



Glyphosate Pretending to be
Glycine: Devastating Consequences

Stephanie Seneff, MIT CSAIL

AutismOne 2016

In a time of universal deceit,
telling the truth is a revolutionary act.

— George Orwell

Outline

- Review
- Glyphosate Insertion Into Peptides
 - Neurological Diseases
 - Neural Tube Defects
 - Diabetes, Obesity and Adrenal Insufficiency
 - Impaired Blood Flow
 - Kidney Disease
 - Liver Disease
 - Hyperkeratosis
- How to Safeguard Yourself and Your Family

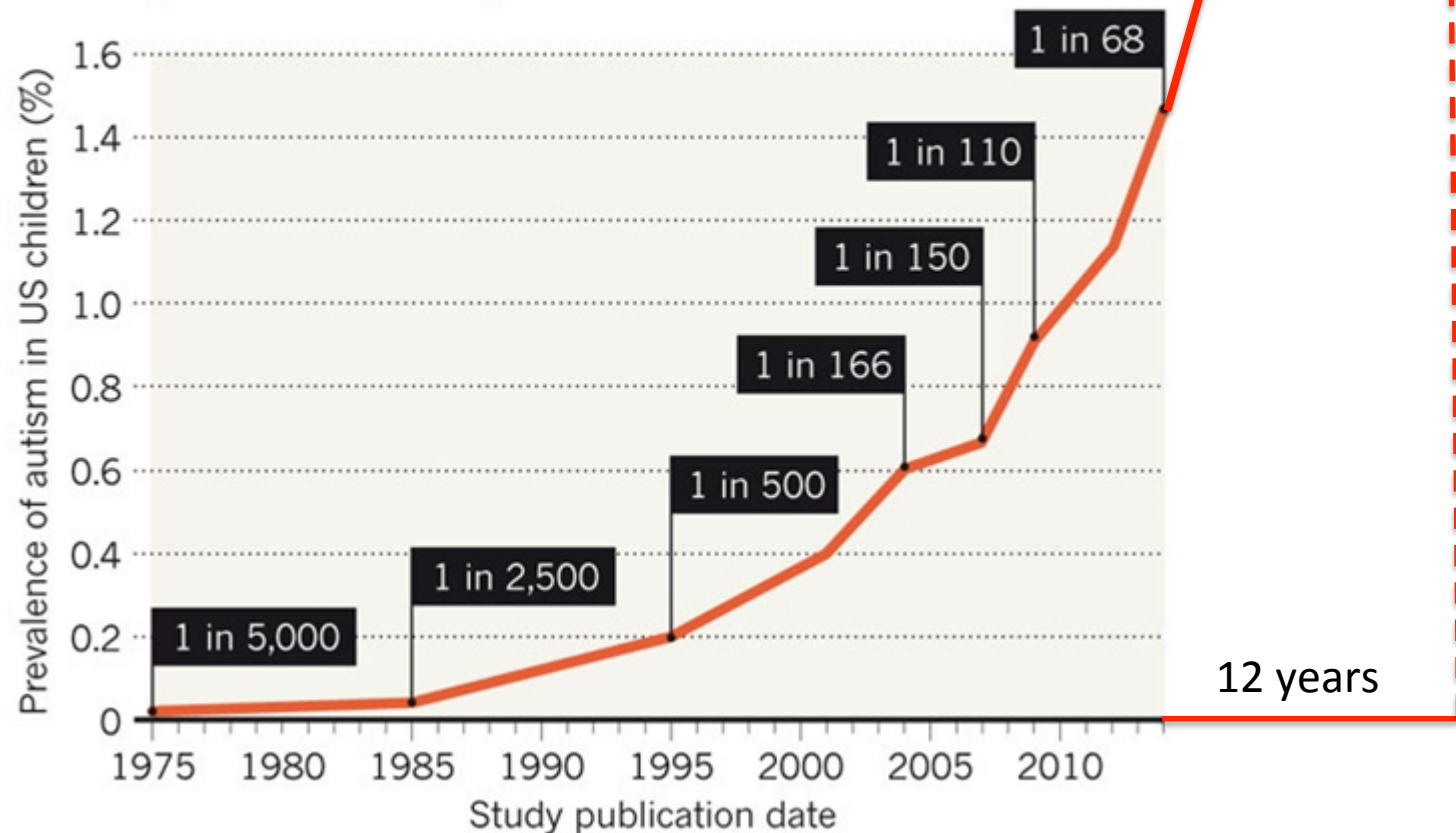
Review

A Frightening Trend*



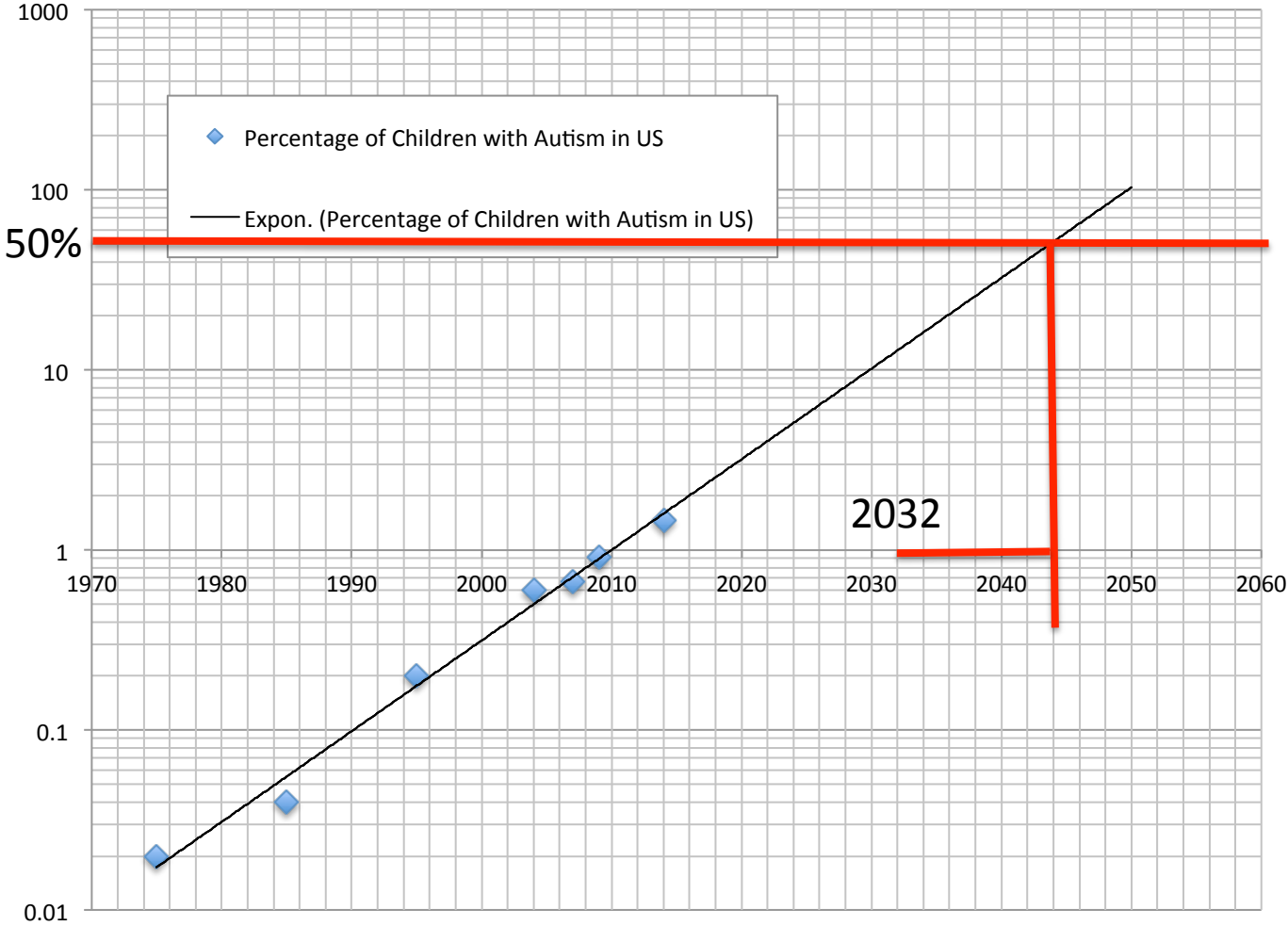
AUTISM DIAGNOSES RISING

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

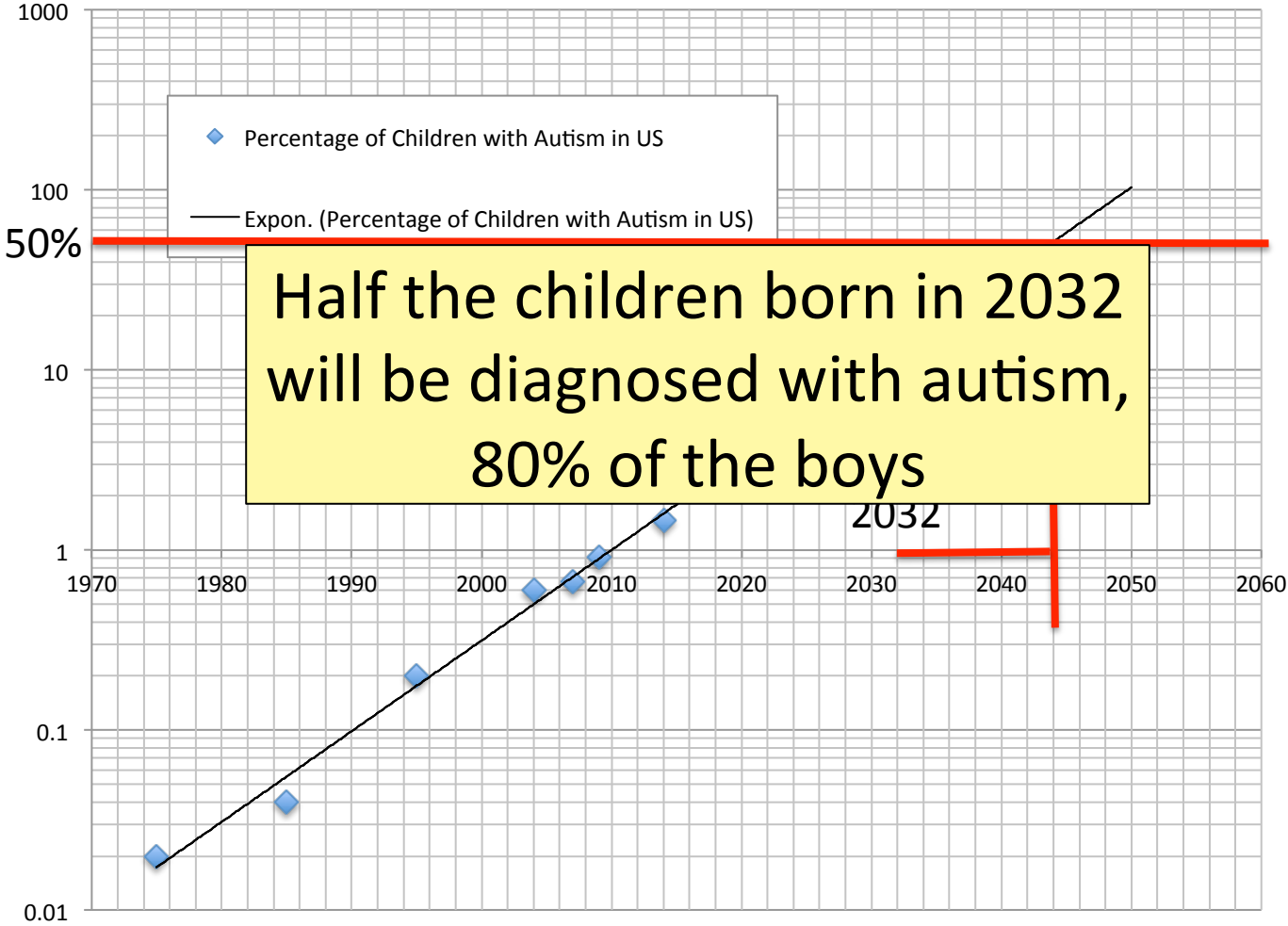


*K. Weintraub, Nature 479, Nov. 3 2011, 22-24.

Percentage of children with Autism in the US

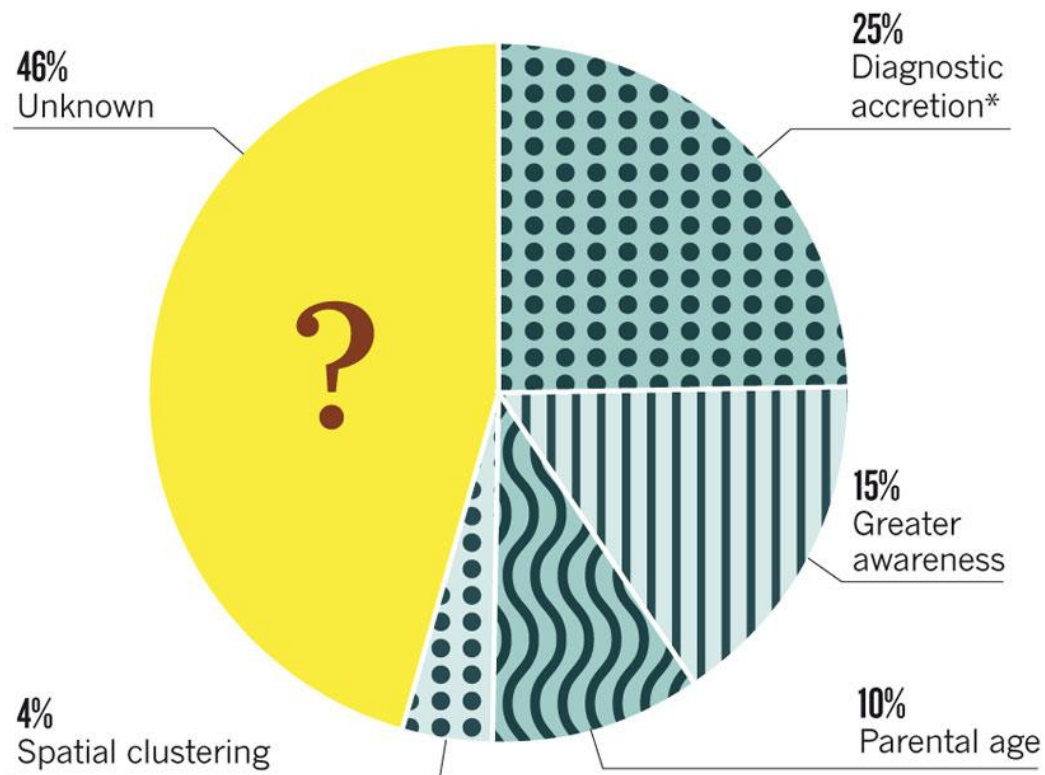


Percentage of children with Autism in the US



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

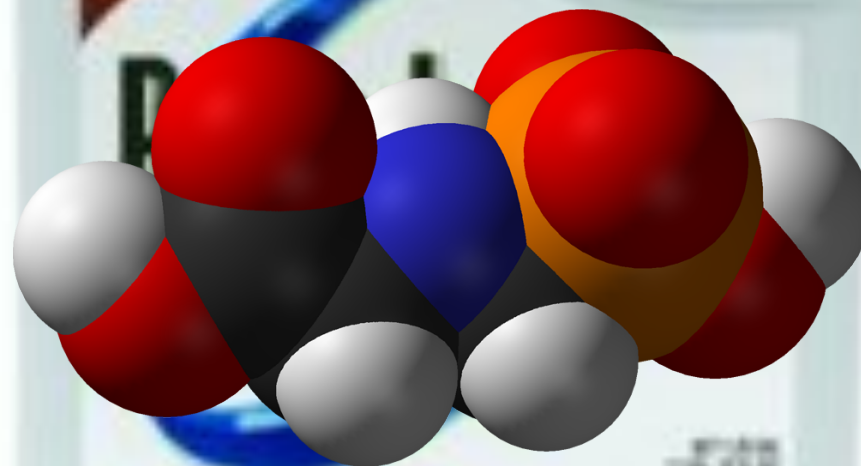
Reasons: unclear



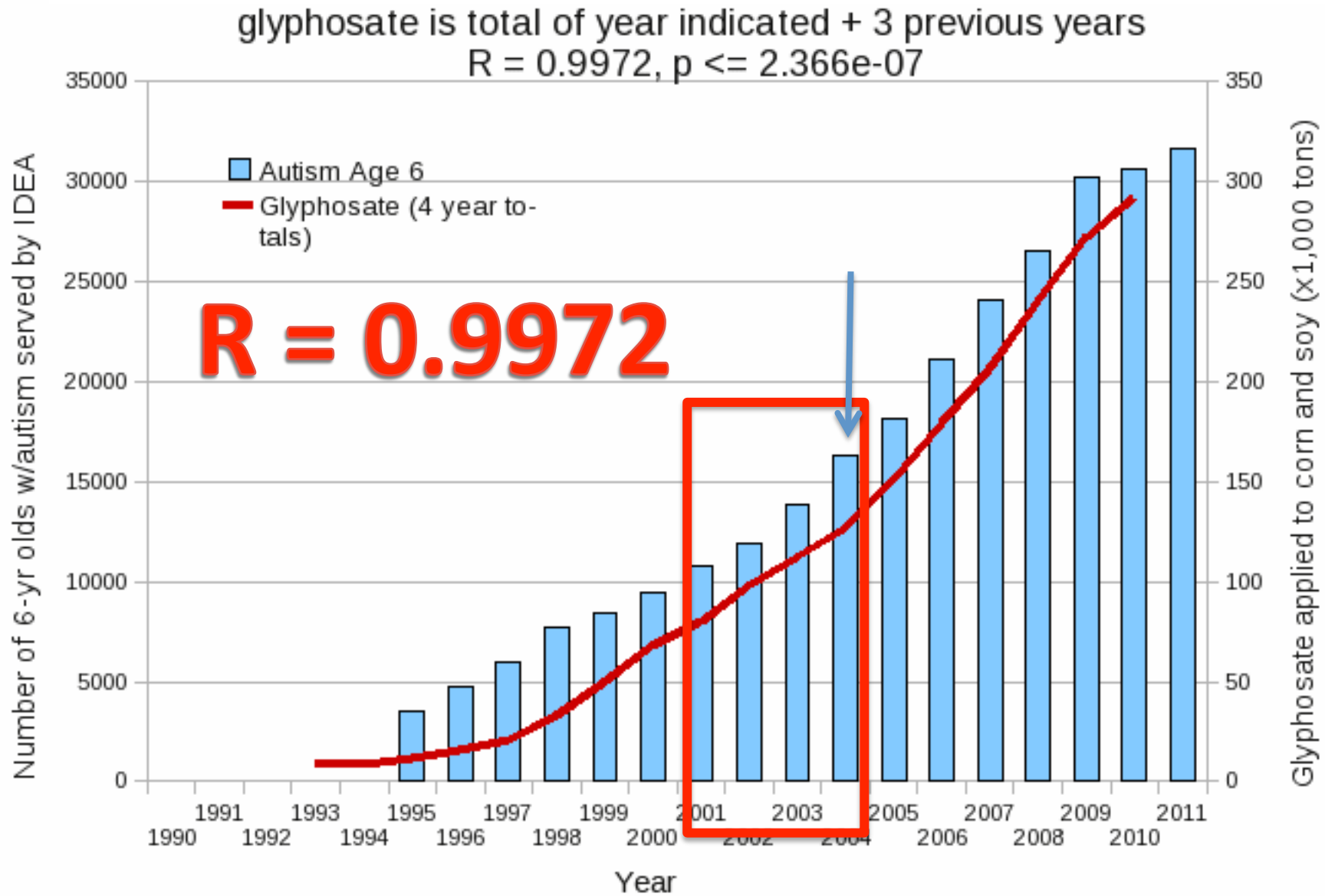
*Children who formerly would have been diagnosed solely with mental retardation

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

GLYPHOSATE

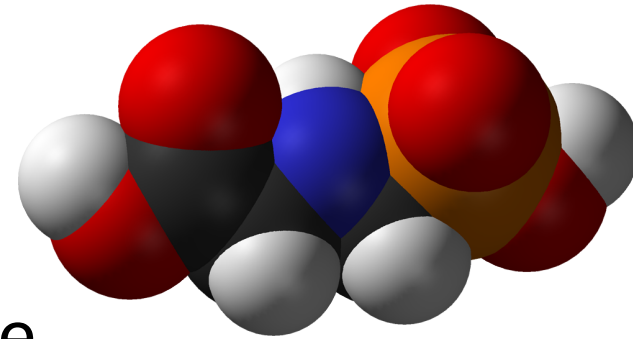


Autism Prevalence: 6 year olds*



* Figure 15, Seneff et al., Agricultural Sciences, 2015, 6, 42-70

Is Glyphosate Toxic?



- 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 and are themselves toxic
- Insidious effects of glyphosate accumulate over time
 - Most studies are too short to detect damage

Main Toxic Effects of Glyphosate*

- 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*

Glyphosate and Autism:

Some Biological Mechanisms

- Disruption of gut microbes¹
 - Children with autism suffer from many digestive issues
- Disruption of sulfur metabolism, glutathione deficiency, impaired methylation pathways¹
- Metal chelation (especially manganese)²
 - Manganese deficiency leads to impaired mitochondrial function and glutamate toxicity in the brain
- Inhibition of pituitary release of thyroid stimulating hormone → hypothyroidism³
 - Moms with hypothyroidism have 4-fold increased risk to autism in the fetus

1. Samsel and Seneff, Entropy 2013;15(4):1416-1463.

2. Samsel and Seneff, Surg Neurol Int. 2015;6:45.

3. Beecham and Seneff, Journal of Autism 2016;3:1.

“Glyphosate Now the Most-Used Agricultural Chemical Ever”*

By Douglas Main, Feb 2, 2016 Newsweek

- Glyphosate usage has increased 50-fold since 1996, when GMO glyphosate-resistant crops were introduced in the US.
- Today, 50 times more glyphosate is allowed by the EPA on corn grain than in 1996
- Half of the American farmers' fields have weeds that are resistant to glyphosate
- New GMO crops offer dual resistance to glyphosate & 2,4-D → Enlist Duo

*www.newsweek.com/glyphosate-now-most-used-agricultural-chemical-ever-422419

Paper Showing Strong Correlations between Glyphosate Usage and Chronic Disease

Journal of Organic Systems, 9(2), 2014

ORIGINAL PAPER

Genetically engineered crops, glyphosate and the deterioration of health in the United States of America

Nancy L. Swanson¹, Andre Leu^{2*}, Jon Abrahamson³ and Bradley Wallet⁴

¹ *Abacus Enterprises, Lummi Island, WA, USA*

² *International Federation of Organic Agricultural Movements, Bonn, Germany*

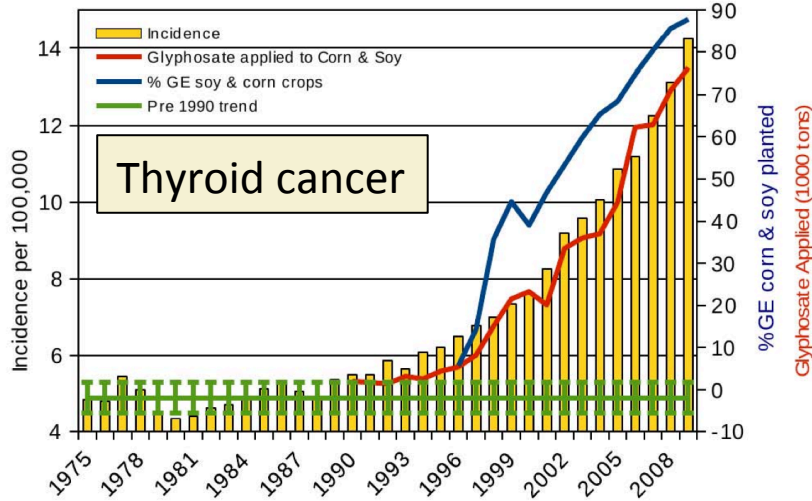
³ *Abacus Enterprises, Lummi Island, WA, USA*

⁴ *Crustal Imaging Facility, Conoco Phillips School of Geology and Geophysics, University of Oklahoma, USA*

* *Corresponding author: andreleu.al@gmail.com*

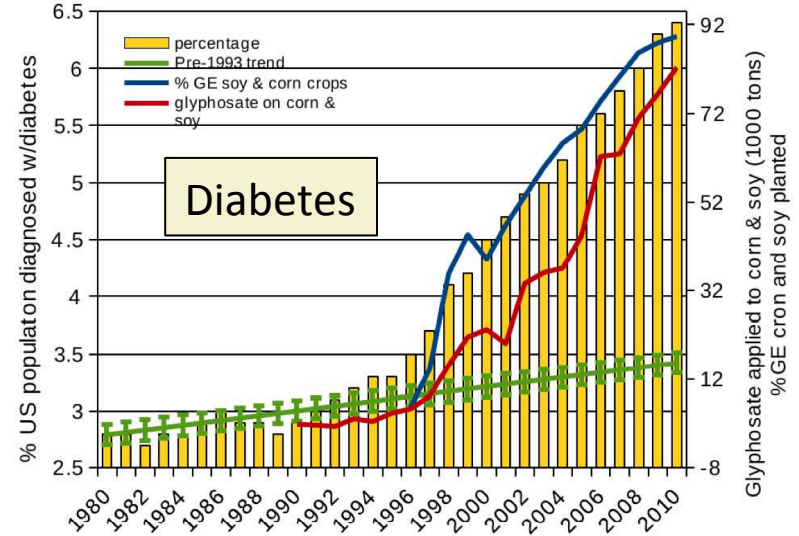
Thyroid Cancer Incidence Rate (age adjusted)

plotted against glyphosate applied to U.S. corn & soy ($R = 0.988$, $p \leq 7.612e-09$)
 along with %GE corn & soy crops $R = 0.9377$, $p \leq 2.152e-05$
 sources: USDA:NASS; SEER



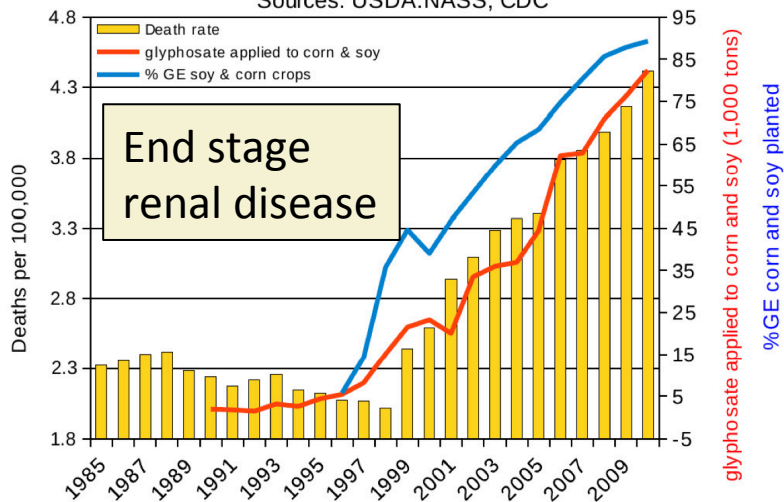
Prevalence of Diabetes in US (age adjusted)

plotted against glyphosate applied to corn & soy ($R = 0.971$, $p \leq 9.24e-09$)
 along with %GE corn & soy grown in US ($R = 0.9826$, $p \leq 5.169e-07$)
 sources: USDA:NASS; CDC



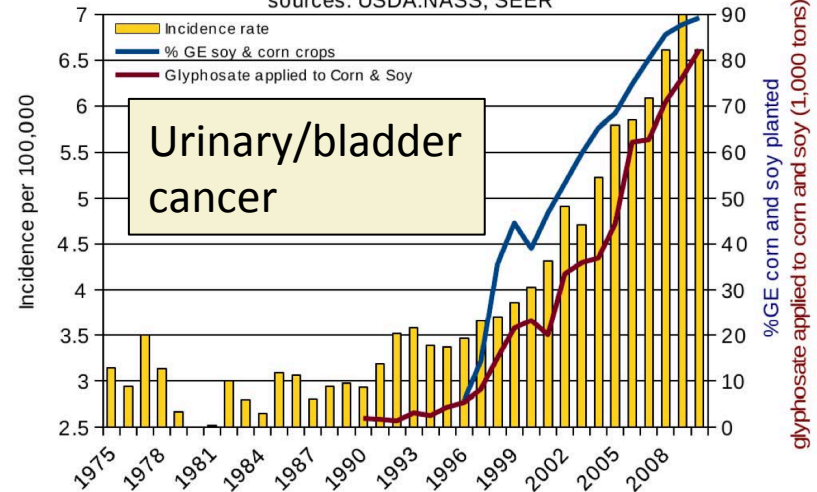
Age Adjusted End Stage Renal Disease Deaths (ICD N18.0 & 585.6)

plotted against %GE corn & soy planted ($R = 0.9578$, $p \leq 4.165e-06$)
 and glyphosate applied to corn & soy ($R = 0.9746$, $p \leq 7.244e-09$)
 Sources: USDA:NASS; CDC



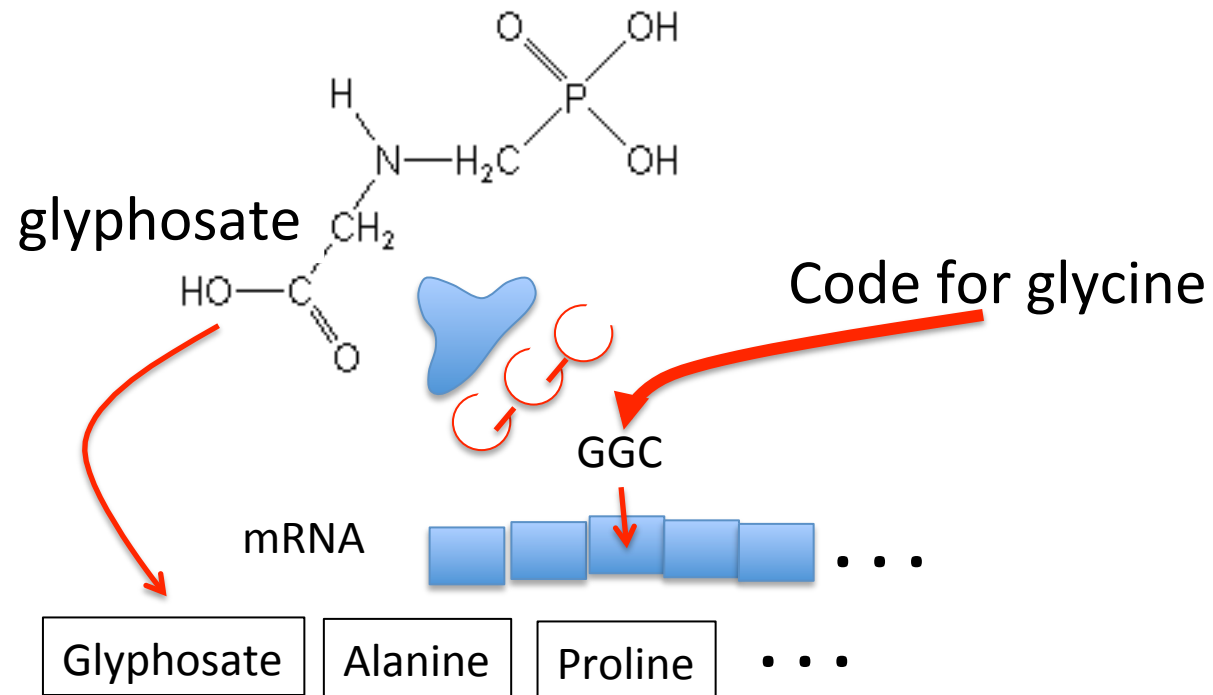
Age Adjusted Urinary/Bladder Cancer Incidence

Plotted against % GE corn and soy ($R = 0.9449$, $p \leq 7.1e-06$)
 and glyphosate applied to corn and soy ($R = 0.981$, $p \leq 4.702e-09$)
 sources: USDA:NASS; SEER



Glyphosate insertion into peptides

What If Glyphosate Could Insert Itself Into Protein Synthesis???



Any proteins with conserved glycine residues are likely to be affected in a major way

Some Predicted Consequences

- Neurological diseases
- Neural tube defects
- Celiac disease
- Impaired collagen → osteoarthritis
- Steatohepatitis (fatty liver disease)
- Obesity and adrenal insufficiency
- Impaired iron homeostasis and kidney failure
- Insulin resistance and diabetes
- Cancer

Circumstantial Evidence from the Rhizosphere*

- Used RNA sequence analysis to quantify changes in microbial protein expression in presence of glyphosate
- Found significant increase in production of enzymes related to protein synthesis and protein breakdown



* MM Newman et al., Science of the Total Environment 553 (2016) 32–41

An Analogy: ALS in Guam

- An epidemic in ALS in Guam was traced to a natural toxin found in cycads
- BMAA is a non-coding amino acid that gets inserted by mistake in place of serine
- Defective versions of a glutamate transporter have been linked to ALS*
- The transporter has an essential serine-rich region in its sequence**

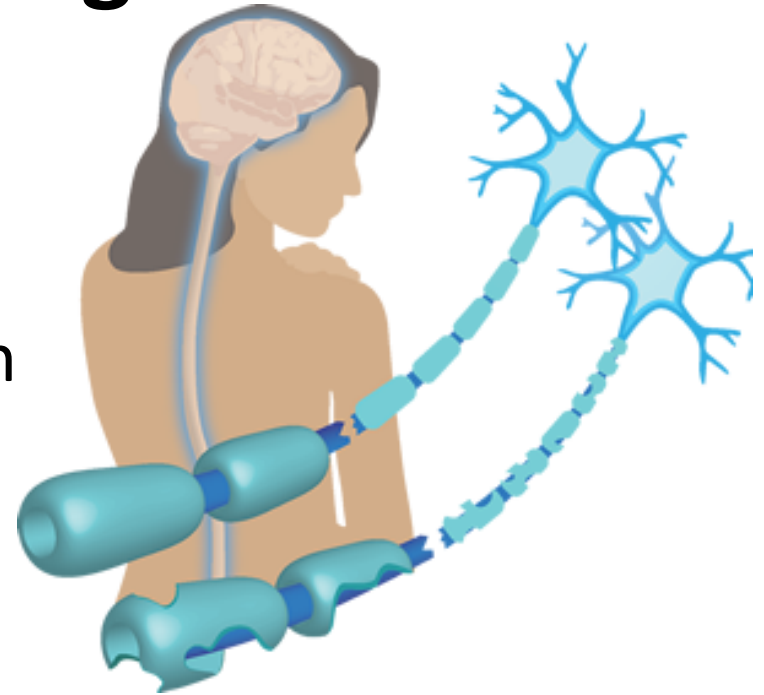


* Antioxidants & Redox Signaling 2009;11: 1587-1602.

** DJ Slotboom et al., PNAS 1999; 96(25): 14282-14287.

Another Analogy: Multiple Sclerosis & Sugar Beets*

- Sugar beets contain an analogue of proline called Aze
- Remarkable correlation between MS frequency and proximity to sugar beet agriculture
- Myelin basic protein contains a cluster of proline residues that are absolutely essential for its proper function



*E. Rubenstein, J Neuropathol Exp Neurol 2008;67(11): 1035-1040.

Vulnerable Proteins: Resulting Pathologies

Conserved Glycines	Disease Profile
Hormone-sensitive Lipase	Obesity
Insulin Receptor	Diabetes
Amyloid Beta Plaque	Alzheimer's Disease
OGG1	DNA Damage → Cancer
Lipocalin	Kidney Failure
ACTH	Adrenal Insufficiency
Cytochrome C Oxidase	Mitochondrial Disease
Alpha Synuclein	Parkinson's Disease
TDP-43	ALS

Neurological Diseases

Glyphosate in Vaccines?

- For MMR, flu vaccine, and rabies vaccine, live virus is grown on gelatin derived from ligaments of cows
 - Cows are fed GMO Roundup-Ready corn and soy feed
- Gelatin contains significant amounts of both glycine and glutamate
 - These two neurotransmitters excite the NMDA receptors in the brain
 - Glyphosate substitution in the protein for glycine is a possibility!
- Glyphosate stimulation of NMDA receptors could cause neuronal burnout

Glyphosate and Glutamate*



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

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

Neurological Diseases and Misfolded Proteins

At least four neurological diseases related to misfolded proteins involve conserved glycine residues:

- Alzheimer's: Amyloid-beta
- Parkinson's Disease: Alpha-synuclein
- ALS: TDP-43
- Madcow/Prion diseases: Prion proteins

Neurological Diseases and Misfolded Proteins

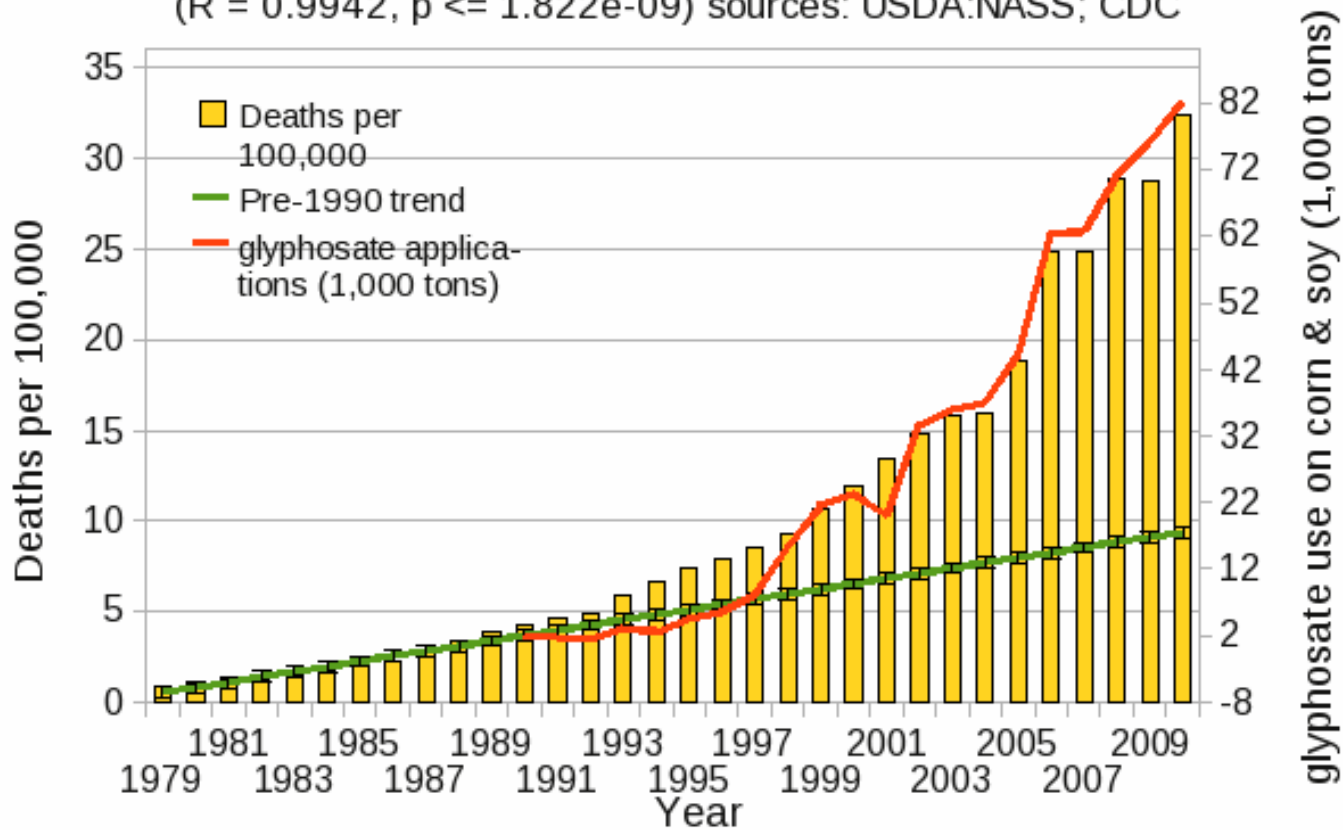
At least four neurological diseases related to misfolded proteins involve conserved glycine

In all cases, the issue is a RARE SOLUBLE peptide rather than the precipitated plaque.

Glyphosate increases the protein's solubility

Deaths from Senile Dementia*

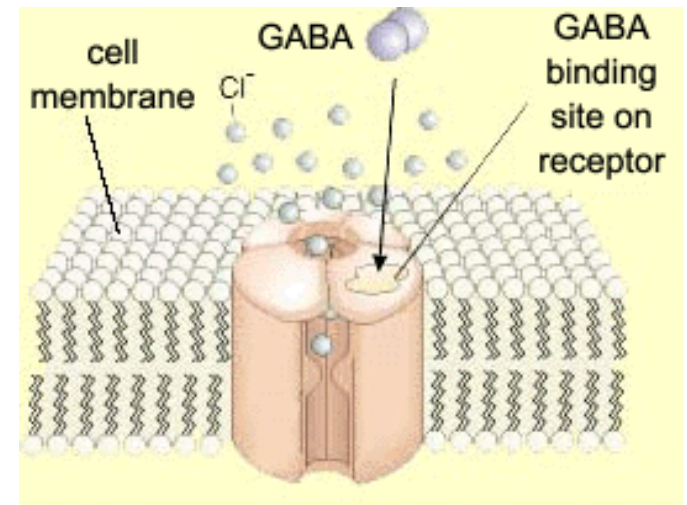
Age Adjusted Deaths from Senile Dementia
(ICD F01, F03 & 290)
plotted against glyphosate applications on corn & soy
($R = 0.9942$, $p \leq 1.822e-09$) sources: USDA:NASS; CDC



*Plot provided by Dr. Nancy Swanson

Impaired GABA Receptor Activity and Autism

- Autism has been linked to a weakened response of the inhibitory GABA receptor to stimuli*
- The GABA receptor has a conserved glycine at the entrance to the first membrane-spanning domain that is essential for its function**



*CD Robertson et al., Current Biology 2016;26: 80-85

**BX Carlson et al., Mol Pharmacol. 2000;57(3):474-84

Neural Tube Defects

Glyphosate and Anencephaly*

- Yakima, Benton and Franklin counties in Washington State have an unusually high number of pregnancies affected by the birth defect, anencephaly
- 75 pesticides were analyzed in studying contamination due to surrounding agriculture
 - 47 (63%) of these were detected
 - Glyphosate was applied in large amounts, but was not studied
- 5% solution of glyphosate was also used heavily around irrigation ditches to control weeds
 - Main herbicide recommended due to its “low toxicity”



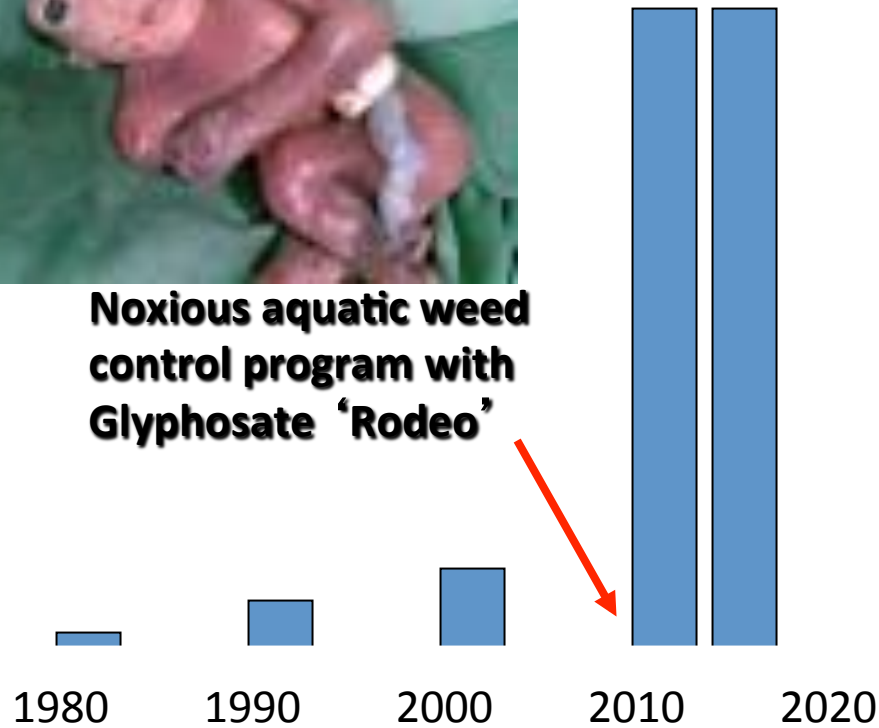
Glyphosate has been linked to anencephaly due to its effect on retinoic acid

*Barbara H. Peterson. Farm Wars, <http://farmwars.info/?p=11137>

“Glyphosate, Brain Damaged Babies, and Yakima Valley - A River Runs Through It”*



Noxious aquatic weed control program with Glyphosate ‘Rodeo’



“Glyphosate, Three Rivers, and Anencephaly”

Yakima Harold Republic

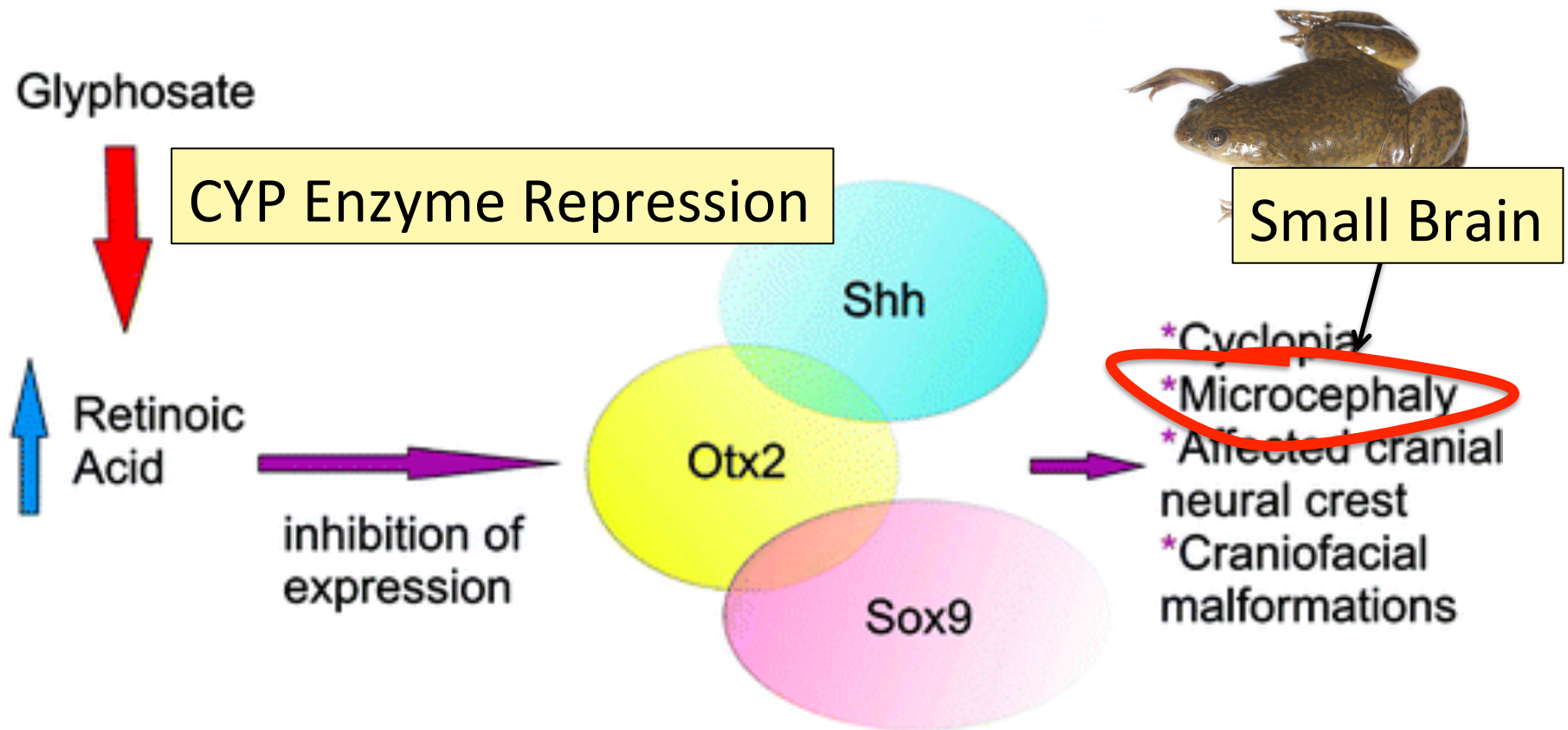
Slide thanks to Prof. Don Huber, with permission

*Farm Wars 3/6/14

How might glyphosate cause anencephaly?

- Neural tube defects linked to folate deficiency
 - Impaired methylation pathway
- Folate production by gut microbes depends on the shikimate pathway (blocked by glyphosate)
 - Gut microbes that synthesize folate are especially sensitive to glyphosate
- Glyphosate interferes with retinoic acid metabolism → toxic accumulation
- Disruption of glycine cleavage system

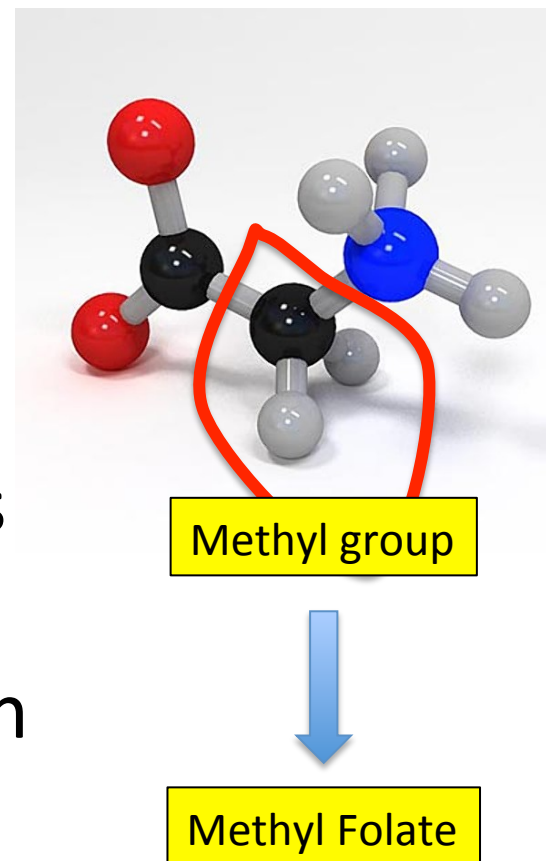
Glyphosate Upregulates Retinoic Acid*



*A. Carrasco, Teratogenesis by glyphosate based herbicides and other pesticides. Relationship with the retinoic acid pathway. In Breckling, B. & Verhoeven, R. (2013) GM-Crop Cultivation – Ecological Effects on a Landscape Scale. Theorie in der Ökologie 17. Frankfurt, Peter Lang.

Glycine, Methyl-folate and One-carbon Metabolism

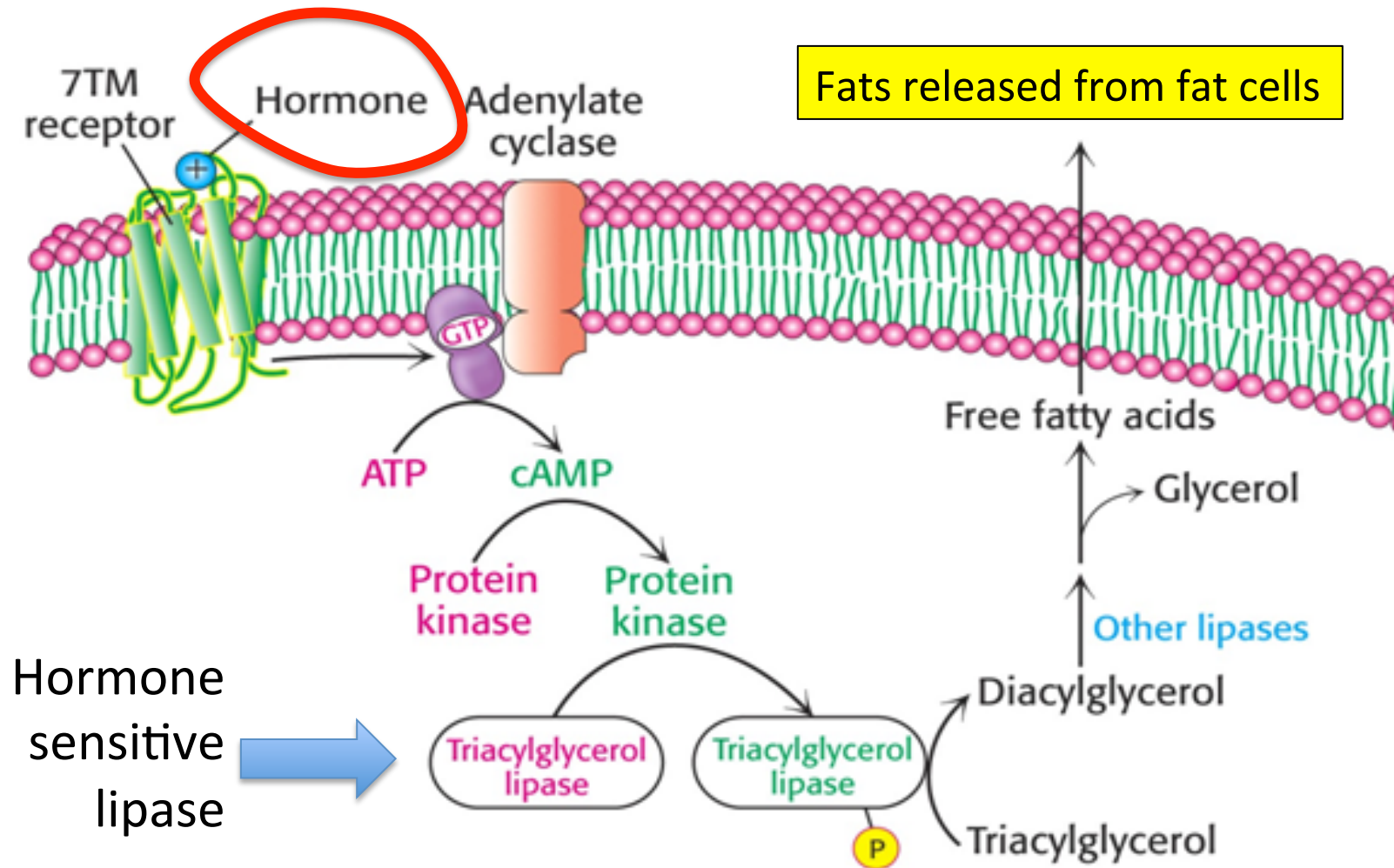
- Glycine is a key source of methyl groups for the one-carbon cycle via the glycine cleavage system
- A glycine-rich region maintains shape and flexibility of glycine decarboxylase, a key enzyme in the glycine cleavage system*



*A Kume et al., JBC 1991; 266(5): 3323-3329.

Diabetes, Obesity and Adrenal Insufficiency

Regulating Fat Release



Impaired Fatty Acid Release from Fat Cells

- Hormone sensitive lipases (aka triacylglycerol lipases)
 - Release fatty acids from fat cells
 - Supply cholesterol to adrenal glands and sex glands for hormone synthesis
 - Respond to glucagon, adrenalin, dopamine, and ACTH
- Depend on multiple conserved glycines*:
 - Contain HGGG motif as “oxyanion hole”
 - Member of the class of “serine proteases” that contain a GX SXG motif essential for enzyme activity

*RC Wilmouth et al. Nat. Struct. Biol 2001;8: 689-694.

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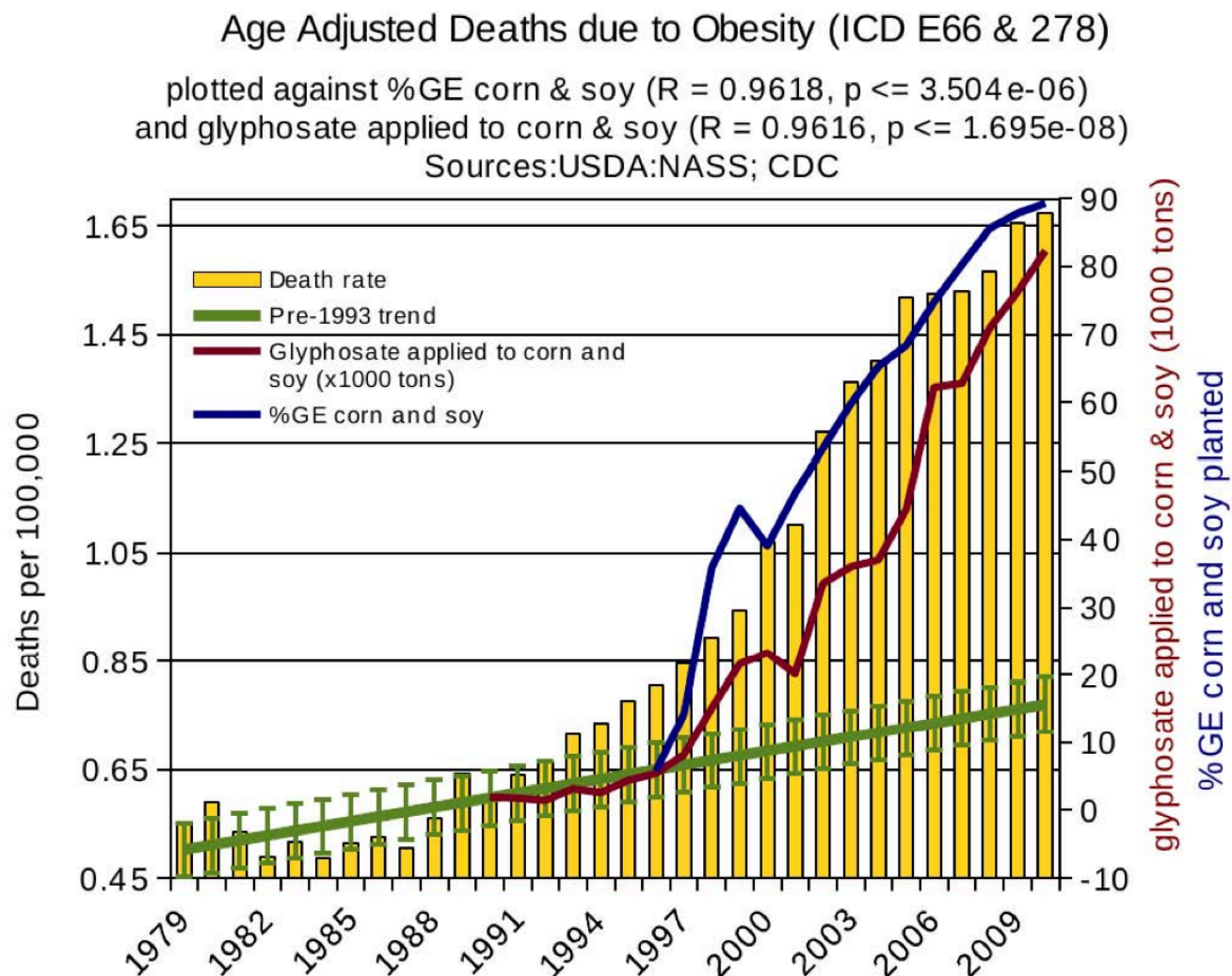
Impaired hormone sensitive lipases have been linked to obesity, atherosclerosis and type II diabetes**

- Contain HGGG motif as “oxyanion hole”
- Member of the class of “serine proteases” that contain a GX SXG motif essential for enzyme activity

**SJ Yeaman, Biochem. J. (2004) 379, 11-22.

*RC Wilmouth et al. Nat. Struct. Biol 2001;8: 689-694.

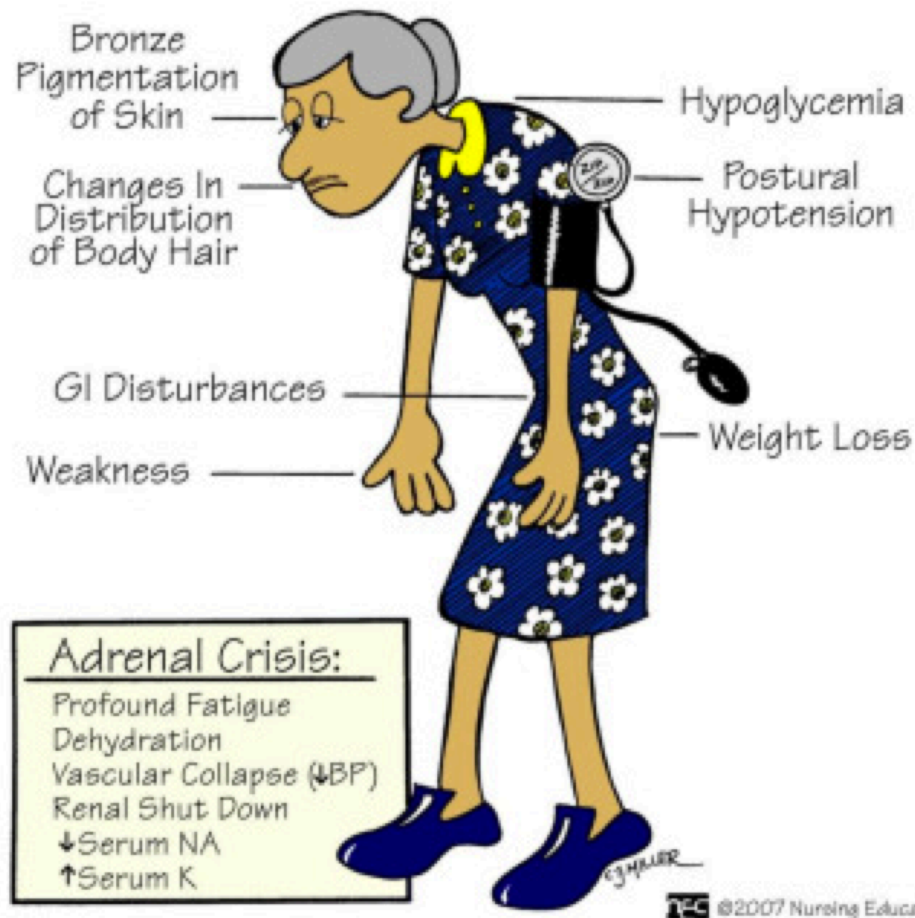
Glyphosate Usage & Death due to Obesity*



*N Swanson et al., *Journal of Organic Systems*, 9(2), 2014

Adrenal Insufficiency

ADDISON'S DISEASE



Roundup has been shown to severely impair adrenal hormone synthesis*

*A Pandey and M Rudraiah, Toxicology Reports 2 (2015) 1075-1085.

Insulin Receptor & Diabetes*,**

- Glucagon release is regulated by insulin receptors (IRs)
 - When IRs are dysfunctional in mice, excess glucose is released from the liver, leading to elevated blood sugar and diabetes
- Eight repeats of a glycine-centered motif determine IR 3-D structure
- ATP-binding site contains a GXGXXG motif***

*PE Cryer, Endocrinology 2012;153(3):1039-1048.

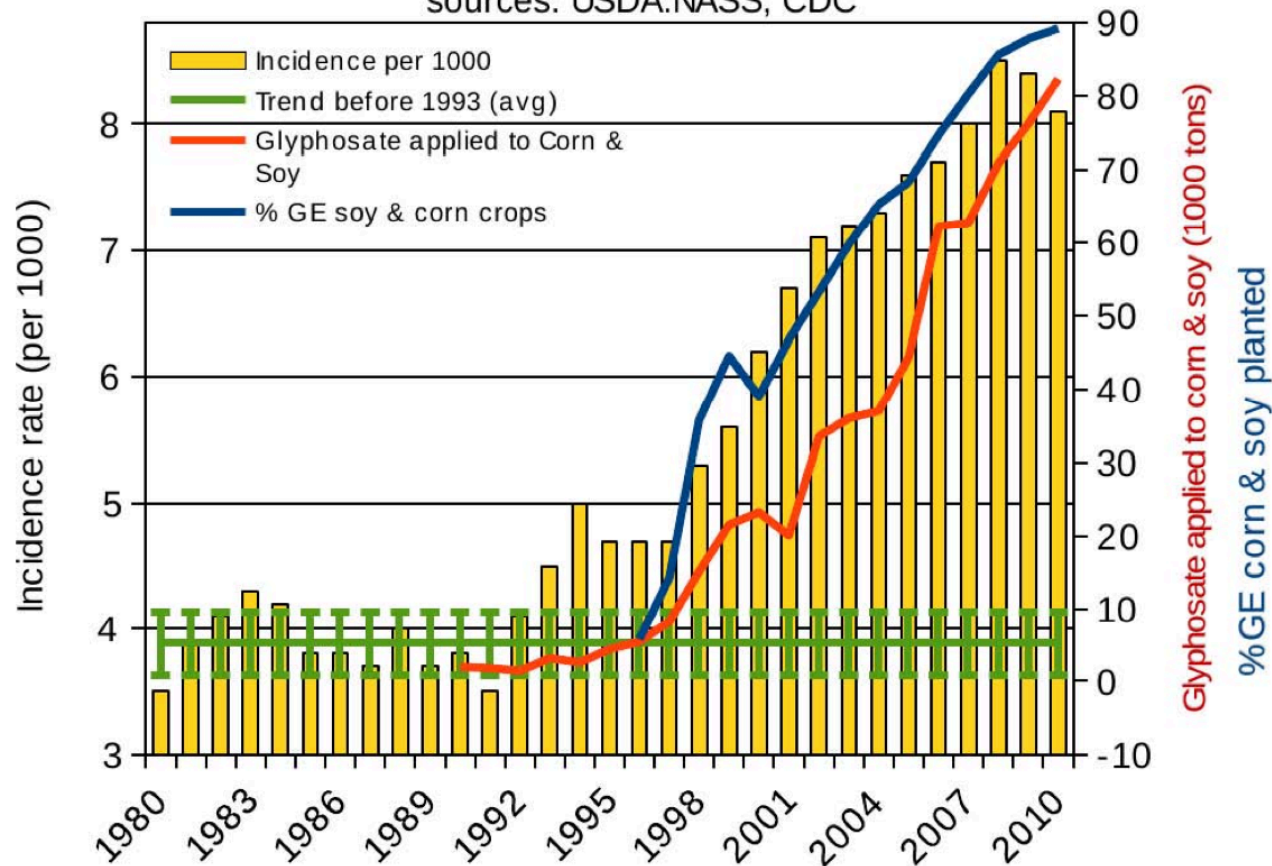
**D Kawamori et al., Cell Metab 2009;9:350-361.

***DR Knighton et al., Proc Natl Acad Sci U S A. 1993;90(11):5001-5

Diabetes and Glyphosate*

Annual Incidence of Diabetes (age adjusted)

plotted against %GE corn & soy crops planted ($R = 0.9547$, $p \leq 1.978e-06$)
along with glyphosate applied to corn & soy in US ($R = 0.935$, $p \leq 8.303e-08$)
sources: USDA:NASS; CDC



*Figure 14, Swanson et al. Journal of Organic Systems 2014; 9(2):6-37.

Celiac Disease and Prolyl Aminopeptidase

- Gluten intolerance and Celiac disease result from inability to break down gluten, which is enriched in proline*
- Prolyl aminopeptidase, the enzyme that breaks down proline-containing peptides, depends on manganese as a catalyst
- Prolyl aminopeptidase also contains a highly conserved GxSxGG motif plus two other regions with conserved glycines**
- Malabsorption due to celiac disease can lead to nutritional deficiencies and symptoms of autism***

*G. Janssen et al., PLoS One 2015; 10(6): e0128065

**F Morel et al., Biochimica et Biophysica Acta 1999;1429: 501-505

***SJ Genuis and TP Bouchard, J Child Neurol. 2010;25(1):114-9

Impaired Blood Flow

Endothelial Nitric Oxide Synthase (eNOS)

- eNOS produces nitric oxide which relaxes blood vessels and promotes blood flow
- We hypothesize that eNOS produces sulfate when it is membrane-bound as a dimer, with sunlight as a catalyst*
- eNOS depends on conserved glycines both for dimer formation and for binding to the membrane
- Replacement of the glycines with larger molecules disrupts both dimer formation and membrane attachment: impairing eNOS function
 - This explains the “pathology” of superoxide release

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

Endothelial Nitric Oxide Synthase (eNOS)

- eNOS produces nitric oxide which relaxes blood vessels and promotes blood flow

Impaired eNOS function leads to oxidative damage in the artery wall, as well as deficient supply of both nitric oxide and sulfate to the vasculature

disrupts both dimer formation and membrane attachment: impairing eNOS function

– This explains the “pathology” of superoxide release

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

Kidney Disease

Bacterial Siderophores & Kidney Disease

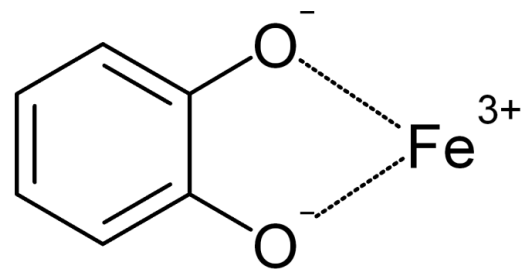
- Alarming incidence of kidney failure among agricultural workers in sugar cane fields
 - Characterized by proximal tubular necrosis
 - Sugar cane sprayed with glyphosate preharvest
- Defective iron uptake from bacterial siderophores in the proximal renal tubule can cause simultaneous iron deficiency and iron toxicity*

*K Mori et al. The Journal of Clinical Investigation 2005;115(3):610-621.

How Proximal Tubule Gets Iron*

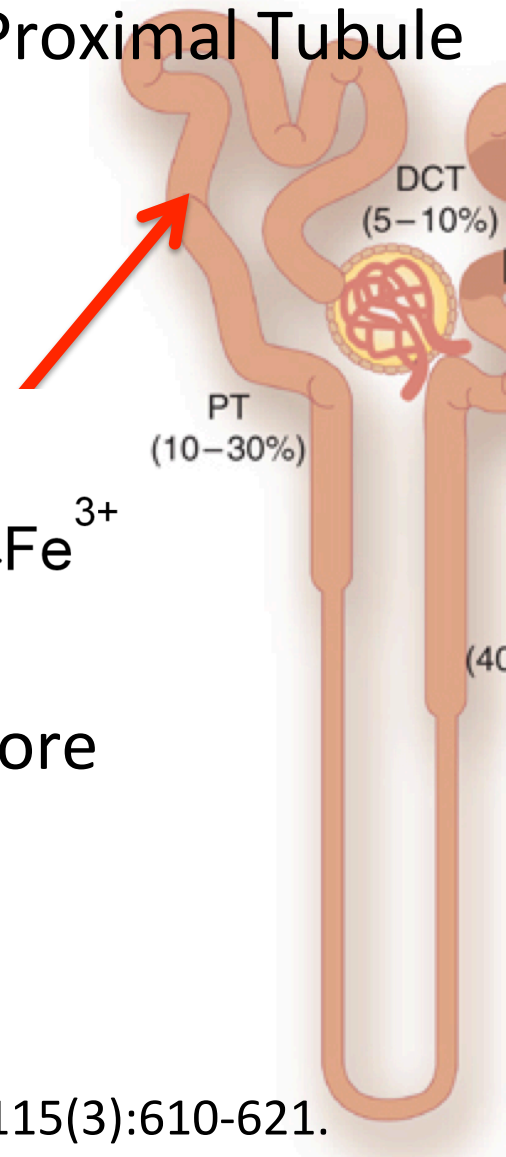
- Protein that synthesizes siderophore in bacillus depends on two conserved glycines
- Protein that uptakes siderophore in renal tubule contain a conserved GXW motif

Bacillus



siderophore

Proximal Tubule



*K Mori et al. The Journal of Clinical Investigation 2005;115(3):610-621.

From Samsel and Seneff: Glyphosate IV*

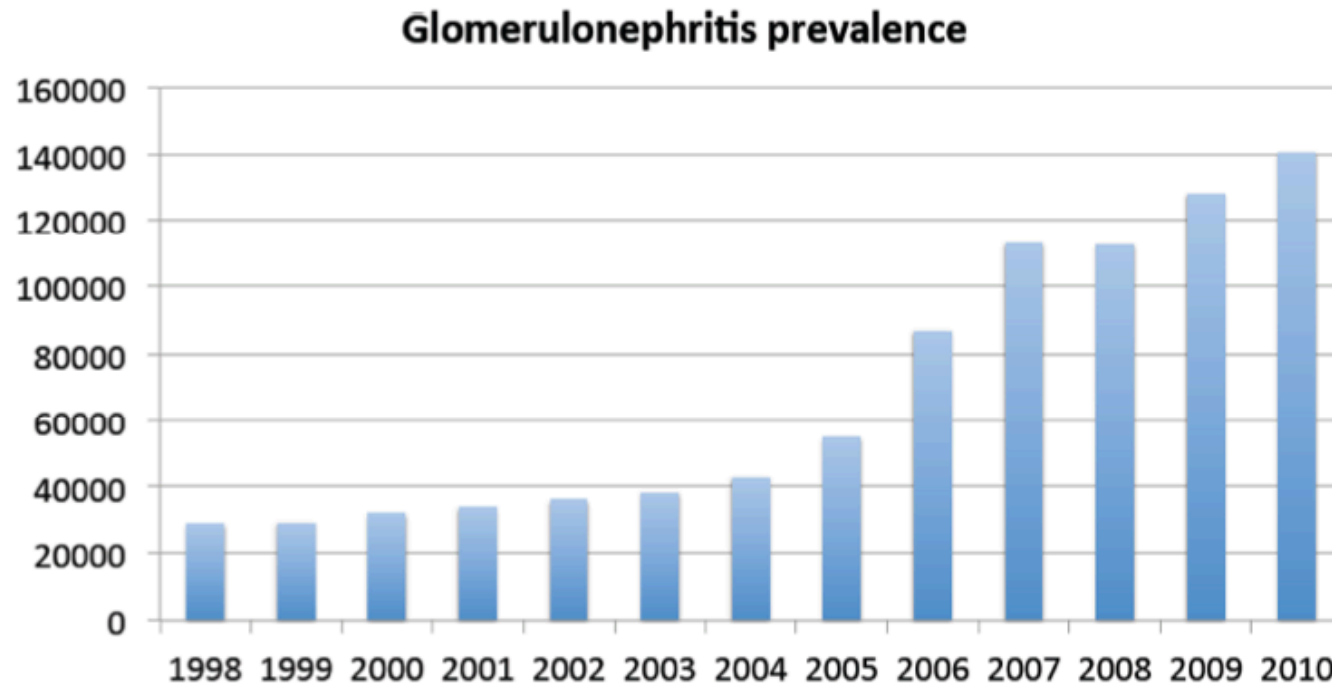


Figure 2. Incidence of nephritis and kidney failure reports in the US CDC's hospital discharge data from 1998 to 2010 normalized to counts per million population each year. This includes all reports of ICD-9 codes from 580 to 589.

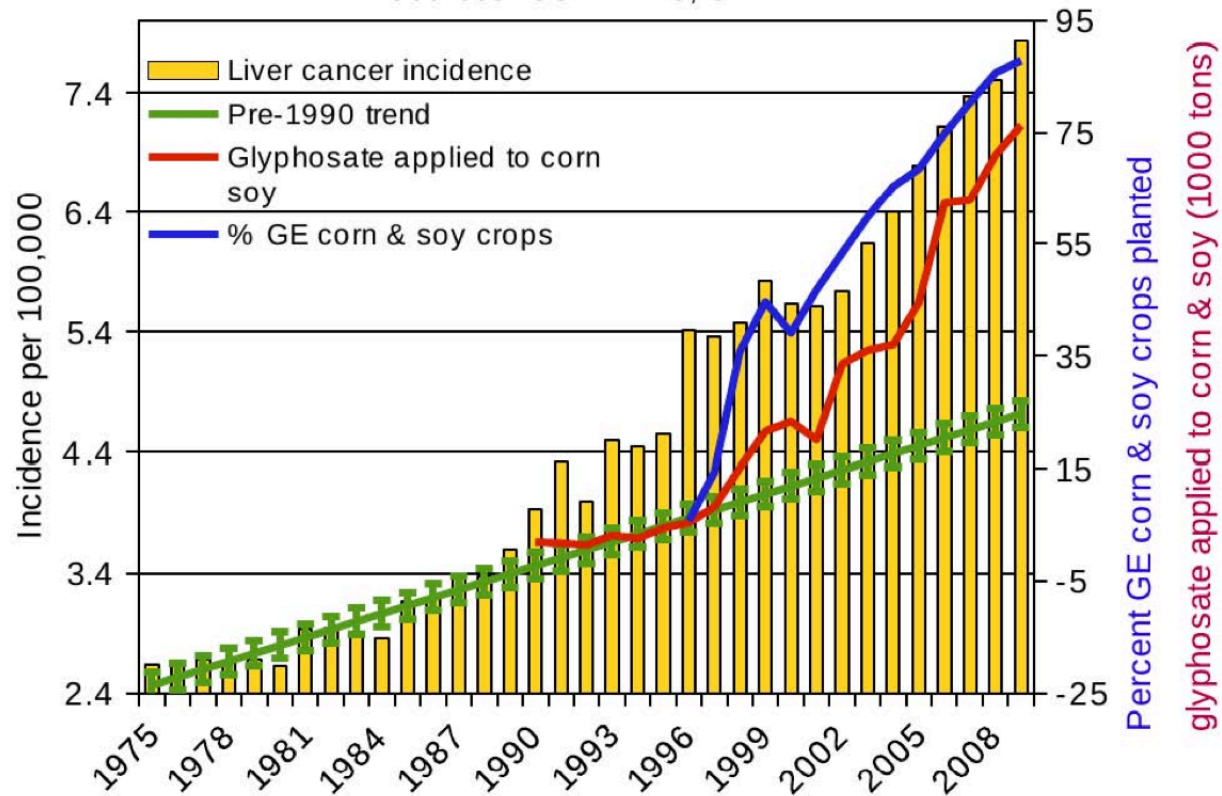
*A Samsel and S Seneff, *Journal of Biological Physics and Chemistry* **15** (2015) 121–159

Liver Disease

Liver Cancer & Glyphosate*

Liver and Intrahepatic Bile Duct Cancer Incidence (age adjusted)

plotted against glyphosate applied to corn & soy ($R = 0.9596$, $p \leq 4.624e-08$)
along with %GE corn & soy planted in U.S. ($R = 0.9107$, $p \leq 5.402e-05$)
sources: USDA:NAS; SEER



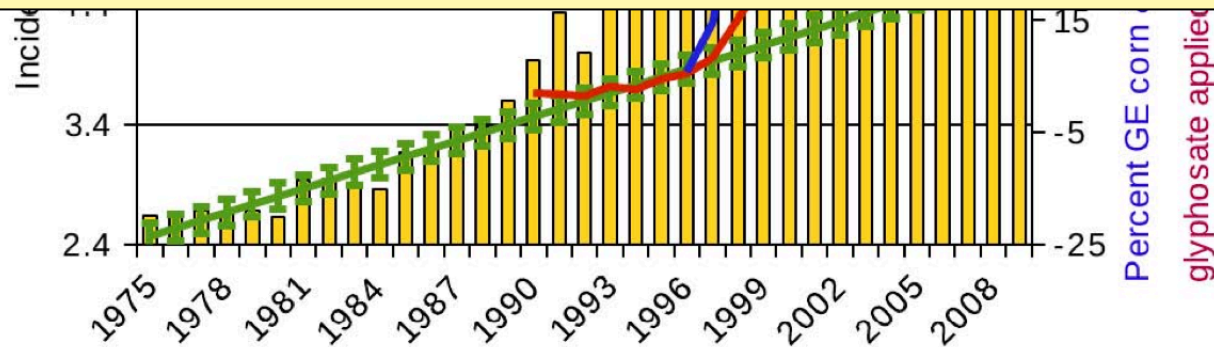
*N Swanson et al., *Journal of Organic Systems*, 9(2), 2014

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Fatty liver disease is a strong risk factor
for liver cancer

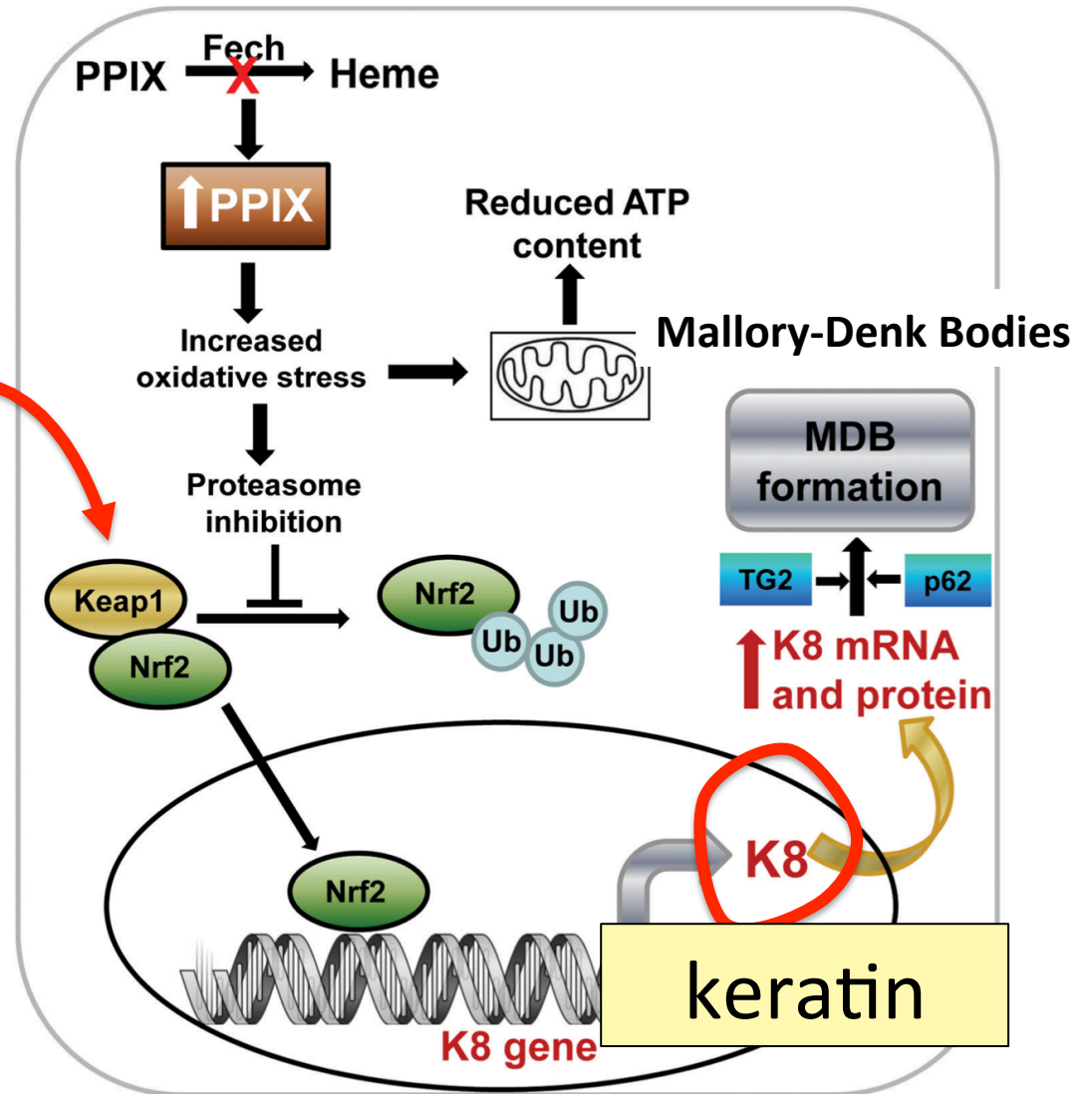


*N Swanson et al., *Journal of Organic Systems*, 9(2), 2014

Steatohepatitis (Fatty Liver Disease)*

Mallory-Denk bodies (MDBs) are liver cell inclusions associated with steatohepatitis (fatty liver disease)

Keap1 has a conserved *double glycine repeat* that anchors it to the cytoskeleton



*A Singla et al., Hepatology 2012 July ; 56(1): 322–331.

Hyperkeratosis

Beak Deformities in Chickadees*

- Beak deformities involving excess *keratin* synthesis have been appearing among chickadees and other birds in the Great Lakes region, in central Alaska and in areas exposed to California agricultural run-off
- No link could be found with investigated toxic chemicals and metals
- Glyphosate was not investigated



*CM Handel and C van Hemert, Environ Toxicol Chem 34, 2015; 314-327.

Beak Deformities in Chickadees*

Chickadees frequent bird feeders to consume sunflower seeds sprayed with glyphosate just before harvest have been appearing

among chickadees and

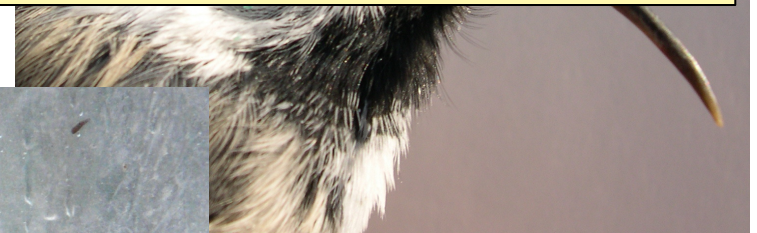
other birds

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*CM Handel and C van Hemert, Environ Toxicol Chem 34, 2015; 314-327.

How to Safeguard Yourself and Your Family

Extracts from Common Plants Can Treat Glyphosate Poisoning*

- Roundup is toxic to hepatic and embryonic cells at doses far below those used in agriculture and at residue levels present in some GM food.
- Extracts from common plants such as dandelions, barberry, and burdock can protect from damage, especially if administered prior to exposure.



*C Gasnier et al. Journal of Occupational Medicine and Toxicology 2011, 6:3

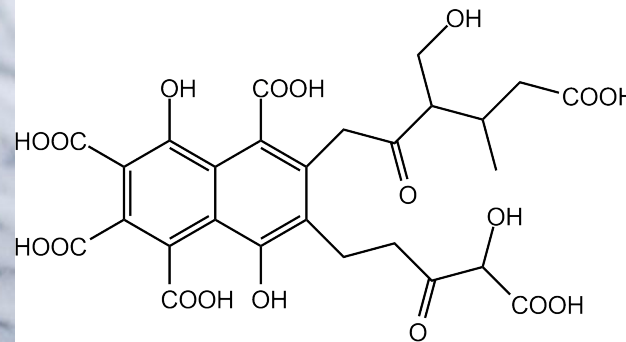
Treating Glyphosate Poisoning in Animals (e.g., cows) *



Activated charcoal, bentonite clay, humic and fulvic acids, and sauerkraut juice have been shown to be effective in reducing urinary levels of glyphosate and improving animal health



Bentonite Clay



Fulvic Acid



Activated Charcoal

*H Gerlach et al., J Environ Anal Toxicol 2014, 5:2

Some Important Nutrients

- Curcumin
- Garlic
- Vitamin C
- Probiotics
- Methyl tetrahydrofolate
- Cobalamin
- Glutathione
- Taurine
- Epsom salt baths

Get Grounded

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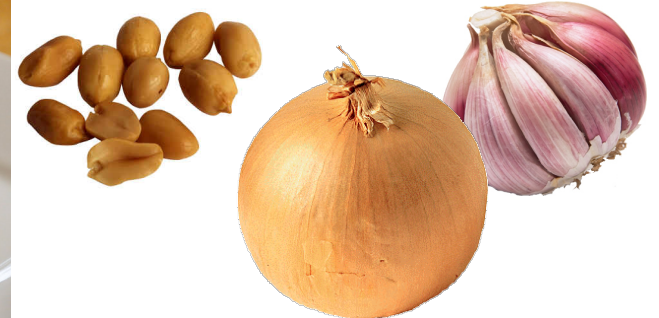
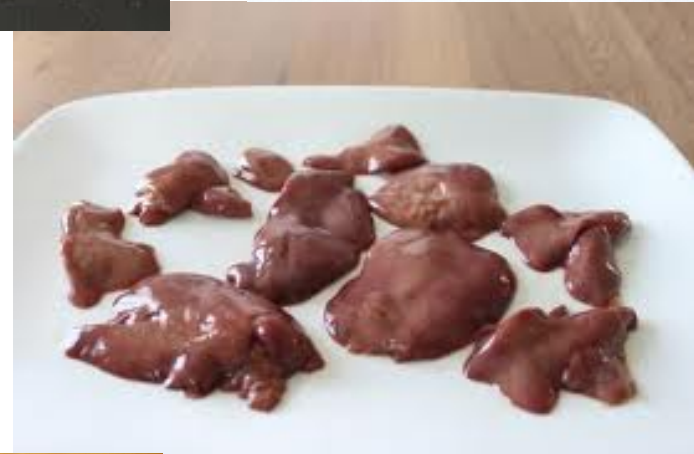
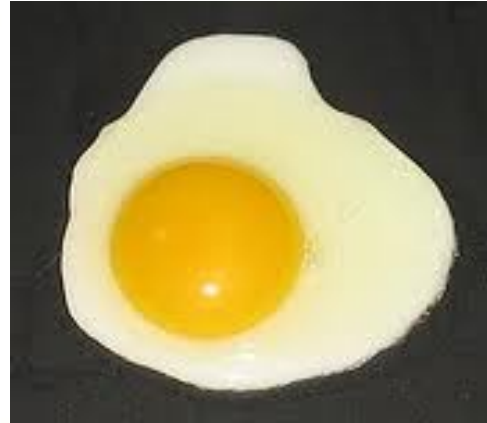
Go Organic!



Eat Foods Containing Manganese



Eat Foods Containing Sulfur



Summary

- Glyphosate contamination in our food supply is a serious threat to health
 - Toxic mechanisms include mineral chelation, disruption of CYP enzymes, and disruption of gut microbes
 - I believe glyphosate is the most important factor in the autism epidemic
- Glyphosate may erroneously replace glycine during protein synthesis
 - Huge consequences to multiple diseases whose incidence is going up in step with glyphosate usage on core crops: diabetes, obesity, Alzheimer's and other neurological diseases, liver and kidney disease, vascular diseases, Celiac disease, etc.
- Eating an organic diet rich in sulfur and manganese and probiotics can help protect from glyphosate poisoning