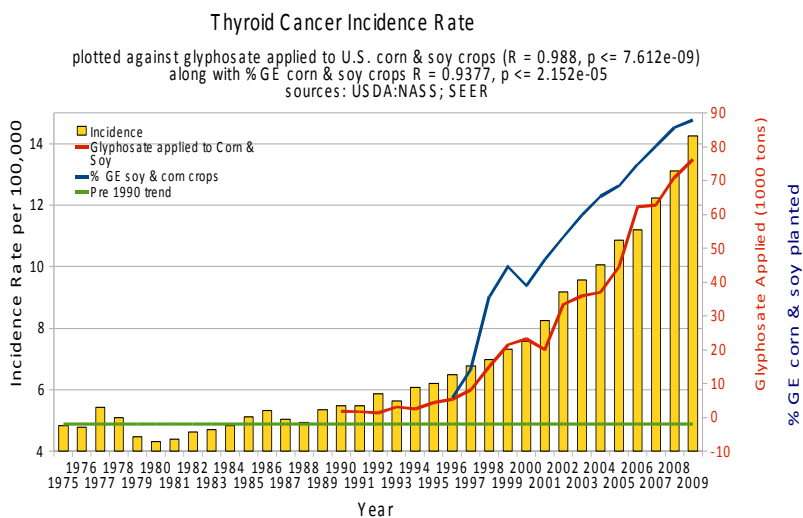
\*<http://www.medscape.com/viewarticle/809718>

## Dopamine and Thyroid Hormone\*

- Like thyroid hormone, dopamine is derived from the aromatic amino acid tyrosine
- Dopamine inhibits thyroid stimulating hormone
  - Corollary: insufficient dopamine leads to overactive thyroid → burnout
- Thyroid hormone promotes synaptogenesis, synaptic vesicle and receptor recycling, neurotransmitter reuptake, and growth factor receptor signaling

\*OP Soldin and M Aschner. Neurotoxicology 2007 September; 28(5):951–956

## Glyphosate and Thyroid Cancer\*



\*Graph kindly provided by Nancy Swanson

## Outline

- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- Glyphosate and aluminum
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- Recommendations and Summary

## Glyphosate and Bone Development\*

- Dams treated with glyphosate in water from days 6 to 15 of their pregnancy
- Effects on pups:
  - Lack of development of the ossification centers of the terminal phalanges (bones in fingers and toes)
  - Larger fontanelles ("soft spot") and incomplete development of skull bones
  - Absence of important bones or parts of bones, shortenings, bendings, asymmetry, fusions or clefts.
  - Surfactant polyoxyethyleneamine increased glyphosate's toxicity



\*E. Dallegrave et al. Toxicology Letters 142 (2003) 45-52.

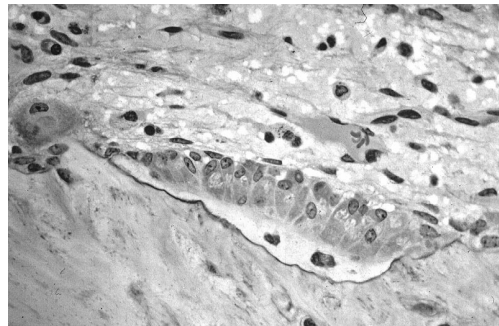
## Manganese and Bones\*

“The multiple cellular effects of Mn deficiency include: decreased bone resorption, production of labile bone, and *decreased synthesis of organic matrix*. The serum level of Mn in a group of osteoporotic postmenopausal women was significantly lower than age-matched controls.”

\*L. Strause and P. Saltman. Role of Manganese in Bone Metabolism. Chapter 5, pp 46–55 in Nutritional Bioavailability of Manganese.

## Osteoblasts build “Ground Substance”

- Ground substance is made of chondroitin sulfate and osteocalcin – collagen is layered over this
- Poor mineralization results from impaired chondroitin sulfate synthesis



Osteoblasts in bone

Childhood osteoarthritis and osteomalacia are an epidemic in the US today

## Chondroitin Sulfate Synthesis in Cartilage depends on Manganese\*

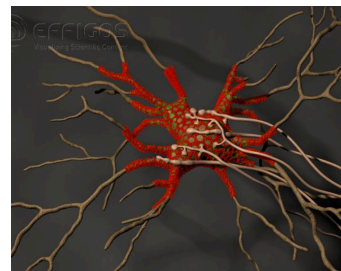
- Two critical enzymes are manganese dependent:
  - Polymerase enzyme forms the polysaccharide
  - Galactotransferase incorporates galactose that links the polysaccharide to the protein associated with it.



\*RM Leach et al. Archives of Biochemistry and Biophysics 133(1), 1969, 22-28.

## Perineuronal Nets\*

- Perineuronal nets (PNs) formed from *chondroitin sulfate* attached to hyaluronan, modulate GABAergic inhibitory signaling
- Removal of PNs increased excitability of interneurons in cultures
- They provide an environment rich in anions (negative charge)

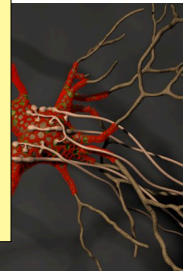


\*G. Bruckner et al. Glia 8(3), 183-200, 1993.



## Perineuronal Nets\*

- Perineuronal nets (PNs) formed from *chondroitin sulfate* attached to hyaluronan, mo
- Re Might manganese deficiency lead to impaired synthesis of perineuronal nets and increased neuronal excitability leading to cell death??
- Th rich in anions (negative charge)



\*G. Bruckner et al. *Glia* 8(3), 183-200, 1993.

## Coral Die-Off & Chondroitin Sulfate\*

- Large amounts of chondroitin sulfate are adsorbed onto coral
- Sulfate groups are of paramount importance to the adsorption process
- Adsorption rate is a direct function of the amount of negative charge



\*N. Volpi. *Biomaterials* 2002 Jul;23(14):3015-22.

## “Disease Causes Starfish to Lose Arms, Dissolve into White Blobs of Goo” \*

- Glyphosate is used to kill seagrass in oyster beds
- "Glyphosate and diuron are among the most frequently detected herbicides in oyster production areas" \*\*
- Starfish eat oysters



\*<http://natureworldnews.com/articles/4749/20131104/disease-causes-starfish-lose-arms-dissolve-white-blobs-goo-video.htm>

\*\*F. Akcha et al. Aquatic Toxicology. 106-107 (pp 104-113), 2012

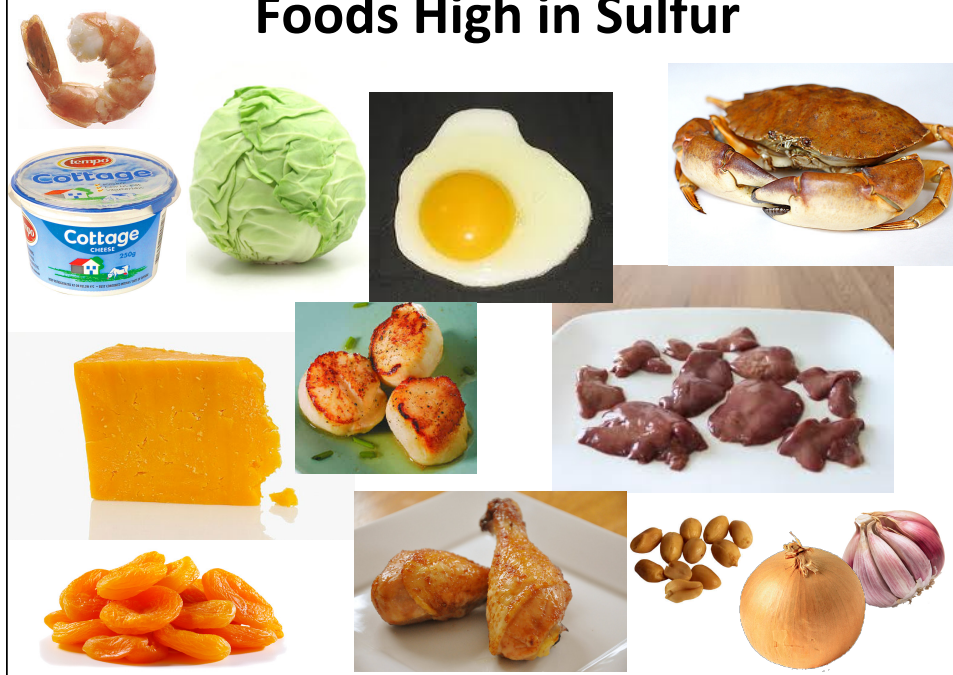
## Recapitulation

- Glyphosate chelates manganese
- Manganese deficiency leads to:
  - Disrupted gut bacteria → anxiety
  - Tyrosine depletion → thyroid disease
  - Glutamate and ammonium toxicity in the brain as well as glutamine deficiency
  - Mitochondrial damage
  - Impaired bone development and osteoporosis
  - Impaired development of perineuronal nets
- Many of these pathologies are associated with autism

## Outline

- Autism and glyphosate: Introduction
- Glyphosate is TOXIC to humans
- My earlier papers reexamined
- Glyphosate and aluminum
- Glyphosate and arsenic
- Glyphosate and manganese
  - Lactobacillus and anxiety
  - Glutamate and ammonia
  - Mitochondrial disorder
  - Thyroid hormone
  - Impaired bone development
- **Recommendations and Summary**

## Foods High in Sulfur



## Foods High in Manganese



## Summary

- Contrary to popular belief, glyphosate is toxic to humans and is likely the number one factor in the autism epidemic
- Glyphosate's chelation of rare minerals is a core component of its toxicity
  - Disrupted gut bacteria leads to multiple problems
  - Aluminum and manganese pathology can account for many aspects of autism
- Dementia may well be the same story
- Autism may be treatable through organic diet enriched in sulfur and manganese