Glyphosate: An Overlooked Factor in Chronic Disease.

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“The earth is not dying, it is being killed, and those who are killing it have names and addresses.”

-- the late activist musician Utah Phillips.

Silent Spring (1962)

Rachel Carson argued that uncontrolled and unexamined pesticide use was harming and even killing not only animals and birds, but also humans.
Outline

• Introduction
• Animal and Human Diseases
• Glyphosate and the Gut
• Glyphosate and Autism
• Glyphosate and Endocrine Disruption
• Transgenerational Effects
• How to Stay Health in a Toxic World
• Conclusion

Introduction
Roundup and GMO Crops

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

What is glyphosate?

Roundup as a Desiccant/Ripener just before Harvest

Wheat, Oats, Barley, Rye, Sugar cane, Beans, Lentils, Peas, Flax, Sunflowers, Pulses, Chick Peas
Glyphosate is now the #1 herbicide in use in the U.S. and is increasingly used around the world

- Developed and patented by Monsanto in the 1970’s
- 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 decade

Is Glyphosate Nontoxic?

- Monsanto has argued that glyphosate is harmless to humans because our cells don’t have the shikimate biological pathway which is the pathway glyphosate disrupts to kill plants
- However, our gut bacteria DO have this pathway
  - We depend upon them to supply us with essential amino acids produced through that pathway, and with many other nutrients such as vitamins and short chain fatty acids
- 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
- Recently, three successful lawsuits claiming that glyphosate caused non-Hodgkin’s lymphoma are bringing public awareness to glyphosate’s toxicity
Glyphosate disrupts the gut microbiome*

• EPSP synthase is the enzyme in the shikimate biological pathway that glyphosate disrupts as the main toxic effect to kill weeds
• It has been argued that we are safe from glyphosate toxicity because human cells don’t express this enzyme
• However, many species in our gut microbiome do have it, and they use the enzyme to synthesize the three aromatic amino acids, tryptophan, tyrosine and phenylalanine

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

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.”


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
Glyphosate Accumulates in Biofilms*

- Glyphosate polluting waterways is rapidly adsorbed into biofilms
- Concentrations of glyphosate in biofilms were two to four orders of magnitude higher than those in the surrounding water
- Glyphosate appears to rapidly disappear from waterways but this is an illusion
- Juvenile fish and amphibians dwell in the biofilms

“We may be underrecognizing the potential ecological risk of contaminants, like glyphosate, that are bioconcentrating in biofilms and subsequently being consumed.”

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, Bayer agreed 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

A Veterinarian Speaks Out about Glyphosate Damage to Livestock*

Cattle herds in Saskatchewan, Canada, exposed to high glyphosate levels

• One herd:
  • Clostridia overgrowth
  • Large numbers of stillborns and weak calves with skeletal problems
  • Necropsies revealed large fatty livers that were mottled and friable
  • Glyphosate contamination at 448 ppb in the corn feed

• Another herd:
  • Coccidia infection in calves on a creep ration tested at 548 ppb glyphosate contamination
  • Removing feed and supplementing with iron and B vitamins reversed the problems


Ib Pedersen: Pig Farmer in Europe*

• Glyphosate was found in the lungs, liver, kidney, brain, gut wall and heart of 38 malformed euthanized one-day-old Danish piglets
• Highest concentrations were in the lungs and heart
  “The summary of my findings is, without a doubt, that Roundup sprayed on crops is the direct reason for the increase in fertility problems, abortions and deformities in animals and as a farmer, knowing how nature works, I quite expect that people are already affected.”
  “Glyphosate is everywhere.”
  -- Ib Pedersen

# Glyphosate-based formulations: Effect on honeybee behaviors*

**Conclusions**

“In this study, we provided new information on the influence of commercially formulated glyphosate at the recommended concentration on the behaviours of honeybees. Our findings showed that the water responsiveness, sucrose responsiveness, learning and memory ability and climbing ability of honeybees were affected by commercially formulated glyphosate at or below the recommended concentration.”

*Qi-Hua Luo et al., Scientific Reports 2021; 11(1): 2115.

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# Effect of Glyphosate on Water Flea Embryos*

- Water fleas are near the bottom of the aquatic food chain
- Tadpoles, salamanders, newts, aquatic insects and many types of small fish feed on water fleas
- When water fleas are exposed to concentrations of Roundup and glyphosate well below the approved regulatory threshold, they suffered from:
  - Embryonic developmental failure
  - Systemic inflammation
  - Collagen degradation
  - Impaired wound healing
  - Disrupted gut microbes
- The animals that eat the water fleas pick up glyphosate from their food
- Effects on water fleas propagate up the food chain

• 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

Newborn white-tailed deer have severely damaged thymuses*


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.
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.


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

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

*Hoy et al., Poultry Fish and Wildlife Science 2015, 3:1
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***


Glyphosate and the Gut
Inflammatory bowel disease, autoimmune arthritis, obesity and metabolic syndrome, and nonalcoholic fatty liver disease can all be traced to imbalances in gut microbiome.

*Figure 1. RS Goldszmid and G Trinchieri. Nat Immunol 2012;13(10):932-8.

Glyphosate and the Gut: Pathogen Overgrowth

- Glyphosate is an antimicrobial agent that preferentially kills beneficial microbes, allowing pathogens to flourish in the gut
- Pathogens cross a leaky gut barrier
- Immune cells infiltrate the gut tissue and release inflammatory cytokines
  - This causes increased risk to inflammatory bowel diseases such as Crohn’s, ulcerative colitis as well as Celiac disease (gluten intolerance)

Inflammatory Bowel Disease

*Figure 20, NL Swanson et al. Journal of Organic Systems 9(2), 2014, p. 25.

Glyphosate and Celiac Disease

Impaired Digestive Enzymes

- Glyphosate has been found as a contaminant in digestive enzymes trypsin, pepsin and lipase*
- Trypsin impairment prevents proteins like gluten in wheat from being digested
- Undigested proteins induce release of zonulin which opens up gut barrier**
- Undigested proteins in the general circulation induce autoimmune disease


Celiac Disease, Glyphosate and Non-Hodgkin’s Lymphoma

- Glyphosate preferentially kills Bifidobacteria*
- Bifidobacteria are depleted in Celiac disease**
- Celiac disease is associated with increased risk to non-Hodgkin’s lymphoma***
- Glyphosate itself is also linked directly to non-Hodgkin’s lymphoma****

**** M. Eriksson et al., Int J Cancer. 2008 Oct 1;123(7):1657-63.
Pathogen Overgrowth in Poultry Microbes Exposed to Glyphosate*


Glyphosate and Autism

*Plot provided by Dr. Martin Michener
Glyphosate and Autism*


Evidence linking autism to Clostridia overgrowth*

- 14 autistic children with gut disorder compared to 21 controls
- Significant increase in *Clostridia* species in the gut in autistic children
- Associated with reduced tryptophan levels and increased expression of inflammatory markers
  - Tryptophan is a product of the shikimate pathway, which glyphosate blocks
  - Macrophages in inflamed tissue take up tryptophan, reducing bioavailability to the brain
- Proposed role for antibiotics
  - Glyphosate is a patented antimicrobial agent (2010)

*RA Luna et al., Cellular and Molecular Gastroenterology and Hepatology 2017;3(2): 218-230
Elevated Urinary Glyphosate and Clostridia Metabolites With Altered Dopamine Metabolism in Triplets With Autistic Spectrum Disorder or Suspected Seizure Disorder: A Case Study *

William Shaw, PhD

- Triplets: two boys, one girl. Both boys have autism and girl has seizure disorder
- Very high levels of glyphosate in urine in all three
- *Clostridia* overgrowth due to glyphosate disruption of gut microbes
  - Clostridia produce toxins which block the conversion of dopamine to norepinephrine.
  - Damage to neurons in the brain through oxidative stress

*W. Shaw. Integrative Medicine 2017;16(1);50-57.

"In this work, we state a possible link between Gly[phosate]-induced dysbiosis and cognitive and motor aggravations in neurodegenerative and neurodevelopmental pathologies, such as autism spectrum disorder (ASD). Hence, we review the negative impact that Gly[phosate]-induced dysbiosis may have on depression/anxiety, autism, Alzheimer’s and Parkinson’s diseases."
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

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 \(\rightarrow\) low estrogen and low vitamin D
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**


“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

CYP Enzymes Activate Vitamin D3*

This takes place in the liver, and the same enzymes detoxify a number of pharmaceutical drugs

* Figure 1 in Glenville Jones et al., Anticancer Research 26: 2589-2596 (2006)

“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.
“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.

“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.
Recapitulation

• Glyphosate causes over-representation of Clostridia in the gut, depleting tryptophan → this maps to brain damage through inflammation
• 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

Glyphosate and Endocrine Disruption
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  
  - Diminished serum progesterone and elevated serum estrogen in exposed mice  
- 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]  

Zen Honeycutt on Glyphosate as an Endocrine Disruptor  

- Zen Honeycutt is the Founder of the advocacy group Moms Across America  
- On Dec. 10, 2020, a meeting of the Developmental and Reproductive Toxicant Identification Committee (DARTIC) was assembled to determine which chemicals might be endocrine disruptors  
  - Under the California EPA’s Office of Health Hazard Assessment (OEHHA)  
- Zen Honeycutt presented slides showing compelling evidence that glyphosate is an endocrine disruptor  
  - The committee subsequently voted that glyphosate should be labelled as a HIGH probability endocrine disruptor on the Prop 65 list  

*https://www.momsacrossamerica.com/winGlyphosateOne
“Glyphosate-Based Herbicides Produce Teratogenic Effects on Vertebrates by Impairing Retinoic Acid Signaling”* 

* Glyphosate 

- Retinoic Acid 

  inhibition of expression 

  Shh 

  *Cyclopia* 

  *Microcephaly* 

  *Affected cranial neural crest* 

  *Craniofacial malformations* 

  Otx2 

  Sox9 


** Glyphosate and Anencephaly**

- Yakima, Benton and Franklin counties in Washington State had an unusually high number of pregnancies affected by the birth defect, anencephaly (baby born with no cerebral cortex) during 2012 and 2013.
- 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**

“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

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

Farm Wars 3/6/14

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The evidence reviewed in this paper offers a multitude of very specific routes by which glyphosate might be impairing embryological and fetal development in ways that significantly increase the risk of anencephaly, and epidemiological and animal studies on glyphosate support a link to impaired neurodevelopment in the brain.”

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“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.
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 children (F1), (F2) and great-grandchildren (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.


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Epigenetic transgenerational toxicology through germline alterations by glyphosate*

“Negligible pathology was observed in the F0 or F1 generations from direct exposure, but a significant increase in pathology and disease was observed in the grand offspring F2 generation and great-grand offspring F3 generation.”

“Therefore, the previous observations demonstrate negligible disease in the direct-exposed generations, but significant disease in subsequent generations, termed generational toxicology, that is mediated through glyphosate-induced epigenetic transgenerational inheritance mechanisms.”

How to Stay Healthy in a Toxic World

Go Organic!
Eat Natural Probiotic Foods

• Sauerkraut and apple cider vinegar contain Acetobacter, one of the very few classes of microbes that can metabolize glyphosate
• Kombucha and kimchi do too!

Some Important Nutrients

• Curcumin
• Garlic
• Vitamin C
• Methyl tetrahydrofolate
• Cobalamin (B12)
• N-acetyl cysteine
• Glutathione
• Taurine
• Epsom salt baths
Treating Glyphosate Poisoning in 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.

Biochar, Bentonite and Zeolite to maintain healthy microbial distribution in poultry*

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

My New Book!

- Expected to be released in June 2021
- Presents extensive data on glyphosate toxicity to animals and humans
- Argues 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
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 causes gut dysbiosis, which is increasingly recognized as a major driver behind multiple chronic diseases
• Glyphosate’s disruption of gut microbes, sex hormones and CYP enzymes can play a role in autism
• Many papers published in the last few years are revealing remarkably severe effects of low doses of glyphosate in animal studies, including transgenerational effects
• I believe that glyphosate should be banned worldwide

“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