

"A truth's initial commotion is directly proportional to how deeply the lie was believed... When a wellpackaged web of lies has been sold gradually to the masses over generations, the truth will seem utterly preposterous and its speaker, a raving lunatic."

- Dresden James

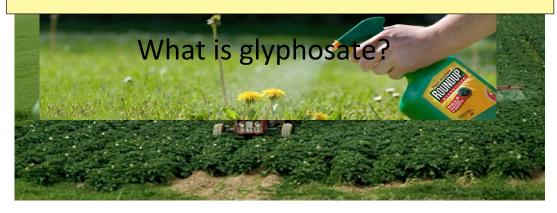
Outline: Part I

- Introduction
- Glyphosate Displacing Glycine in Protein Synthesis
- Dysfunctional PEP Carboxykinase: Multiple Consequences
- The California Lawsuits: Glyphosate and non-Hodgkin's Lymphoma

Introduction

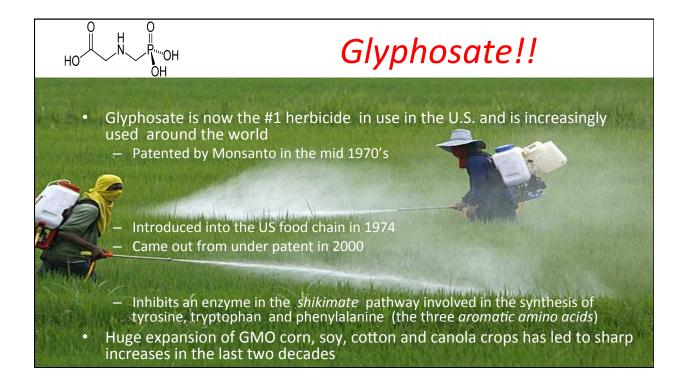
Roundup and GMO Crops

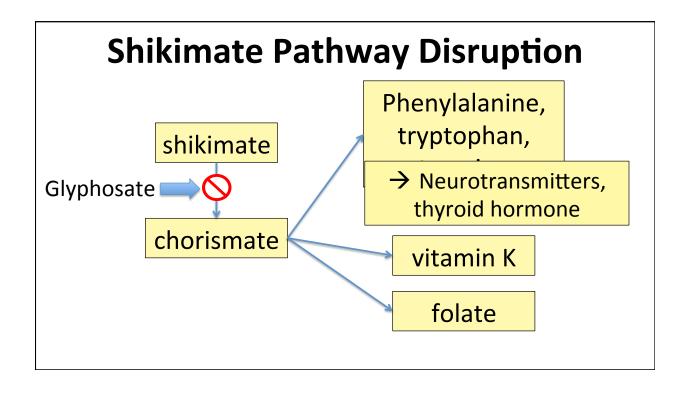
GMO Roundup-Ready corn, soy, canola, sugar beets cotton, tobacco and alfalfa

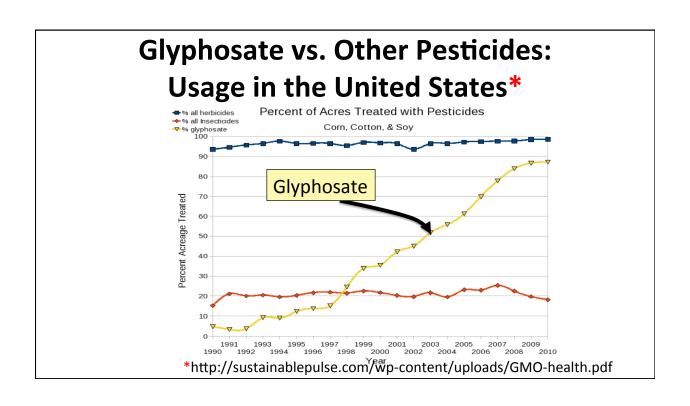


Roundup as a Desiccant/Ripener just before Harvest

Wheat, Oats, Barley, Rye,
Sugar cane, Beans, Lentils,
Peas, Flax, Sunflowers,
Pulses, Chick Peas



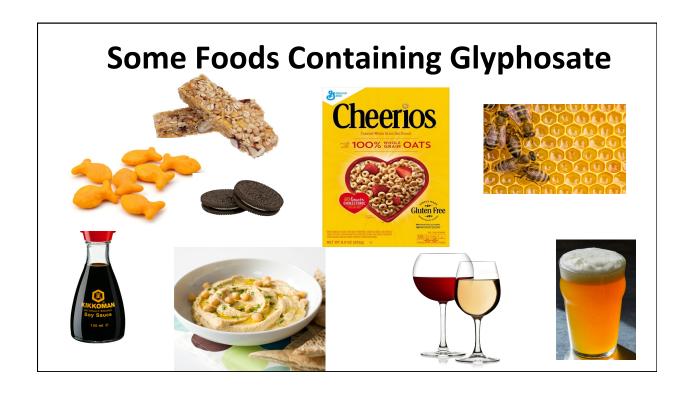


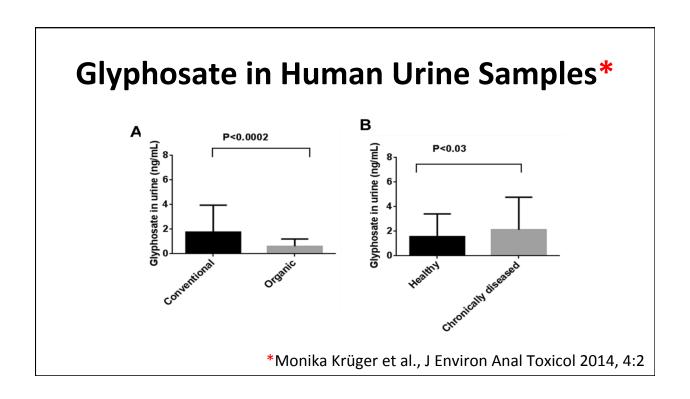


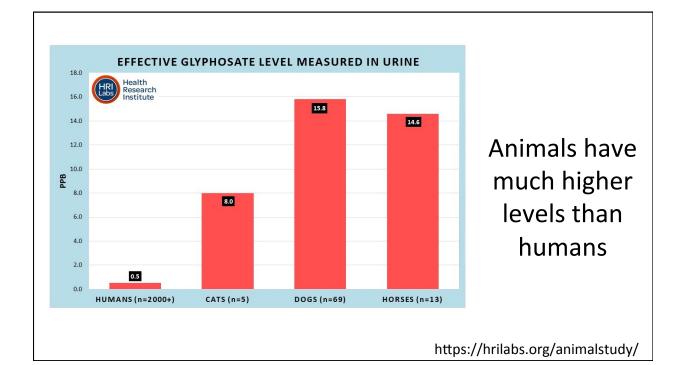
Environmental Working Group Results*



*www.ewg.org/childrenshealth/glyphosateincereal/







Paper Showing Strong Correlations between Glyphosate Usage and Chronic Disease

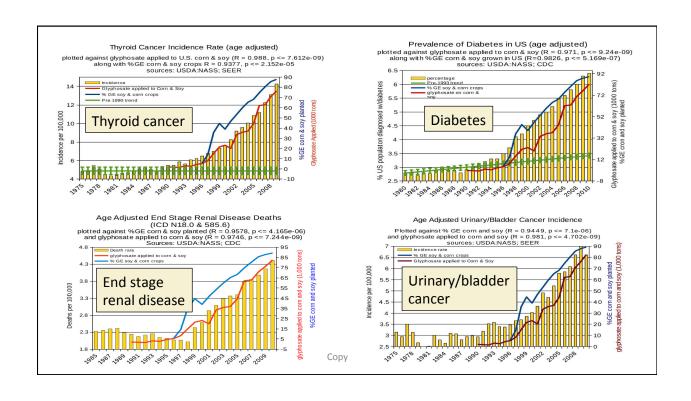
Journal of Organic Systems, 9(2), 2014

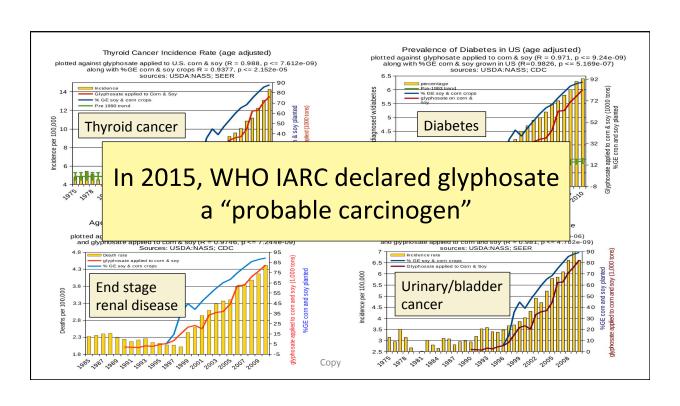
ORIGINAL PAPER

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

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- ² International Federation of Organic Agricultural Movements, Bonn, Germany
- ³ Abacus Enterprises, Lummi Island, WA, USA
- Crustal Imaging Facility, Conoco Phillips School of Geology and Geophysics, University of Oklahoma, USA
- * Corresponding author: andreleu.al@gmail.com

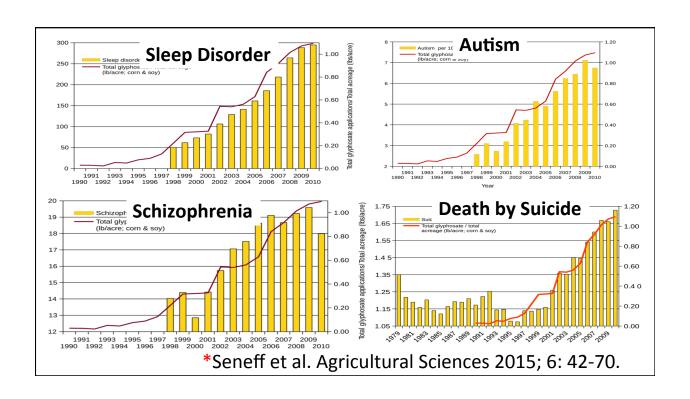




Quote from the Conclusion*

"Although correlation does not necessarily mean causation, when correlation coefficients of over 0.95 (with *p*-value significance levels less than 0.00001) are calculated for a list of diseases that can be directly linked to glyphosate, via its known biological effects, it would be imprudent not to consider causation as a plausible explanation."

*NL Swanson et al. Journal of Organic Systems 9(2), 2014, p. 32,



List Compiled by Prof. Don Huber

Diseases Increasing in Incidence (Epidemic) (after Fox, 2012; Antoniou et al., 2012; Samsel & Seneff, 2013; Swanson, 2013) Allergies, Asthma Diabetes Alzheimer *s Difficale diarrhea Arthritis Gluten intolerance Atopic dermatis Indigestion Autism Infertility Autoimmune diseases Inflammatory bowel diseas Bipolar, Attn deficit (ADHD) Irritable bowel disease Birth defects Leaky gut syndrome Bloat (fatal) Liver abnormalities Bowel disease Miscarriage Cancer (some) Morgellan 's (NEW) Celiac disease Multiple sclerosis Chronic fatigue syndrome Obesity Pancreas ahnormalities 200*Barkinson* (s07 2009 2011 Sudden Infant Death Syndrome

Decreasing IQ scores after 1975*

"scores increased by almost
3 percentage points each decade
for those born between 1962 and
1975 -- but then saw a steady



decline among those born after 1975."

"What specific environmental factors cause changes in intelligence remains relatively unexplored."

*Rory Smith, CNN.

https://www.cnn.com/2018/06/13/health/falling-iq-scores-study-intl/index.html

Decreasing IQ scores after 1975*

"scores increased by almost 3 percentage points each decade

for th 1975

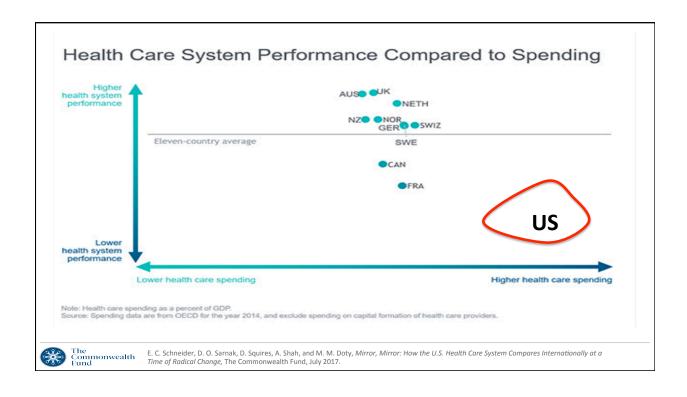
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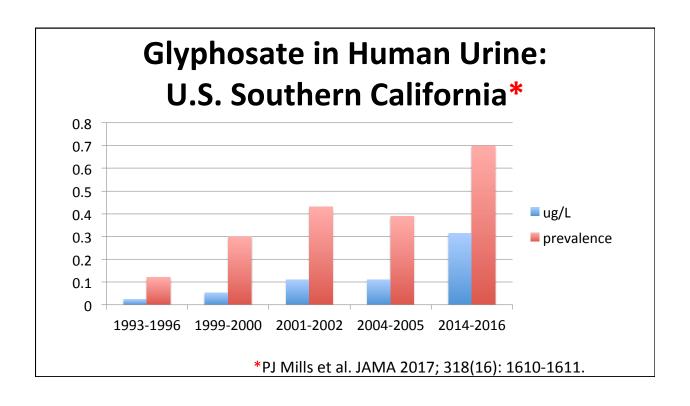
Glyphosate was introduced on the market in 1975

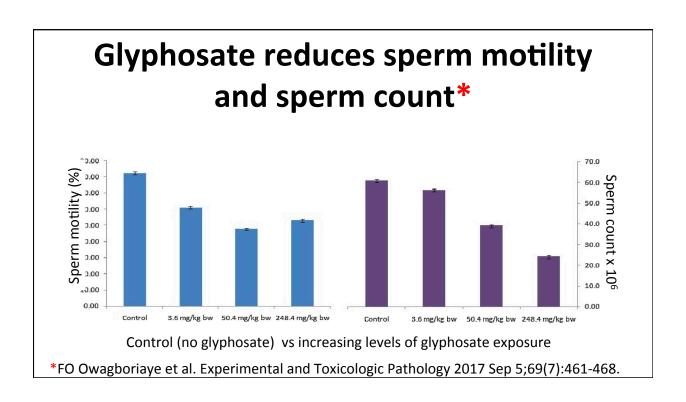
"What specific environmental factors cause changes in intelligence remains relatively unexplored."

*Rory Smith, CNN.

https://www.cnn.com/2018/06/13/health/falling-iq-scores-study-intl/index.html







Glyphosate Damages Second Generation*

- Pregnant rats exposed to glyphosate starting at day 9 of gestation
- Two exposure levels (low, high), both levels considered to be safe according to regulators
- Neither the rats nor their offspring showed any obvious effects
- The second generation offspring from both exposed groups showed delayed growth, lower fetal weight and length and a higher incidence of abnormally small fetusus
- Most surprising: there were three cases (each from a different mother) among the second generation offspring with major fetal abnormalities (conjoined fetuses and abnormal limb development)

*MM Milesi et al. Archives of Toxicology June 9, 2018 [Epub ahead of print]

America's Children are in Trouble!

- It is now "normal" for a kindergarten child to have 12 colds every year and for a baby to have nine
- Fourfold increase in childhood obesity
- Double the asthma rate since the 1980's
- "Chronic illnesses" rose from 1.8% in 1960 to 7% in 2004
 - Today, 43% of US children are chronically ill
- 1 in 6 children in the USA has a neurodevelopmental disability
 - 1 in 38 boys are autistic
- US has the worst neonatal death rate of all industrialized countries
- Today's children in the US will have a shortened life span compared to their parents

Source: http://www.vaccineviolence.com/

What's Making Our Children SICK?

How Industrial Food Is Causing an Epidemic of Chronic Illness, and What Parents (and Doctors) Can Do About It

EXPLORING THE LINKS BETWEEN

GM FOODS, GLYPHOSATE, AND GUT HEALTH

Michelle Perro, MD and Vincanne Adams, PhD

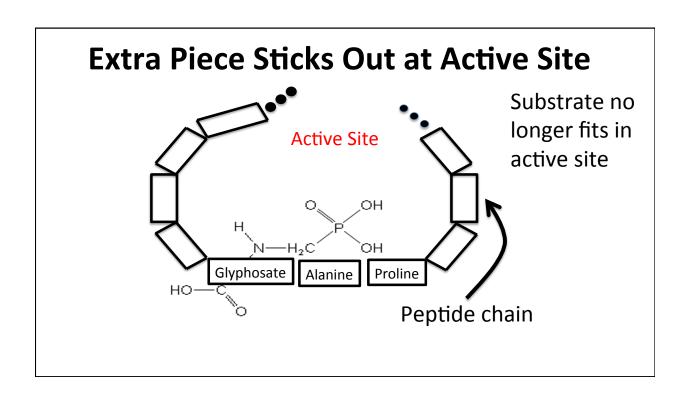


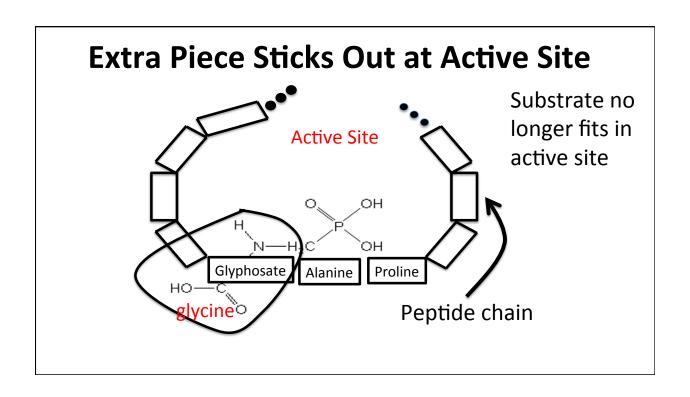
Genetically Modified Children

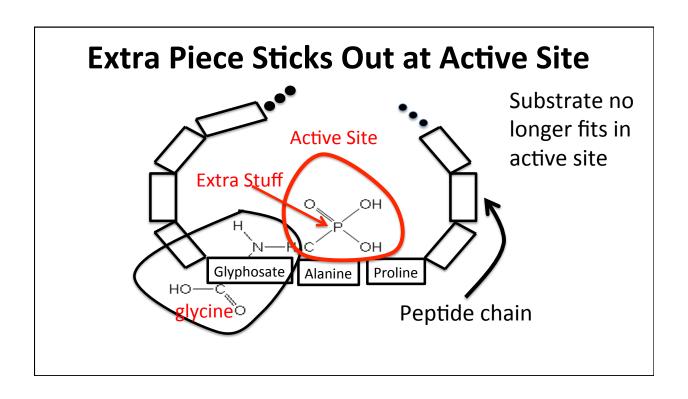


Glyphosate Displacing Glycine in Protein Synthesis

What if Glyphosate could Insert itself into Proteins during Synthesis??? glyphosate Glyphosate Alanine Proline -- Any proteins with conserved glycine residues are likely to be affected in a major way







Extra Piece Sticks Out at Active Site

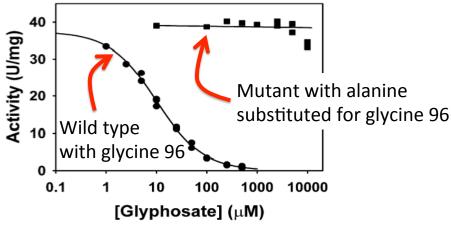
Substrate no This explains how glyphosate disrupts EPSPS in the shikimate pathway: Multiple bacteria have developed resistance by replacing active site glycine with alanine and this is the basis for GMO Roundup Ready crops*

*T Funke et al., Molecular basis for the herbicide resistance of Roundup Ready crops. PNAS 2006:103(35):13010-13015.

fits in

site





*Figure 3, S Eschenburg et al. Planta 2002;216:129-135.

DowDupont Experiments on Maize*

- Designer gene introduced into maize using CRISPR technology
- Tweaked native EPSP synthase to produce glyphosateresistant version
- First step: mutate glycine to alanine at residue 101 (GNAG → GNAA)
 - Completely erases any glyphosate sensitivity
 - [corresponds to 96 in E coli]
- Modify additional nearby residues to increase space for EPSP substrate

*Y Dong et al. J Biol Chem 2019; 294(2): 716-725.

Monsanto Study (1989)*

- Study exposed bluegill sunfish to carbon-14 radiolabelled glyphosate
- Measured radiolabel in tissues greatly exceeded measured glyphosate levels
- Proteolysis recovered more glyphosate
 - -20% yield \rightarrow 70% yield

*WP Ridley and KA Chott. Monsanto unpublished study. August, 1989.

Monsanto Study (1989)*

- Stud
- Measeexce
- Prote- 20

"Proteinase K hydrolyses proteins to amino acids and small oligopeptides, suggesting that a significant portion of the 14C activity residing in the bluegill sunfish tissue was tightly associated with *or incorporated into* protein."

*WP Ridley and KA Chott. Monsanto unpublished study. August, 1989.

Some Predicted Consequences*

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

*A. Samsel and S. Seneff. Journal of Biological Physics and Chemistry 2016;16:9-46.

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: MS & 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 concentration of proline residues that are absolutely essential for its proper function

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

I want to teach you how to fish!



How to Fish

Myosin alignments

- L. Find a glycine residue in an important protein class that is highly conserved across multiple species
- 2. Find papers describing the functional role of that glycine in the protein
- 3. Find an example of a genetic mutation mapping that glycine to something else and identify the resulting disease profile
- 4. Ideally: find papers that describe dysfunction of that protein linked to glyphosate exposure or a symptom profile of glyphosate exposure that could be explained by that protein's dysfunction

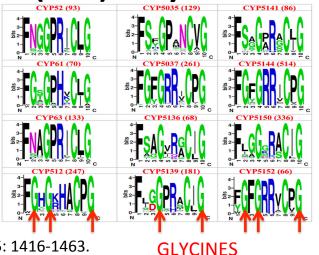
Vulnerable Proteins: Resulting Pathologies

Conserved Glycines	Disease Profile	
Hormone-sensitive Lipase	Obesity	
Insulin Receptor	Diabetes	
Amyloid Beta Plaque	Alzheimer's Disease	
GABA Receptor	Autism	
Lipocalin	Kidney Failure	
ACTH	Adrenal Insufficiency	
Cytochrome C Oxidase	Mitochondrial Disease	
Alpha Synuclein	Parkinson's Disease	
Myosin	Chronic Fatigue Syndrome	

^{*}A Samsel and S Seneff, Journal of Biological Physics and Chemistry 2016;16:9-46.

Glyphosate Disrupts Cytochrome P450 (CYP) Enzymes*

- Glyphosate severely suppresses CYP enzymes in rat liver
- CYP enzymes have a unique FGXGXRXCXG motif with two and often three critical glycine residues**



*A Samsel and S Seneff. Entropy 2013; 15: 1416-1463.

**K Syed and SS Mashele. PLOS ONE 2014; 9(4): | e95616.

Glyphosate Disrupts Cytochrome P450 (CYP) Enzymes* Glyphosate severely CYP enzymes are needed to produce bile acids for digesting fats, to activate vitamin D and to detoxify many environmental toxicants Unique PGAGARACAG motif with two and often three critical glycine residues** *A Samsel and S Seneff. Entropy 2013; 15: 1416-1463. *K Syed and SS Mashele. PLOS ONE 2014; 9(4): e95616.

Dysfunctional PEP Carboxykinase: Multiple Consequences

Overview of PEP Carboxykinase (PEPCK)

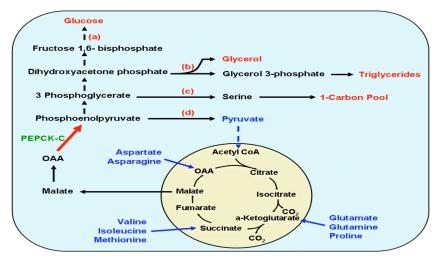
- PEPCK is a crucial enzyme in gluconeogenesis
 - It is a major regulatory enzyme in metabolism
- Defective PEPCK is linked to many diseases and conditions
 - Fatty liver disease
 - Neonatal hypoglycemia
 - Type 1 diabetes
 - Sudden Infant Death Syndrome
 - Fungus overgrowth
 - High oxalate and kidney stones

Basic Chemistry

PEPCK Oxalacetate + GTP ←----⇒ PEP + GDP + CO₂

- PEPCK is a cataplerotic enzyme and a feeder reaction for downstream metabolic processes
 - Cataplerosis: the removal of intermediate metabolites in the citric acid cycle, to prevent their accumulation in the mitochondrial matrix.
- PEPCK supports the synthesis of many important metabolites by "stealing" oxaloacetate from the citric acid cycle

Cytosolic PEPCK and Metabolism*



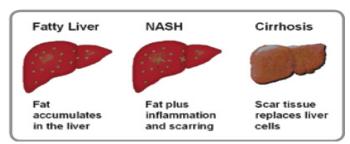
*Figure 1. Jianqi Yang et al. JBC 2009; 284, 27025-27029

PEP Carboxykinase and Fatty Liver Disease*

- Mice with defective PEP carboxykinase (PEPCK) develop dramatic hepatic steatosis
 - TCA cycle intermediates build up and this blocks fatty acid metabolism
- Glucocorticoids stimulate gluconeogenesis in liver and kidney by promoting PEP carboxykinase synthesis**
- * Shawn C Burgess et al. JBC 2004; 279(47): 48941-48949 **Taiyi Kuo et al. Adv

Exp Med Biol. 2015;

872: 99–126.

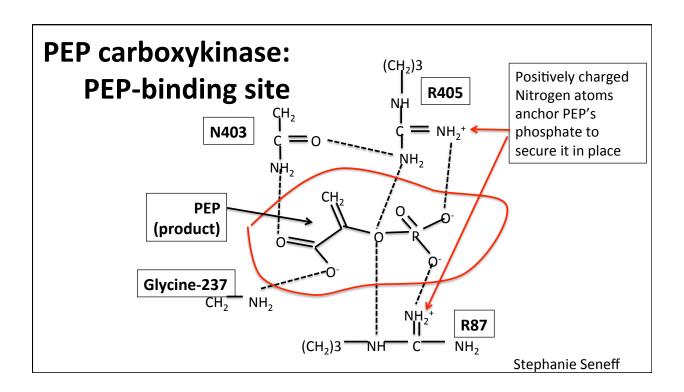


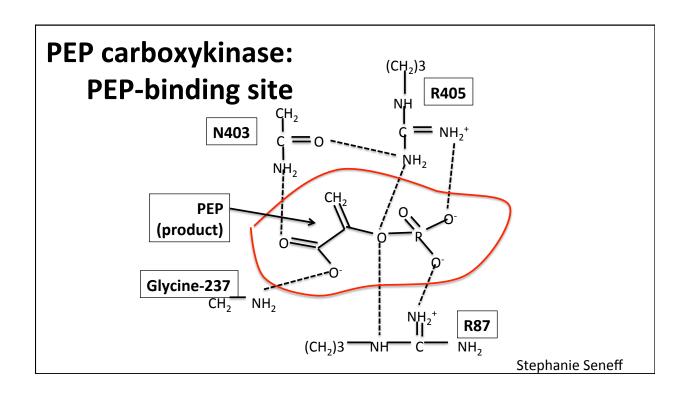
Is Glyphosate Causing an Epidemic in Fatty Liver Disease?

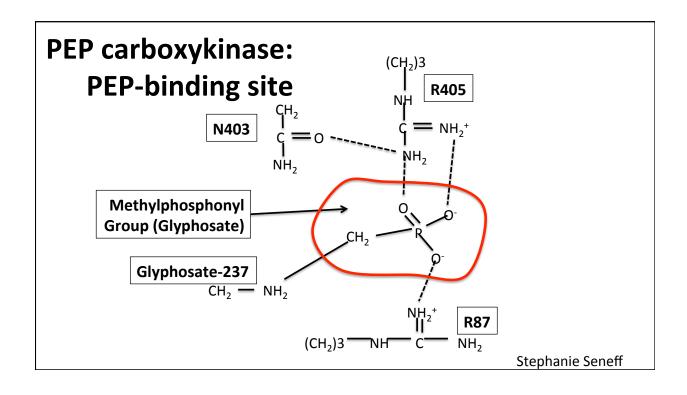
- We have a worldwide epidemic in fatty liver disease today*
- "Multiomics reveal non-alcoholic fatty liver disease in rats following chronic exposure to an ultra-low dose of Roundup herbicide."**
- Glyphosate causes fatty liver disease in humans***
 - * Chris Estes et al. Hepatology 2018; 67(1): 123-133.
 - ** Robin Mesnage et al. Sci Rep 2017; 7: 39328.
 - *** PJ Mills et al. Clinical Gastroenterology and Hepatology 2019 [Epub ahead of print].

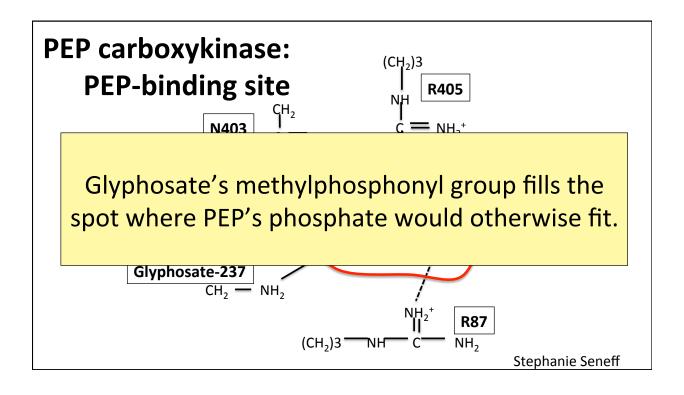
"Glyphosate Excretion is Associated With Steatohepatitis and Advanced Liver Fibrosis in Patients With Fatty Liver Disease"*

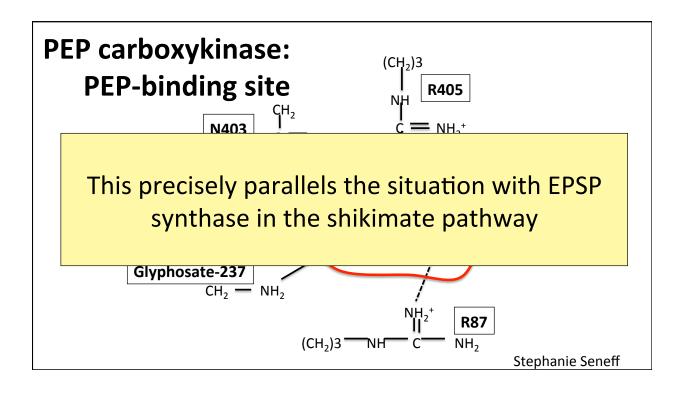
- Patients with liver disease at UC San Diego were carefully screened for NASH
- Glyphosate excretion was significantly higher in patients with NASH than in patients without NASH
- Patients with advanced fibrosis had significantly higher glyphosate than patients with less fibrosis
 - * PJ Mills et al. Clin Gastroenterol Hepatol 2019 [Epub ahead of print]











Mitochondrial PEPCK Controls Insulin Secretion in Beta Cells*

- PEPCK exists in both mitochondrial and cytoplasmic forms
- Mitochondrial PEPCK is constitutional, whereas cytoplasmic forms are regulated
- Beta cells in pancreas contain only mitochondrial form
- "Silencing PEPCK-M prevents insulin secretion in response to glucose"

*Romana Stark et al. Biochim Biophys Acta 2014; 1840(4): 1313–1330

Mitochondrial PEPCK Controls Insulin Secretion in Beta Cells*

- PEPCK exists in both mitochondrial and cytoplasmic
- Glyphosate suppression of PEPCK in mitochondria of beta cells could lead to
- suppressed insulin release type 1 diabetes

"Silencing PEPCK-M prevents insulin secretion in response to glucose"

*Romana Stark et al. Biochim Biophys Acta 2014; 1840(4): 1313–1330

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Designer Mice: Wow!*

- Designer mice with ten-fold excess expression of cytoplasmic PEPCK localized to skeletal muscle
 - Eat 60% more than control pups but weigh half as much
 - Lived almost 2 years longer; increased fertility
 - Violate pillar of aging research: limiting food intake increases longevity
- Eat a huge amount but are so hyperactive that they burn off most of the calories and stay thin.
- Increased insulin sensitivity and recruitment of GLUT-4 to the cell surface in muscle

*Jianqi Yang et al. JBC 2009; 284, 27025-27029

Possible Mechanism to Explain the Phenotype of the PEPCK-C^{mus} mice PEPCK-C in muscle † Glyceroneogenesis † Triglyceride † FA oxidation † CO₂ production † Adipose tissue ↓ Leptin, MCP-1 ↓ Reproduction † Food intake † *Figure 1. Jianqi Yang et al. JBC 2009; 284, 27025-27029

More Details on these Designer Mice

- Overexpression of PEPCK in skeletal muscle during development → excessive mitochondria in muscles
 → hyperactive as early as 10 days after birth
- Increase in citric acid flux → more mitochondria
- Excess PEPCK in muscle → synthesis of glycerol & triglycerides
 - Triglycerides fuel muscle overactivity

*Jianqi Yang et al. JBC 2009; 284, 27025-27029

What is the Opposite of This?

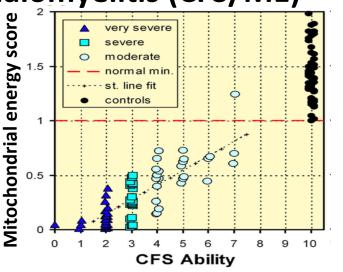
- Reduced mitochondrial density in muscle
- · Reduced ability for muscle to utilize fat
- Increased adiposity
- Low energy; hypoactivity
- Insulin resistance and reduced GLUT-4
- Shortened lifespan; decreased fertility

Chronic Fatigue Syndrome???

Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (CFS/ME)*

"Our results strongly suggest that the immediate cause of the symptoms of CFS/ME is mitochondrial dysfunction."

*S. Myhill et al. Int J Clin Exp Med 2009; 2: 1-16.



Ractopamine

- Ractopamine is a steroid-like drug used as a feed additive to increase lean meat yield in livestock
 - Banned in most countries, including EU, China, Russia, Taiwan, etc., but not US
 - US uses Ractopamine on > 60% of its livestock
- Ractopamine increases activity of PEPCK*
- Exposed pigs are more aggressive and can lose mobility as a side effect
- Most countries view it as unsafe for human consumption



*DM Brown et al. Scientific Reports 2016; 6:28693

Sugar Addicted Newborns: the Silent Epidemic*

- Diabetic moms with high blood sugar supply too much sugar to their fetus during pregnancy
- Infant produces too much insulin, which induces hypoglycemia following birth
 - Symptoms include lethargy, tachycardia, poor feeding, seizures, and even coma
- Excessive growth in utero leads to complicated birth
- Infant normally upregulates PEP carboxykinase at birth, but glyphosate exposure could be inhibiting protein activity

*www.dunkthejunk.org/blog/2016/1/19/sugar-addicted-newborns-the-silent-epidemic

Glycine mutation in PEP carboxylase leads to hypoglycemia and liver disease

- Three cases of homozygous mutation of PEP carboxykinase in Finland
- All three had a mutation of glycine at residue 309 to arginine which produced a nonfunctional version of the enzyme
- Clinically presented as childhood hypoglycemia, liver dysfunction, and elevations of fumarate and other citric cycle intermediates in the urine

* P Viera et al., Mol Genet Metab 2017; 120(4):337-341.

Critical diaphragm failure in sudden infant death syndrome*

- "Critical Diaphragm Failure" hypothesis for SIDS
 - Weak diaphragm → breathing difficulties
 (due to PEPCK impairment?)
- PEPCK deficiency in liver → impaired gluconeogenesis

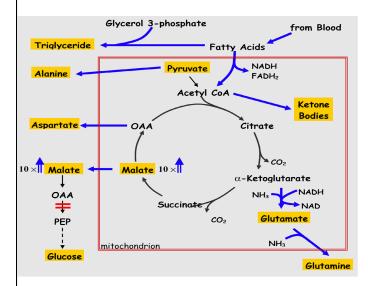


 SIDS often occurs at night after child begins to sleep through the night → acute hypoglycemia

*PMA Siren and MJ Siren.

Upsala Journal of Medical Sciences 2011; 116: 115–123.

PEPCK Deficiency: Metabolic Derailments*



Fish exposed to glyphosate had low liver glucose, elevated ALT and AST, and elevated lactate and triglycerides**

*Parvin Hakimi et al. Nutrition and Metabolism 2005: 2:33

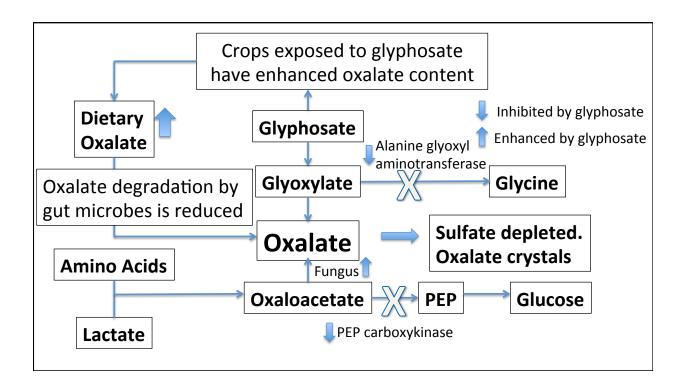
**FR de Maura et al. Environ Toxicol Pharmacol 2017; 56: 241-248.

Could PEP Carboxykinase Deficiency Cause High Serum Oxalate and Fungus Overgrowth?

- We have a worldwide epidemic in fungus diseases*
- PEP Carboxykinase converts oxaloacetate to PEP
- PEP Carboxykinase deficiency leads to excess oxaloacetate
- White rot fungus synthesizes oxalate from oxaloacetate**
- This leads to accelerated growth and a more pathogenic form

*GD Brown et al. Sci Transl Med 2012; 4: 165rv13.

** Nina Elisabeth Nagy et al. MPMI 2012; 25(11): 1450-1458.



Low Sulfate, High Oxalate Phenotype*

- Gut Dysbiosis
 - Decreased sulformicins, colitis, IBD, leaky gut
 - Increased susceptibility to pathogens
- Fatty liver disease
 - Reduced detox of heavy metals and toxic chemicals
 - Elevated serum LDL
- Decreased insulin function
- Adrenal insufficiency
- Increased cancer risk
- · Stunted growth, slow metabolism
- Serotonin deficiency in brain
- Autism linked to sulfate wasting in kidneys

*Dr. Rostenberg

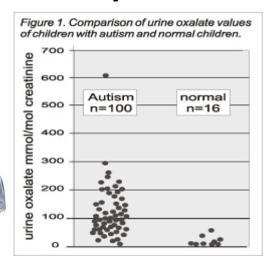
www.beyondmthfr.com/side-high-oxalates-problems-sulfate-b6-gut-methylation

Autism Linked to Oxalate Crystals*

 Crystals of oxalate form kidney stones and cause great discomfort

 Study has shown at least 3fold higher serum and urinary levels of oxalate in autistic kids**

*William Shaw, The Role of Oxalates in Autism and Chronic Disorders WAPF, March 26, 2010



**J Konstantynowicz et al., European Journal of Paediatric Neurology 16(5), 2012, 485-491

Oxalate Causes Sulfate Flushing through Urine*

- Sulfate is essential for:
 - Synthesis of extracellular matrix glycoproteins
 - Synthesis of cerebroside sulfate, in myelin in nerve fibers
 - Detoxification of many environmental toxins
- Sulfate is flushed (lost) when kidney oxalate levels are high
- Oxalobacter microbes degrade oxalate but they are killed by antibiotics such as Cipro
 - Oxalate decarboxylase depends on manganese as catalyst**
 - *W Krick et al., Am J Physiol Renal Physiol 2009;297: F145-F154.
 - **A Tanner et al. J Biol Chem. 2001;276(47):43627-34

Recapitulation

- Glyphosate may be disrupting PEPCK in the same way it disrupts EPSP synthase
- If so, it explains glyphosate's well established association with fatty liver disease
- It also explains the epidemic we see today in:
 - chronic fatigue syndrome– oxalate overload
 - neonatal hypoglycemiafungus infection
 - sudden infant deathtype 1 diabetes
 - autism

The California Lawsuits: Glyphosate and non-Hodgkin's Lymphoma

DeWayne Lee Johnson Lawsuit

- Johnson was a groundskeeper for the school district in Benicia, CA, just north of San Francisco
- He was diagnosed with non-Hodgkin's lymphoma (NHL) in 2014, at age 42.
- In 2015, WHO's IARC classified glyphosate as "probably carcinogenic to humans"
- Donna Farmer, Monsanto's "product protection lead" said in email to colleagues:
 - "You cannot say that Roundup does not cause cancer."
- Timothy Litzenburg, one of Johnson's lawyers, said:
 - "so much of what Monsanto has worked to keep secret is coming out."

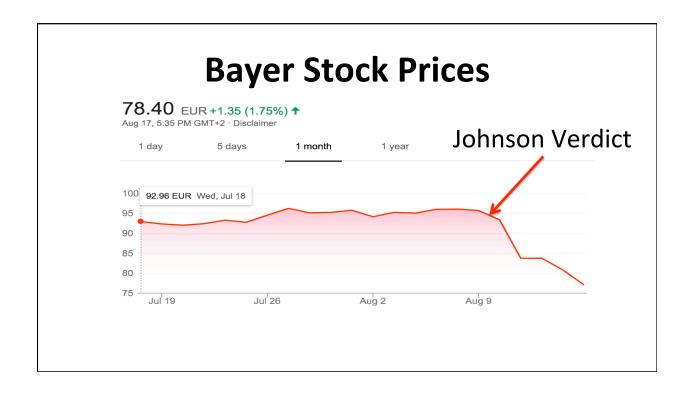


"We're going to see for the first time evidence that nobody has seen before, evidence that has been in Monsanto's files that we've obtained from lawyers and the people in Monsanto... I don't think it's a surprise after 20 years Monsanto has known about the cancer-causing properties of this chemical and has tried to stop the public from knowing it, and tried to manipulate the regulatory process."

-- Robert F Kennedy, Jr. Co-counsel for Johnson

"We're going to see for the first time evidence that nobody has seen before, evidence that has been in Monsa " If we get a large award in this case, fter the pe 20 yea it could easily threaten the future ng prope financial viability of the company." public regula -- Robert F Kennedy, Jr. -- Rob Co-counsel for Johnson

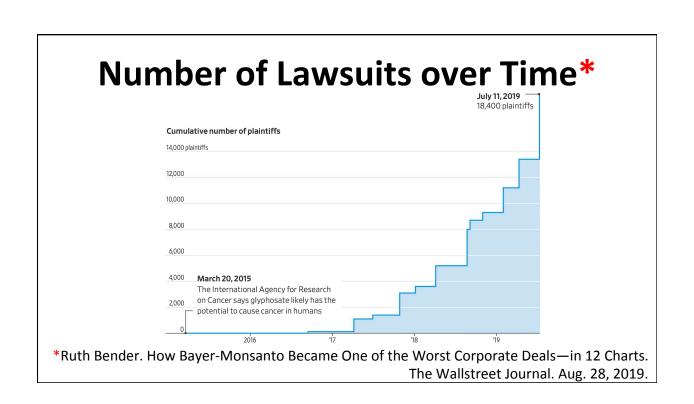




Four Ongoing Lawsuits

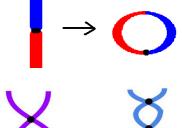
Plaintiff	Location	Jury Award	Judge's Ruling
DeWayne Johnson	California	\$289 million	\$78 million
Edwin Hardeman	California	\$80 million	\$25 million
Alva and Albert Piliod	California	\$2 billion	\$86 million
Sharlean Gordon	Missouri	-	-

>42,000 more in the works!



"In vitro evaluation of genomic damage induced by glyphosate on human lymphocytes"*

- In vitro exposure of human lymphocytes to glyphosate at levels of 0.5, 0.1, 0.050, 0.025 and 0.0125 µg/ml
- 0.5 is considered an "acceptable daily exposure level"
- Chromosomal aberrations and micronuclei frequencies were significantly high at all except the lowest exposure levels.





*A Santovito et al. Environ Sci Pollut Res Int 2018;25(34):34693-700.

"In vitro evaluation of genomic damage induced by glyphosate on human lymphocytes"* In vitro exposure of human lymphocytes to the state of the stat

- Lymphocytes are the cell type that transforms into cancer cells in non-Hodgkin's lymphoma
- Chromosomar abenrations and micronuclei frequencies were significantly high at all except the lowest exposure levels.





*A Santovito et al. Environ Sci Pollut Res Int 2018;25(34):34693-700.

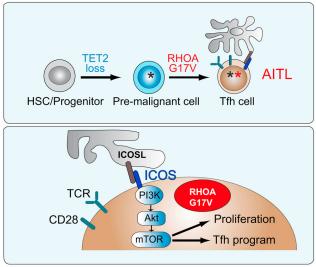
Two Papers on Glyphosate and NHL

- Retrospective study involving 244 patients with diffuse large B-cell lymphoma (variant of NHL)*
 - 2-year event-free survival was only 56% among those with agricultural occupational exposure compared to 83% for the unexposed group
- Meta-analysis involving 65,000 participants in 6 studies**
 - Those highly exposed to glyphosate-based formulations had an increased risk ratio of 1.41.

*Sylvain Lamure et al. JAMA Netw Open 2019; 2(4): e192093.

**Luoping Zhang et al., Mutation Research 781 (2019): 186-206.

Angioimmunoblastic T Cell Lymphoma (a rare but virulent form of NHL)*



 70% of cases have the Glycine-17-Valine mutation

> *Jose R. Cortes et al., Cancer Cell 33, 259–273, 2018.

Outline: Part II

- Experiments on Breast Cancer Cells
- Glyphosate, Sulfate, Oxalate, Autism
- Roundup, StAR and Sterol Homeostasis
- A Failed System and A Growing Food Movement
- How to Safeguard Yourself and Your Family
- Conclusions