

Toxic Legacy: How the Weedkiller Glyphosate is Destroying Our Health

Stephanie Seneff, MIT CSAIL

AutismOne, September 2021



1

“Future historians may well look back upon our time and write, not about how many pounds of pesticide we did or didn’t apply, but by how willing we are to sacrifice our children and future generations for this massive genetic engineering experiment that is based on flawed science and failed promises just to benefit the bottom line of a commercial enterprise.”

-- Prof. Don Huber

2

Outline

- Introduction
- Human and Animal Diseases
- Glyphosate and Autism
- Glyphosate and Endocrine Disruption
- Transgenerational Effects
- Conclusion

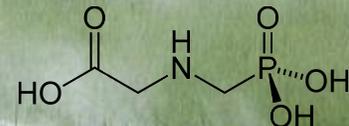
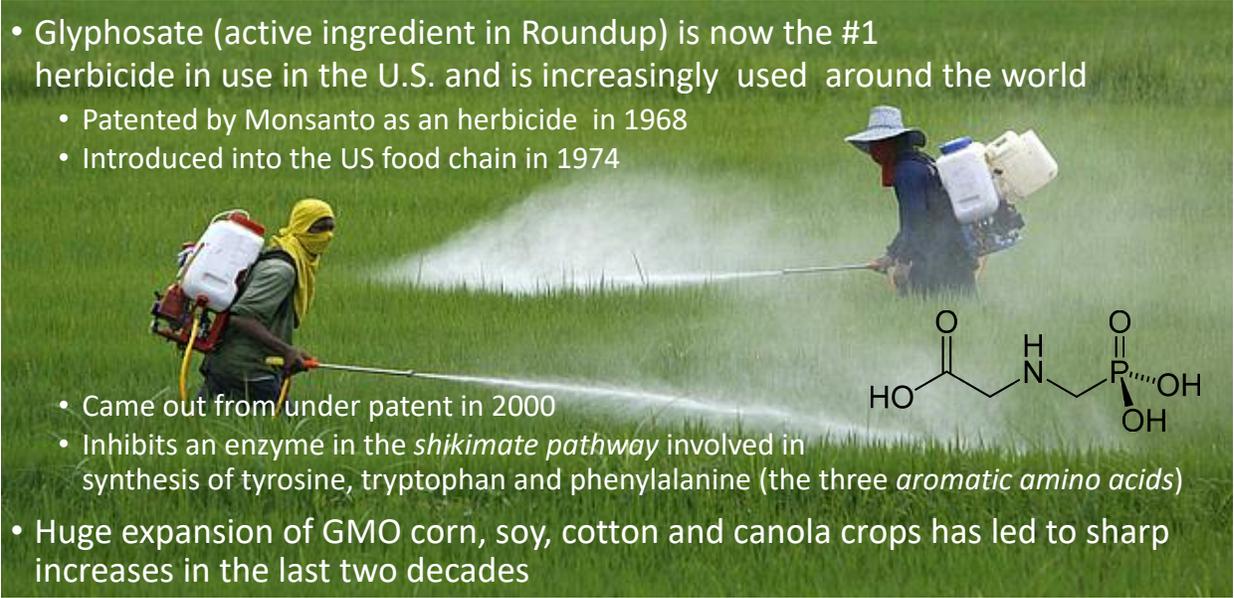
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Introduction

4

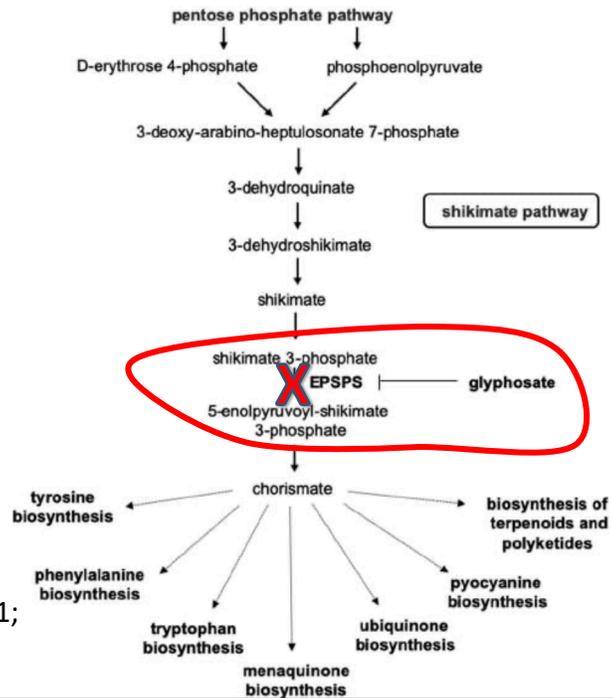
A Brief History of Glyphosate

- Glyphosate (active ingredient in Roundup) is now the #1 herbicide in use in the U.S. and is increasingly used around the world
 - Patented by Monsanto as an herbicide in 1968
 - Introduced into the US food chain in 1974
- Came out from under patent in 2000
- Inhibits an enzyme in the *shikimate pathway* involved in synthesis of tyrosine, tryptophan and phenylalanine (the three *aromatic amino acids*)
- Huge expansion of GMO corn, soy, cotton and canola crops has led to sharp increases in the last two decades



5

Glyphosate Blocks EPSP Synthase in the Shikimate Pathway in Plants*



*Figure 1 in Robin Mesnage et al. Environmental Health Perspectives 2021; 129(1): 017005.

6



Research paper

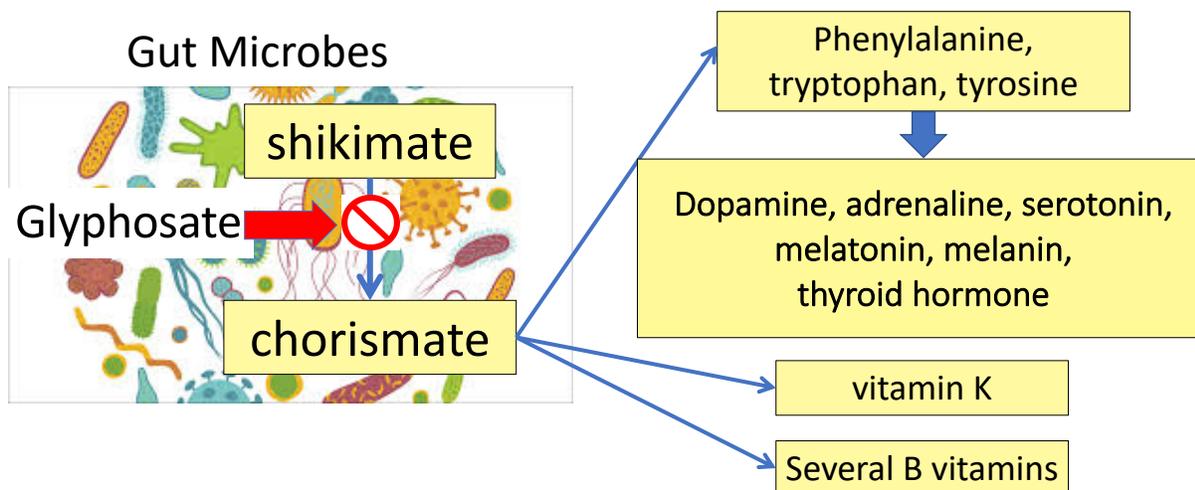
Classification of the glyphosate target enzyme (5-enolpyruvylshikimate-3-phosphate synthase) for assessing sensitivity of organisms to the herbicide

“A conservative estimate from our results shows that **54%** of species in the core human gut microbiome are sensitive to glyphosate.” *

*Lydia Leino et al. Journal of Hazardous Materials 2021; 408: 124556.

7

Shikimate Pathway Disruption



8

Main Toxic Effects of Glyphosate*

- Kills beneficial gut bacteria and allows pathogens to overgrow
- Interferes with function of cytochrome P450 (CYP) enzymes in the liver
 - These enzymes serve many important roles, including making bile acids, activating vitamin D, detoxifying many toxic chemicals and breaking down prescription drugs
- Chelates (binds tightly to) important minerals like cobalt, manganese and zinc, making them unavailable to the cells
- Interferes with the synthesis of aromatic amino acids and methionine
- Disrupts sulfate synthesis and sulfate transport

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

9

“Glyphosate: Plasma and Bone Marrow Levels Following Intraperitoneal Injection”*

- Significant amounts of radiolabeled glyphosate were found in plasma and bone marrow following intraperitoneal injection in rats
- Glyphosate in bone marrow reached 340 ppm after 1/2 hour, and it remained at about that level throughout the duration of the study (10 hours)



**WP Ridley et al. Monsanto commissioned study ML-83-218; EHL No. 830109. 1983.*

10

Glyphosate and Cancer*

- In April 2015, the World Health Organization's International Agency for Research on Cancer (IARC) identified glyphosate as a probable human carcinogen
- Three trials involving cases where glyphosate was claimed to cause non-Hodgkin's lymphoma resulted in a successful lawsuit
 - The plaintiffs were awarded \$25-80 million in each case
- In June, 2020, Bayer offered to pay up to \$10.9 billion to roughly 125,000 people in thousands of lawsuits arguing Roundup was responsible for their non-Hodgkin lymphomas

*<https://sustainablepulse.com/2020/12/24/environmental-and-farming-groups-start-us-legal-action-in-attempt-to-ban-glyphosate/>

11

Human and Animal Diseases

12

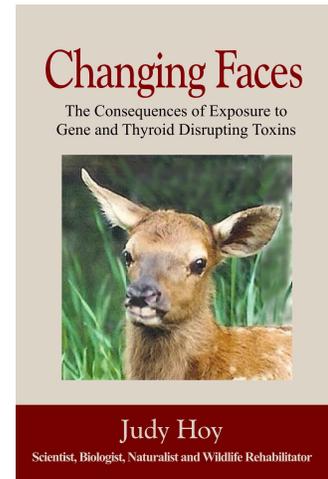


The High Cost of Pesticides: Human and Animal Diseases

Judy Hoy¹, Nancy Swanson² and Stephanie Seneff^{3*}

- The first author, Judy Hoy, runs a wildlife rehabilitation center in the Bitterroot Valley in Western Montana
- She has been tracking the dwindling numbers and decreasing health status of wildlife there for decades
- Dr. Nancy Swanson and I collaborated with her to compare health issues of the animals with those of humans in the United States

*Hoy et al. Poultry, Fisheries and Wildlife Sciences 2015; 3:1.



13

Newborn white-tailed deer have severely damaged thymuses*



*Judy Hoy et al., Poultry, Fisheries & Wildlife Sciences 2015; 3(1): 1000132.

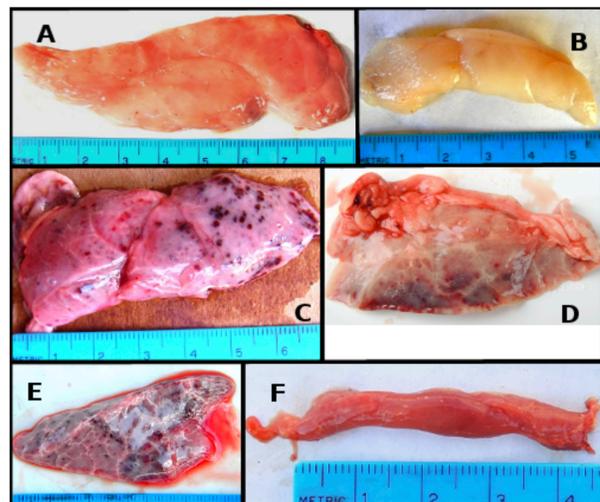


Figure 14: Newborn white-tailed deer thymus conditions. A and B. Normal thymus color and shape. C and D. Thymus with red spots throughout. E. Odd shaped, mostly red thymus. F. Undersized thymus, red throughout.

14

Some Correlations between Human Diseases and Glyphosate*

- Compared US government data on glyphosate usage and on human disease patterns over time from the 1998-2010 hospital discharge data
- Found striking correlations between the rise in glyphosate usage and the rise in multiple health issues in newborn babies:



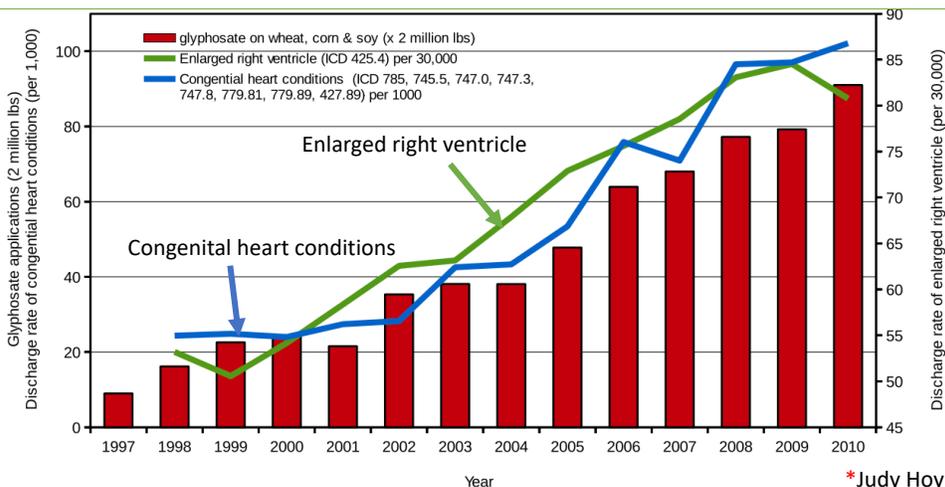
- | | |
|-------------------------------|--------|
| • head and face anomalies | R=0.95 |
| • blood disorders | R=0.92 |
| • skin disorders | R=0.96 |
| • metabolic disorders | R=0.95 |
| • genitourinary disorders | R=0.96 |
| • congenital heart conditions | R=0.98 |
| • lung problems | R=0.95 |

R is the correlation coefficient characterizing how similar the two curves are. 1.0 is the highest value it can take, representing a perfect match.

*Judy Hoy et al., Poultry, Fisheries & Wildlife Sciences 2015; 3(1): 1000132.

15

Congenital heart conditions (newborns) $p < 0.000009$ and enlarged right ventricle (adults) $p < 0.00003$ *



*Judy Hoy et al., Poultry, Fisheries & Wildlife Sciences 2015; 3(1): 1000132.

16

Cardiovasc Toxicol (2015) 15:117–126
 DOI 10.1007/s12012-014-9282-y

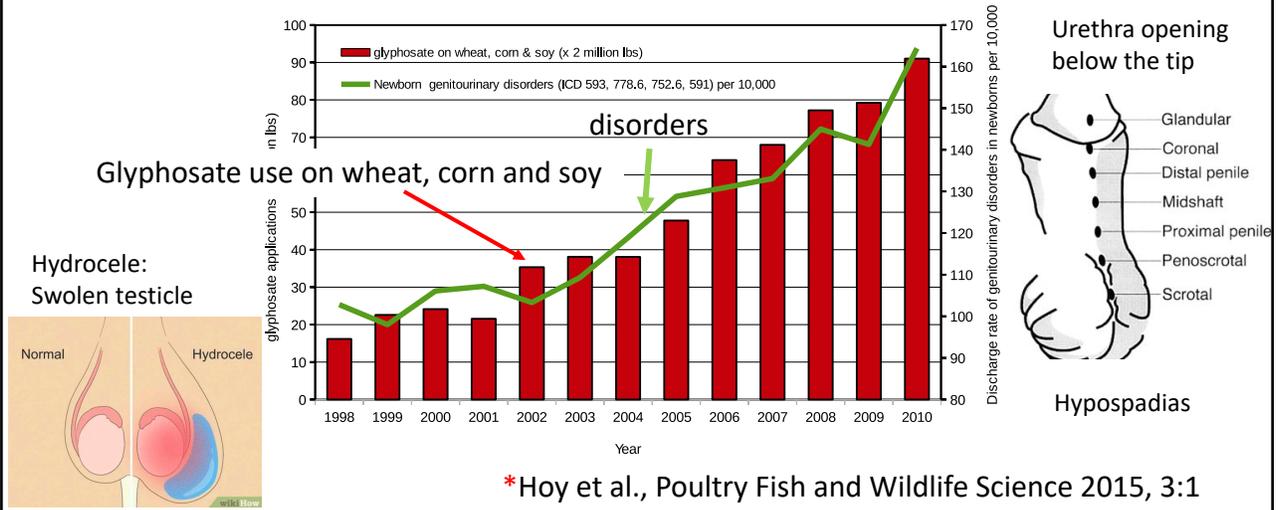
Glyphosate-Based Herbicides Potently Affect Cardiovascular System in Mammals: Review of the Literature

Steeve Gress · Sandrine Lemoine · Gilles-Eric Séralini · Paolo Emilio Puddu

- Long-QT syndrome, atrioventricular block, arrhythmias in both humans and animals
- “In fatalities, the common symptoms were cardiorespiratory arrest, cardiovascular shock, hemodynamic disturbances, intravascular disseminated coagulation and multiple-organ failure”

17

Newborn Genitourinary Disorders (Hypospadias, Hydrocele, etc.) $p < 0.000024$



18

Is Glyphosate Causing an Epidemic in Fatty Liver Disease?

- 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 correlated with fatty liver disease in humans***



Non-Alcoholic Fatty Liver Disease (NAFLD)



* Chris Estes et al. Hepatology 2018; 67(1): 123-133.

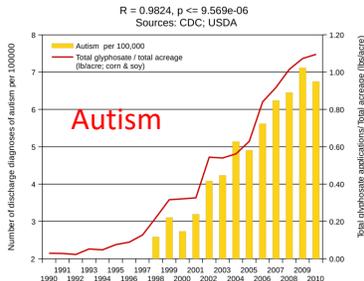
** Robin Mesnage et al. Sci Rep 2017; 7: 39328.

*** PJ Mills et al. Clinical Gastroenterology and Hepatology 2020;18(3):741-743.

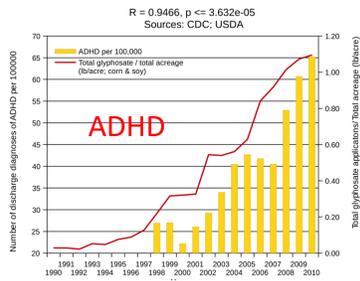
19

Glyphosate and Neurological Diseases*

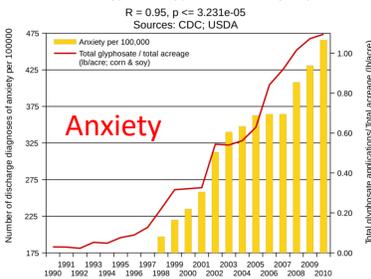
Hospital Discharge Diagnoses of Autism (ICD 299.0) & Glyphosate applied to corn & soy crops



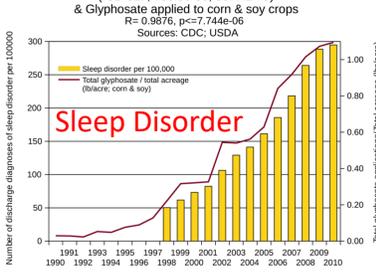
Hospital Discharge Diagnoses of ADHD (ICD 314.00-01) & Glyphosate applied to corn & soy crops



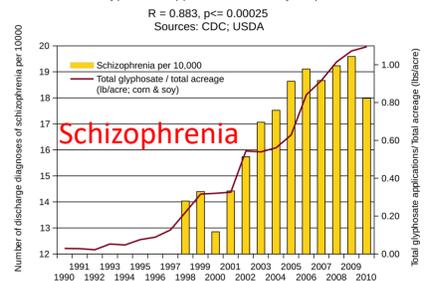
Hospital Discharge Diagnoses of Anxiety (ICD 300) & Glyphosate applied to corn & soy crops



Hospital Discharge Diagnoses of Sleep Disorders (ICD 327, 780.50-59, 307.41-49) & Glyphosate applied to corn & soy crops



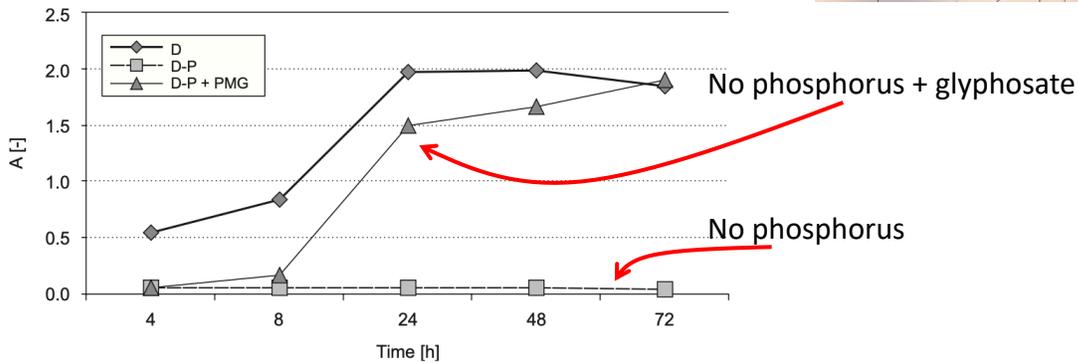
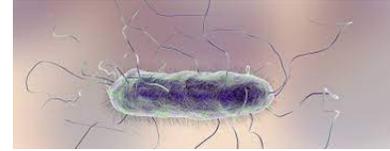
Hospital Discharge Diagnoses of Schizophrenia (ICD 295) & Glyphosate applied to corn & soy crops



* S Seneff et al. Agricultural Sciences 2015; 6: 42-70.

20

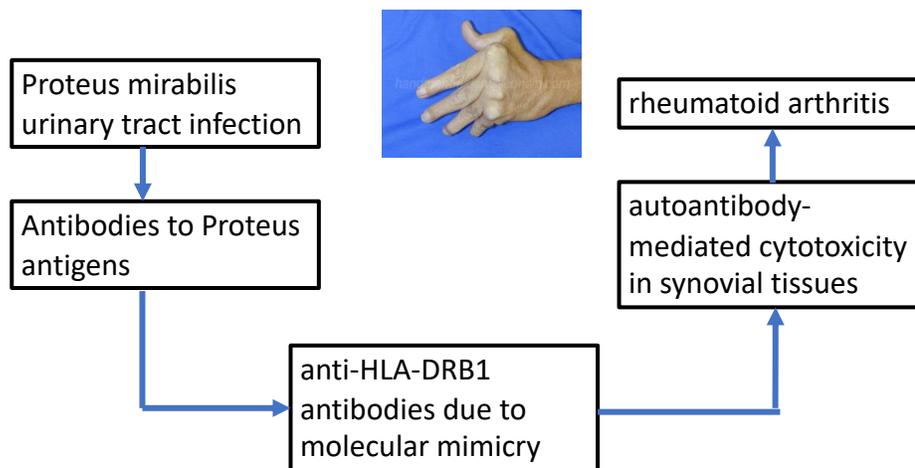
Proteus mirabilis can fully metabolize glyphosate and use its phosphorus atom as a source of phosphorus*



*Z. Wybranych et al. Ecol Chem Eng A. 2015; 22(2): 185-193.

21

“Rheumatoid arthritis is an autoimmune disease triggered by Proteus urinary tract infection”*



*A. Ebringer and T Rashid. Clinical & Developmental Immunology 2006; 13(1): 41-48.

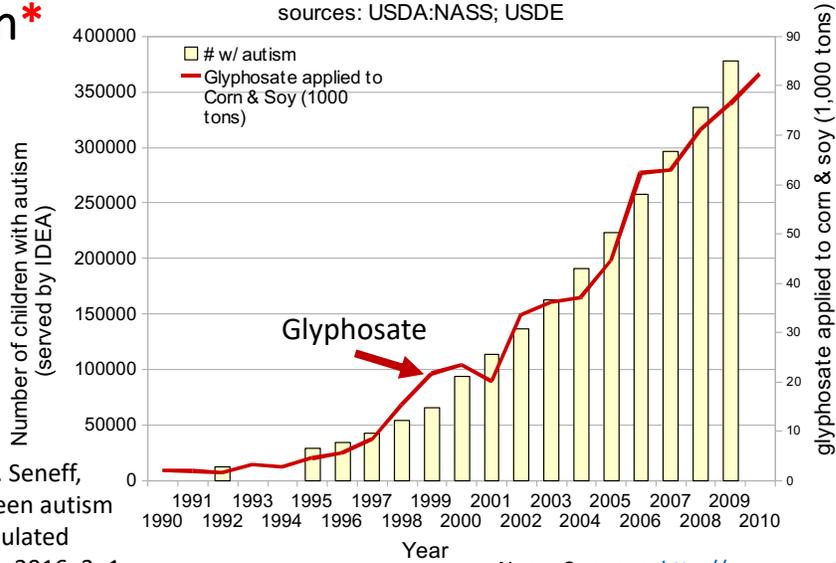
22

Glyphosate and Autism

23

Glyphosate and Autism*

Number of children (6-21yrs) with autism served by IDEA plotted against glyphosate use on corn & soy (R = 0.9869, p <= 1.103e-06)
sources: USDA:NASS; USDE



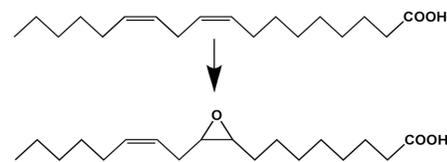
*J.E. Beecham and S. Seneff, "Is there a link between autism and glyphosate-formulated herbicides?" J Autism 2016; 3: 1.

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

24

Autism-like Symptoms following Maternal Glyphosate Exposure*

- Exposure to herbicides during pregnancy might increase risk for autism in progeny
- Exposure of pregnant mice to high-dose glyphosate during pregnancy and lactation induced autism-like symptoms in juvenile offspring
 - Associated with gut microbiome imbalance and disrupted fatty acid metabolism
- Increased expression of **soluble epoxyhydrolase (sEH)** in prefrontal cortex of the brain
 - Produces pro-inflammatory fatty acid derivatives
- High sEH has been linked to depression, autism, schizophrenia and Parkinson's disease



*Yaoyu Pu et al. PNAS 2020; 117 (21): 11753-11759

25

How to explain this

- The story links together vitamin D, Cytochrome P450 (CYP) enzymes, aromatase, estrogen, testosterone and sEH
- Maternal vitamin D deficiency causes high testosterone in male offspring
- Aromatase deficiency causes low estrogen, high testosterone in the brain
- Estrogen suppresses synthesis of sEH [low estrogen = high sEH]
- Vitamin D activation depends on CYP enzymes
- Aromatase is a CYP enzyme
- Glyphosate suppresses CYP enzymes → low estrogen and low vitamin D

26

Glyphosate Suppresses Aromatase in the Placenta*

- Some agricultural workers using glyphosate have fertility problems
- Glyphosate is toxic to human placental JEG3 cells at concentrations lower than those found with agricultural use
- The additional ingredients in Roundup increase glyphosate toxicity
- Roundup disrupts aromatase activity

Aromatase is a cytochrome P450 (CYP) enzyme, and glyphosate has been shown to suppress CYP enzymes in the liver**

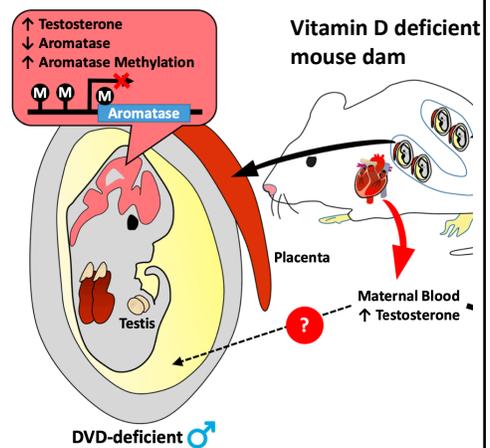
*Sophie Richard et al. Environmental Health Perspectives 2005; 113(6):716-720.

**Mohamed Ahmed Fathi et al. Environmental Science and Pollution Research 2020; 27(14): 16865-16875.

27

“Developmental vitamin D deficiency increases foetal exposure to testosterone”*

- Vitamin D regulates gene expression via methylation
- Vitamin D deficiency causes hypermethylation of the promoter for aromatase
 - This results in reduced aromatase expression in male brains
- Aromatase converts testosterone to estrogen
- Excess testosterone in male foetal brains.
 - autism

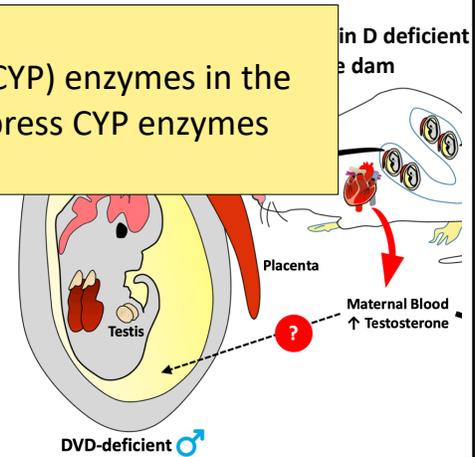


*Asad Amanat Ali et al. Molecular Autism (2020) 11:96.

28

“Developmental vitamin D deficiency increases foetal exposure to testosterone”*

- Vitamin D is activated by Cytochrome P450 (CYP) enzymes in the liver, and glyphosate has been shown to suppress CYP enzymes
- This results in reduced aromatase expression in male brains
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- Excess testosterone in male foetal brains.
→ autism



*Asad Amanat Ali et al. Molecular Autism (2020) 11:96.

29

“Glyphosate exposure induces synaptic impairment in hippocampal neurons and cognitive deficits in developing rats”*

- Glyphosate-treated hippocampal neurons in culture showed a decrease in dendritic complexity and spine formation
- Rat pups were exposed to glyphosate (every two days from 7 days old to 27 days old)
 - Induced cognitive impairments
 - Reduced synaptic protein expression in hippocampus

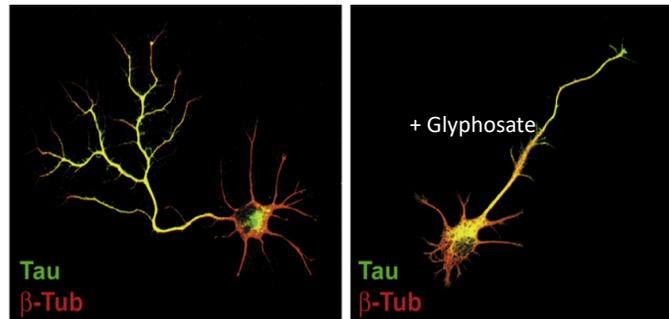


*Sebastian Luna et al. Archives of Toxicology (2021) [Epub ahead of print]

30

“Neuronal development and axon growth are altered by glyphosate through a WNT non-canonical signaling pathway”*

- Neurons grown in culture & exposed to glyphosate
- “They elicited shorter and unbranched axons and they also developed less complex dendritic arbors compared to controls”

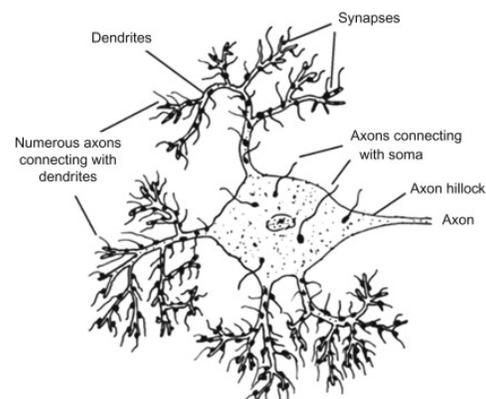


*RP Coullery et al., NeuroToxicology 2016;52:150-161.

31

“Dendrite and spine modifications in autism and related neurodevelopmental disorders in patients and animal models” *

"Specifically, autism has been linked to a decrease in the density of spines with mature morphology, indicating a general spine immaturity state in autism."



*Verónica Martínez-Cerdeño, Dev Neurobiol 2017 Apr; 77(4): 393–404.

32

“Environment permissible concentrations of glyphosate in drinking water can influence the fate of neural stem cells from the subventricular zone of the postnatal mouse”*

"Our findings demonstrated that the permissible concentrations of glyphosate in drinking water recognized by environmental protection authorities are capable of inducing neurotoxicity in the developing nervous system."

"Our findings signify the need to review the safety standards established by environmental protection agencies concerning safe glyphosate concentrations in drinking water."

*Muhammad Irfan Masood et al., Environmental Pollution 270 (2021) 116179.

33

Recapitulation

- Glyphosate causes autism-like symptoms in male mice linked to increased expression of soluble epoxyhydrolase (sEH)
 - Estrogen decreases expression of sEH
 - Aromatase converts testosterone to estrogen
- Aromatase expression in the placenta is suppressed by glyphosate
 - This explains glyphosate’s effects and the link to autism
 - Low estrogen leads to high sEH
- Maternal vitamin D deficiency leads to excess testosterone in males
 - Vitamin D depends on liver CYP enzymes for activation, which glyphosate suppresses
- Aromatase is also a CYP enzyme and this explains how glyphosate suppresses it
- Glyphosate suppresses maturation of neuronal dendritic spikes – a characteristic feature of autism

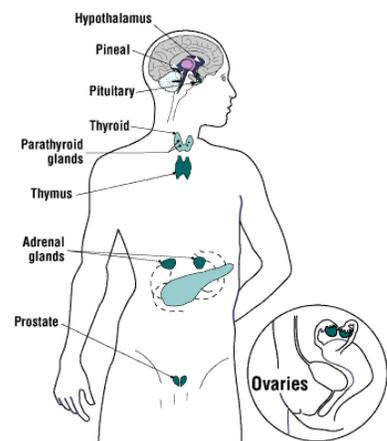
34

Glyphosate and Endocrine Disruption

35

Glyphosate is an Endocrine Disruptor*

- Glyphosate at parts per trillion triggers estrogen-sensitive breast cancer cells to proliferate
- Glyphosate increases expression levels of estrogen and progesterone receptors
- Glyphosate-based herbicides disrupt the hypothalamic-pituitary-thyroid (HPT) axis
- Glyphosate alters circulating levels of hormones
- Glyphosate induced hypothyroidism in female Wistar rats
- Glyphosate-based formulations altered reproductive developmental parameters in animal models
- Glyphosate induced malformation in zebrafish embryos



*Juan P. Muñoz et al. Chemosphere October 19, 2020 [Epub ahead of print]

36

"Maternal urinary levels of glyphosate during pregnancy and anogenital distance in newborns in a US multicenter pregnancy cohort"*

- Glyphosate in urine measured mid-pregnancy
- Anogenital distance in girls was longer (more male typical) in association with higher urinary levels of glyphosate
- An earlier study on rats found a similar result**
- Glyphosate suppresses aromatase, which converts testosterone to estrogen
- Confirms that glyphosate is an endocrine disruptor in humans



*Corina Lesseur et al. Environmental Pollution 2021; 280: 117002.

**Manservigi et al. Environmental Health 2019; 18: 15.

37

Longer anogenital distance in females is linked to infertility

- Women in the highest tertile of anogenital distance had an 18-fold increased risk of having polycystic ovary syndrome (PCOS)*
 - Associated with irregular periods or no menstrual cycle, plus excess growth of hair
- PCOS is the most common cause of female infertility, affecting as much as 20% of the world's female population
- Women with PCOS have an increased risk of being diagnosed with autism and of having progeny with autism**

*Yingchen Wu et al. Human Reproduction 2017 Apr 1;32(4):937-943.

**Maria Katsigianni et al. Molecular Psychiatry 2019 Dec;24(12):1787-1797

38

Glyphosate and Premature Birth*

- Study based in Puerto Rico
- 53 cases (premature birth); 194 controls
- Models are adjusted for maternal age, education, pre-pregnancy BMI, and smoking
- Measured both glyphosate and AMPA
 - AMPA is a breakdown product of glyphosate
- Women who had high (> 0.65 micrograms/Liter) levels of AMPA in their urine at 26 weeks of gestation had a 4.5-fold increased risk of premature birth ($p < 0.006$). High urinary glyphosate was associated with a 3.77-fold increased risk.



*Monica K Silver et al. Environmental Health Perspectives 2021; 29(5): 057011.

39

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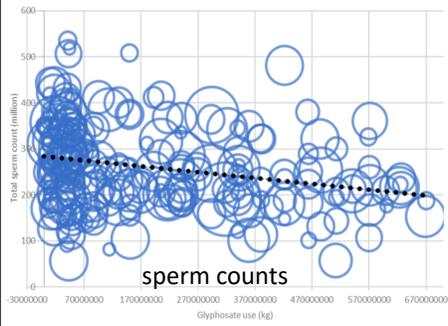
"Preterm birth is a national epidemic, costing the United States \$26.2 billion each year"
-- American Psychological Association



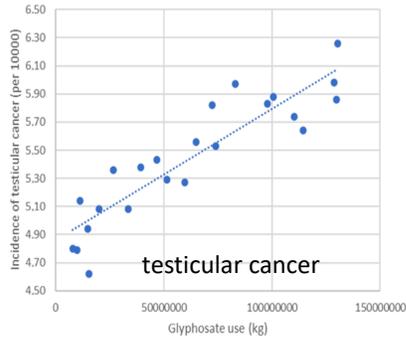
*Monica K Silver et al. Environmental Health Perspectives 2021; 29(5): 057011.

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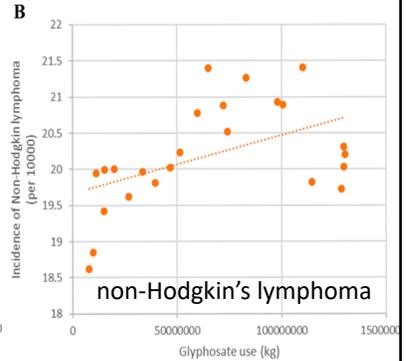
Glyphosate, Sperm Counts and Cancer*



p < .000015



p < . 0.0000000039



p < 0.0053

Data were obtained from publicly available databases maintained by the US government

*B. Sopko et al., ACS Omega 2021 June 2, 2021 [Epub ahead of print]

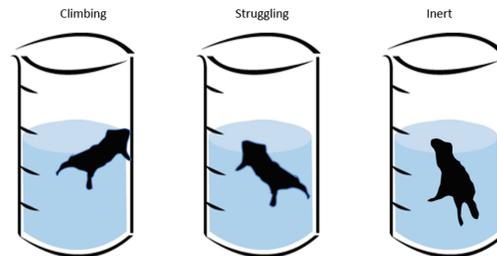
41

Transgenerational Effects

42

“Developmental exposure to glyphosate-based herbicide and depressive-like behavior in adult offspring: Implication of glutamate excitotoxicity and oxidative stress”*

- Mother rats were exposed to glyphosate while pregnant and for fifteen days following birth of the offspring.
- The offspring suffered from glutamate excitotoxicity in their brains persistently even after exposure was terminated.
- When the offspring were 60 days old, they showed signs of depression in a forced swimming test.



*Daiane Cattani et al., Toxicology 2017; 387: 67-80.

43

Epigenetic transgenerational toxicology through germline alterations by glyphosate*,**

- Pregnant rats were exposed to glyphosate at half the No Observable Adverse Effect Level (NOAEL) from day 8 to day 14 of gestation (timed to match germ cell epigenetic programming)
- Offspring were bred to produce pups (F1), grandpups (F2) and great-grandpups (F3)
- Exposed rats showed no symptoms
- F1 generation were mostly fine
- F2 and especially F3 generations suffered from many diseases, including mammary tumors, delayed or early puberty, premature birth abnormalities, prostate disease, kidney disease, and obesity



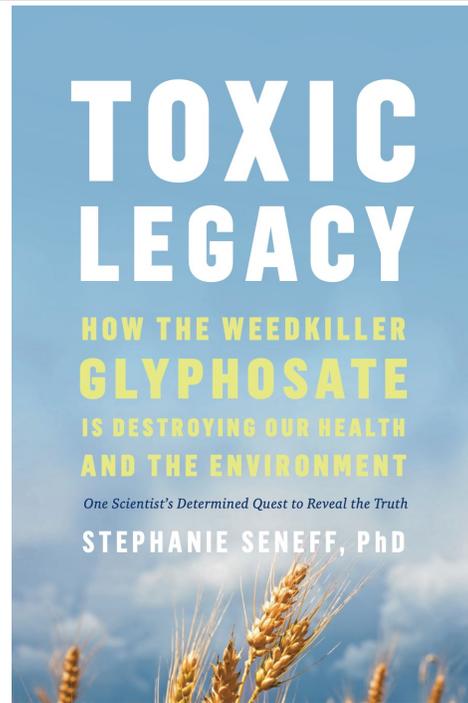
* Millissia Ben Maamar et al. Epigenetics 2020 Dec 9;1-18.

** Deepika Kubsad et al. Scientific Reports 2019; 9:6372.

44

My New Book!

- Released on July 1, 2021
- Presents extensive data on glyphosate toxicity to animals and humans
- Explains in detail how glyphosate exposure leads to autism
- Provides compelling arguments that glyphosate is insidiously, cumulatively toxic through its diabolical insertion into proteins by mistake in place of the coding amino acid glycine
 - This unique feature explains why it is causal in so many diseases



45

Conclusions

- Glyphosate is far more toxic to humans than we have been led to believe
- The rise in glyphosate usage on core crops in the United States correlates with the rise in prevalence of many diseases and conditions
- Glyphosate's disruption of gut microbes, CYP enzymes, and hormones can play a significant role in autism and other neurological diseases
- Glyphosate causes infertility in both males and females, as well as developmental disorders
- Many papers published in the last few years are revealing remarkably severe effects of low doses of glyphosate in animal studies, including transgenerational effects
- Glyphosate should be banned worldwide

46

Conclusions

- Glyphosate is far more toxic to humans than we have been
- The risk of cancer is significantly higher in states with high glyphosate use, and conditions such as obesity, diabetes, and heart disease are also more prevalent
- Glyphosate can be found in the urine of children in high glyphosate use areas, and it is associated with hormonal disorders, reproductive problems, and developmental delays
- Many studies have shown that glyphosate is remarkably toxic to a wide range of animals, including birds, fish, and insects
- Severe effects of low doses of glyphosate in animal studies, including transgenerational effects
- Glyphosate should be banned worldwide

Adopting a 100% certified organic diet is the best thing you can do to assure long term health of your family members

