Glyphosate: Is it the Primary Cause of the Autism Epidemic?

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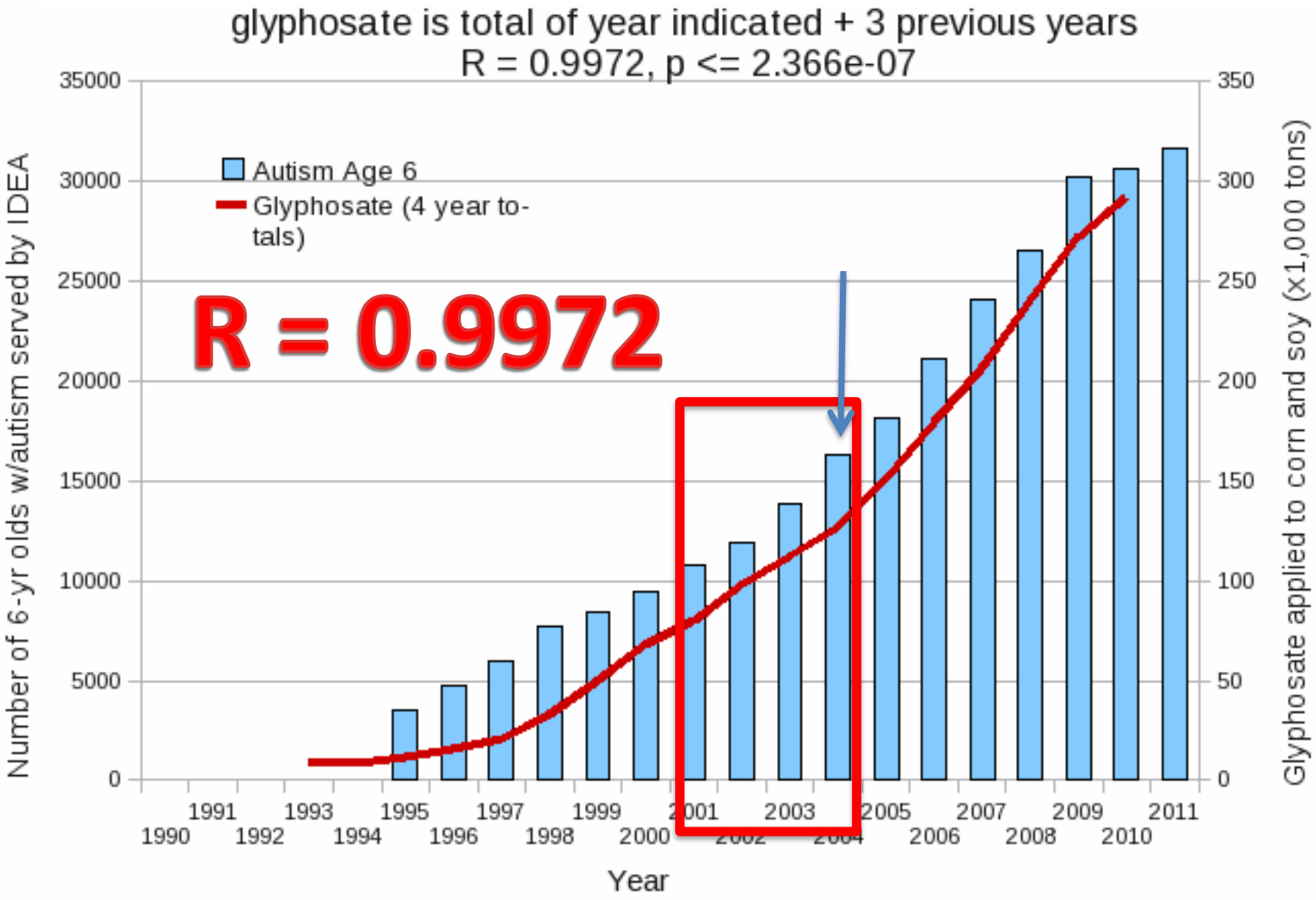
MIT CSAIL
TACA Workshop
March 28, 2019

Outline

- Introduction
- Glyphosate and the Gut
- Glyphosate and Manganese
- What you can do!
- Summary

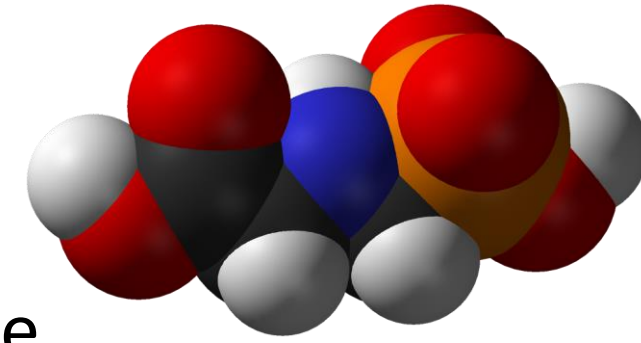
Autism Prevalence: 6 year olds*



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

Some Foods Containing Glyphosate

Is Glyphosate Toxic?



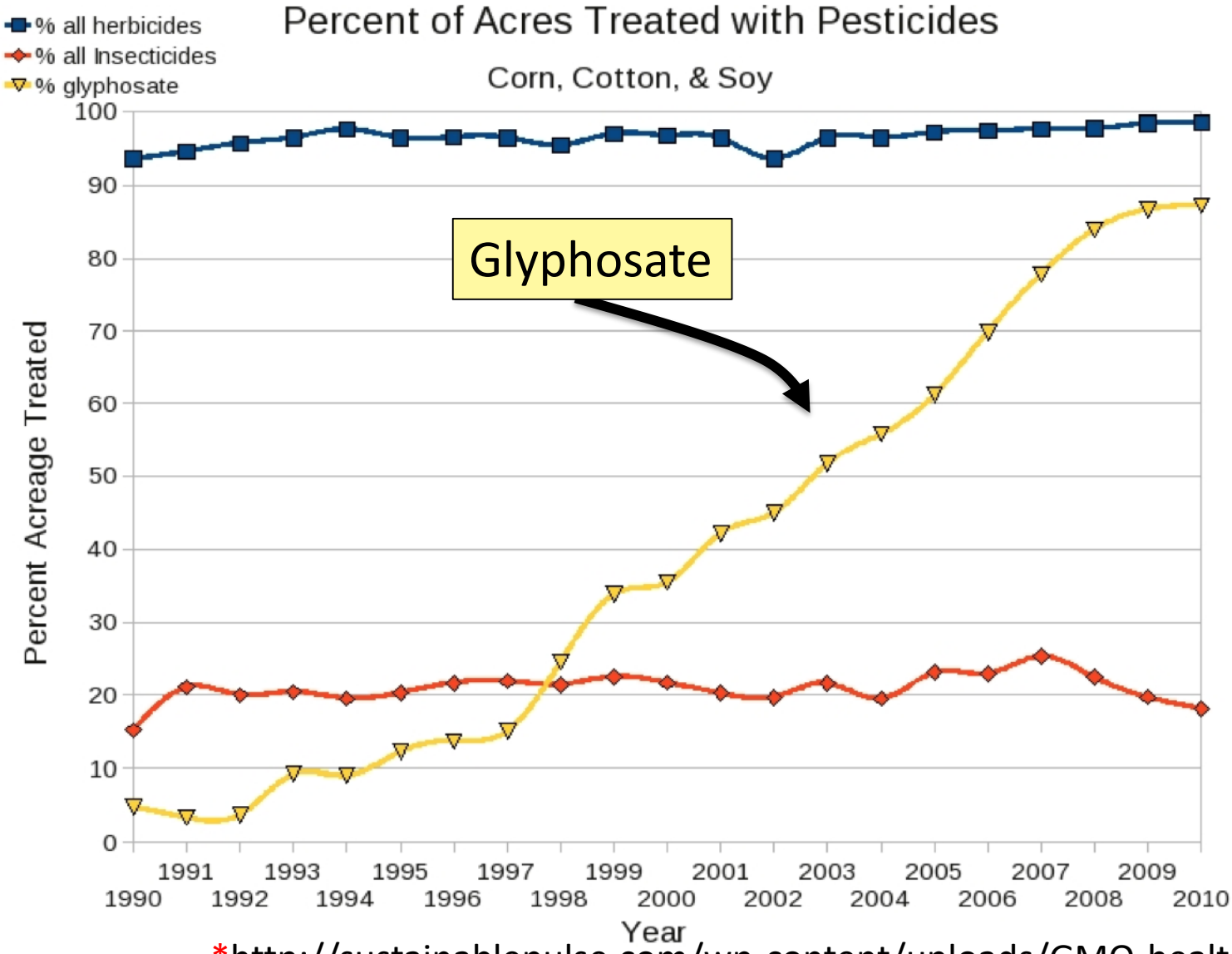
- Monsanto has argued that glyphosate is harmless to humans because our cells don't have the shikimate pathway, which it inhibits
- However, our gut bacteria DO have this pathway
  - We depend upon them to supply us with essential amino acids (among many other things)
- Other ingredients in Roundup greatly 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*

- Disrupts gut microbes leading to overgrowth of pathogens and inflammatory/leaky gut syndrome
- 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
  - Leads to disrupted bile flow and impaired fat digestion

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

Glyphosate vs. Other Pesticides: Usage in the United States*



*http://sustainablepulse.com/wp-content/uploads/GMO-health.pdf

Sobering Statistics on Glyphosate Residues*

- Parts per *trillion (ppt)*: increased proliferation of breast cancer cells in vitro
- 0.1 ppb:
  - Altered the gene function of over 4000 genes in the livers and kidneys of rats
  - Severe organ damage in rats
  - Permitted level for glyphosate and all other herbicides in EU tap water
- 10 ppb: demonstrated toxic effects on the livers of fish
- 700 ppb: Permitted level for glyphosate in U.S. tap water
- 11,900 ppb: found in Genetically Modified (GMO) soybeans

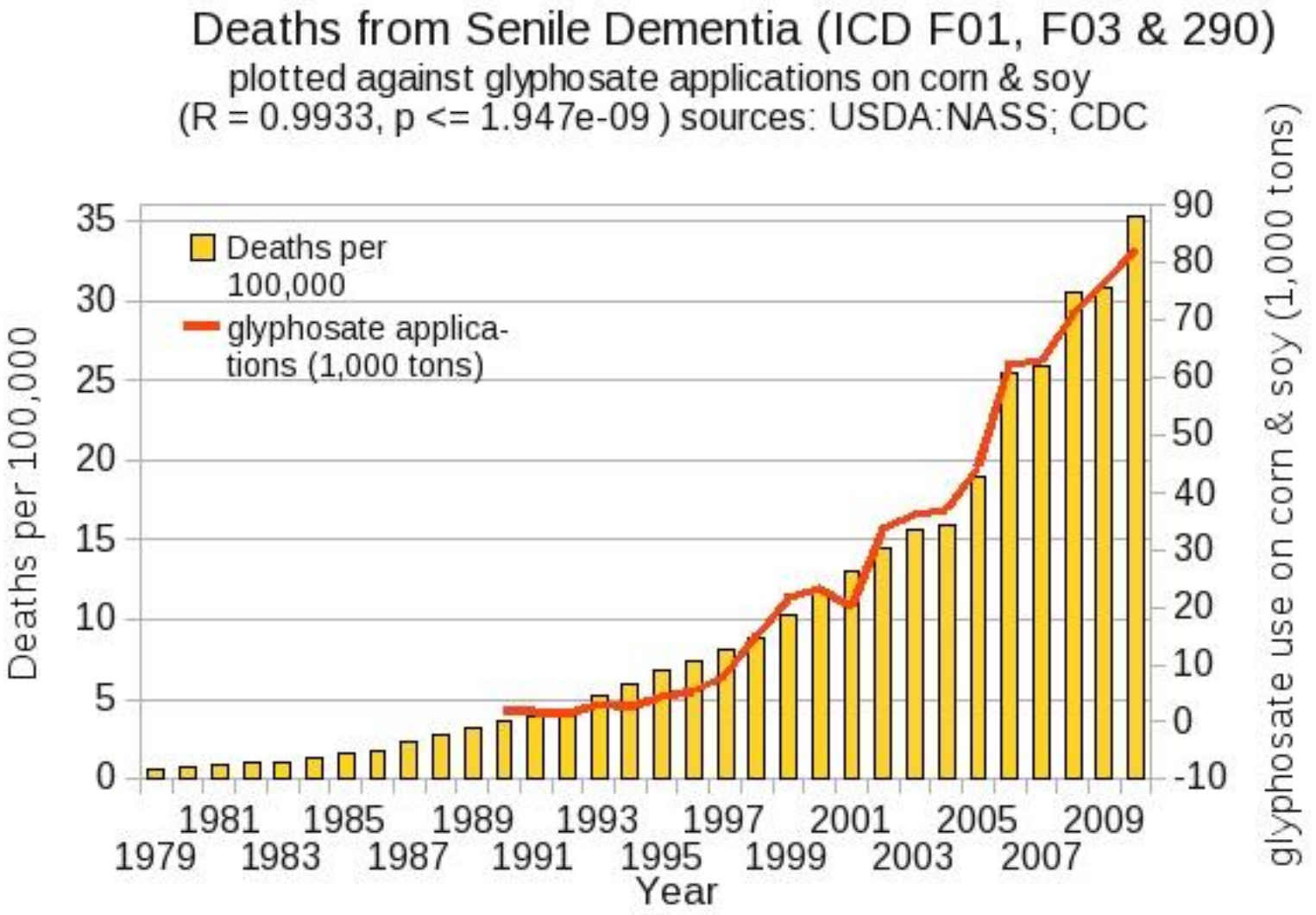
*http://detoxproject.org/glyphosate-in-numbers/

Some Biomarkers for Autism

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

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

Dementia and Autism Have Much in Common



Plot kindly provided by Nancy Swanson

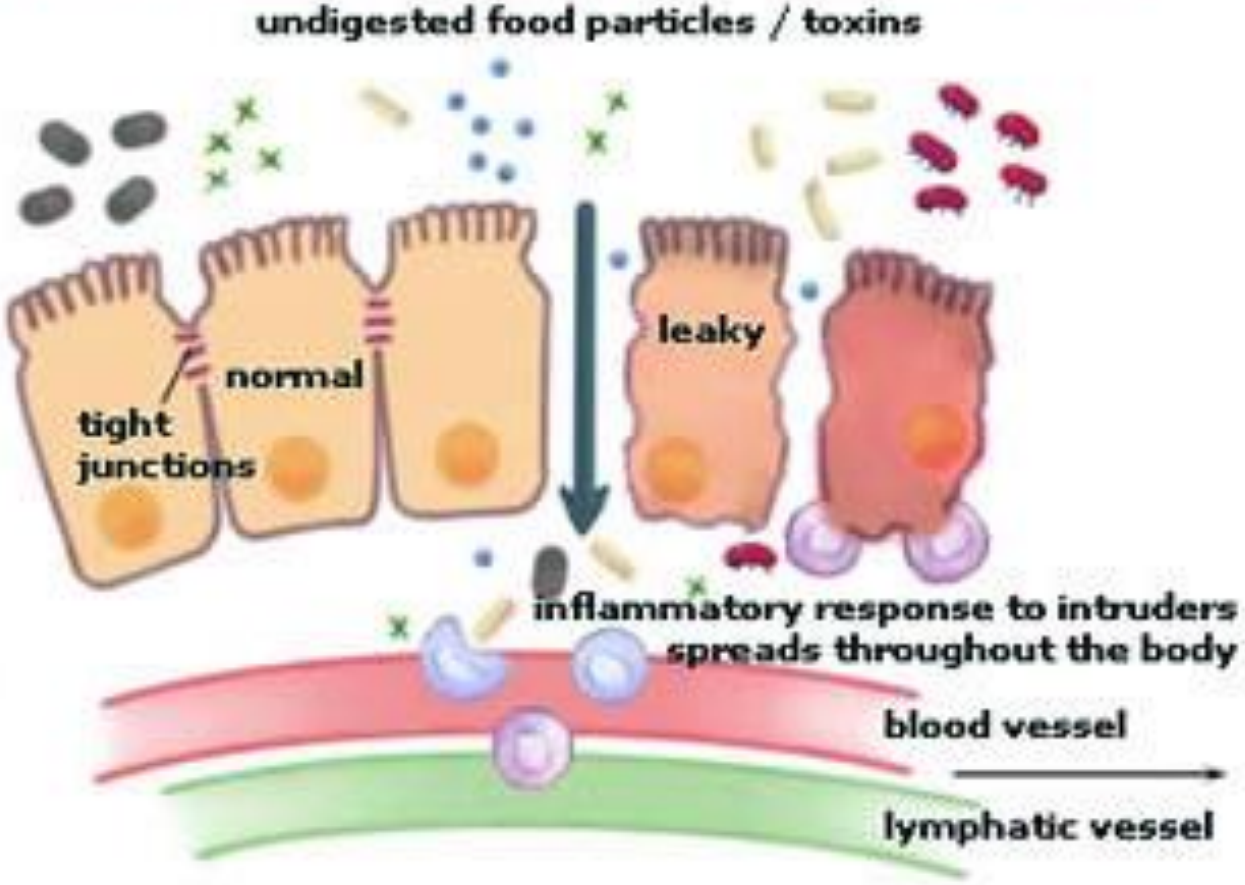
Glyphosate and the Gut

Autism and the Gut*

"Prospective, controlled studies suggest that as many as 70% of autistic children exhibit chronic GI-related symptoms [1,5,6] including diarrhea, laxative-dependent constipation, abdominal distension, failure to thrive, weight loss, feeding problems, and abdominal pain related to extreme irritability, aggression, and self-injury."

*SJ Walker et al. PLOS One March 2013; 8(3):e58058.

LEAKY GUT


undigested food particles / toxins
normal
tight
junctions
leaky
inflammatory response to intruders
spreads throughout the body
blood vessel
lymphatic vessel

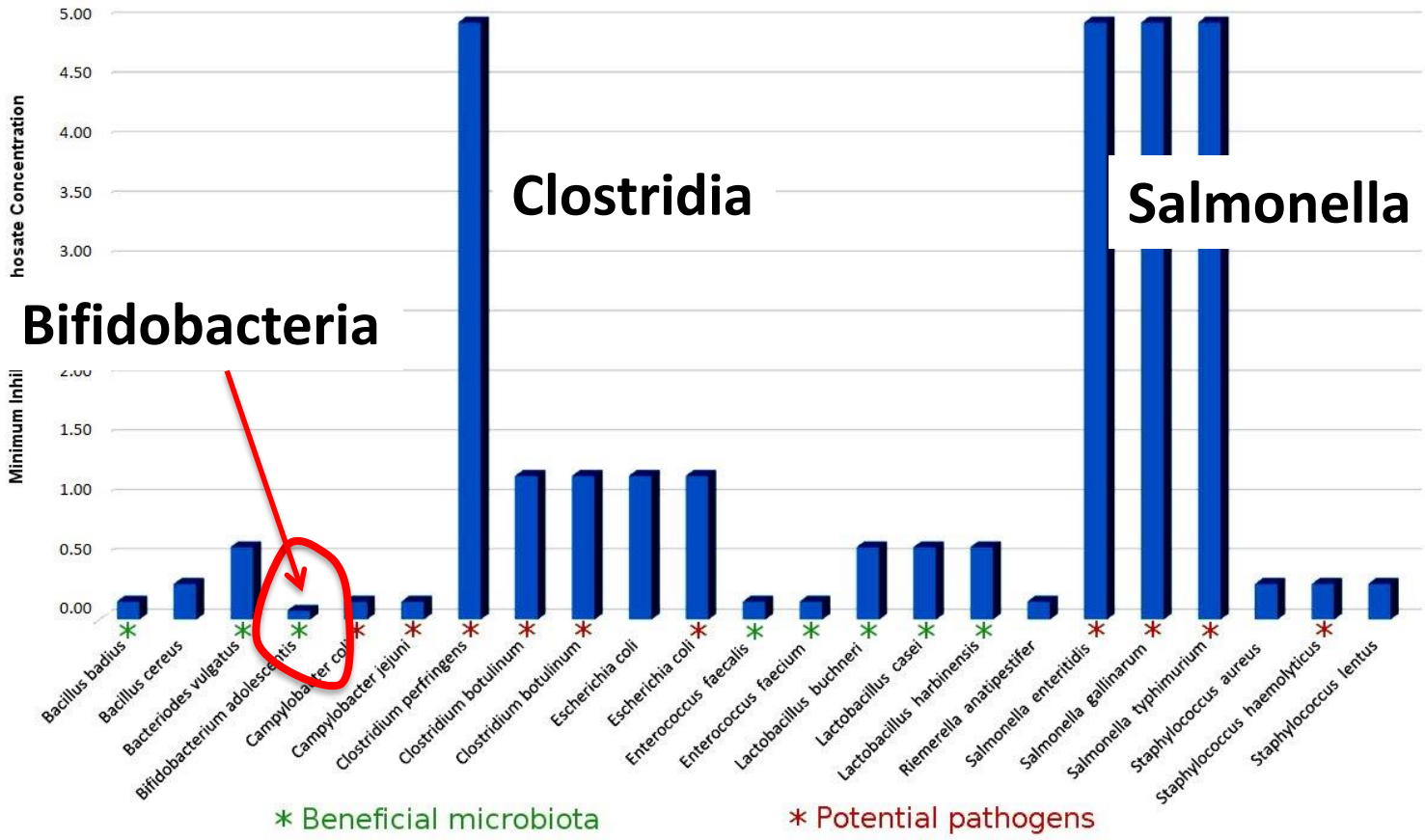
Glyphosate and the Gut: Pathogen Overgrowth*

- Glyphosate is an antimicrobial agent that preferentially kills beneficial microbes, allowing pathogens to flourish in the gut
- Immune cells invade the gut and release inflammatory cytokines
  - This causes increased risk to inflammatory bowel diseases such as Crohn's and ulcerative colitis

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

Pathogen Overgrowth in Poultry Microbes Exposed to Glyphosate*

Shehata AA, Schrödl W, Aldin AA, Hafez HM, Krüger M. The effect of glyphosate on potential pathogens and beneficial members of poultry microbiota in vitro. Curr Microbiol. 2013 Apr;66(4):350-8.



*Plot provided by Dr. Martin Michener

Glyphosate and the Gut: Digestive Enzymes

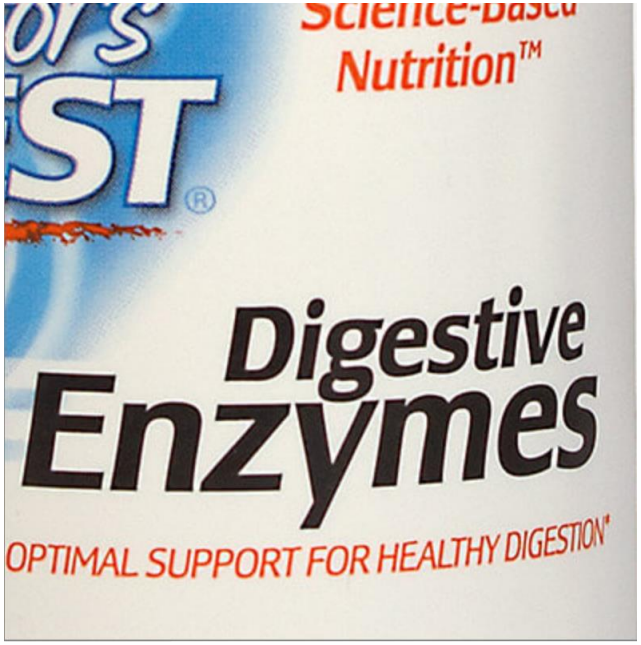
- Glyphosate has been found as a contaminant in digestive enzymes trypsin, pepsin and lipase*
- Trypsin impairment prevents proteins like gluten in wheat from being digested
- Undigested proteins induce release of zonulin which opens up gut barrier**
- Zonulin lingers because trypsin is defective

*A Samsel and S Seneff. J Biol Phys Chem 2017;17:8-32

** JJ Gildea et al. J Clin Nutr Diet. 2017, 3:1.

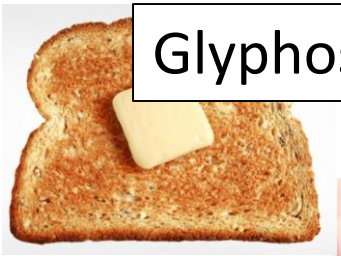
Trypsin, Pepsin and Lipase are all contaminated with glyphosate*

Enzyme	Glyphosate (PPB)
Pepsin (ELISA)	<40
Pepsin (GC-MS)	430
Pepsin (HPLC-MSMS)	290
Trypsin (ELISA)	62
Lipase (ELISA)	24

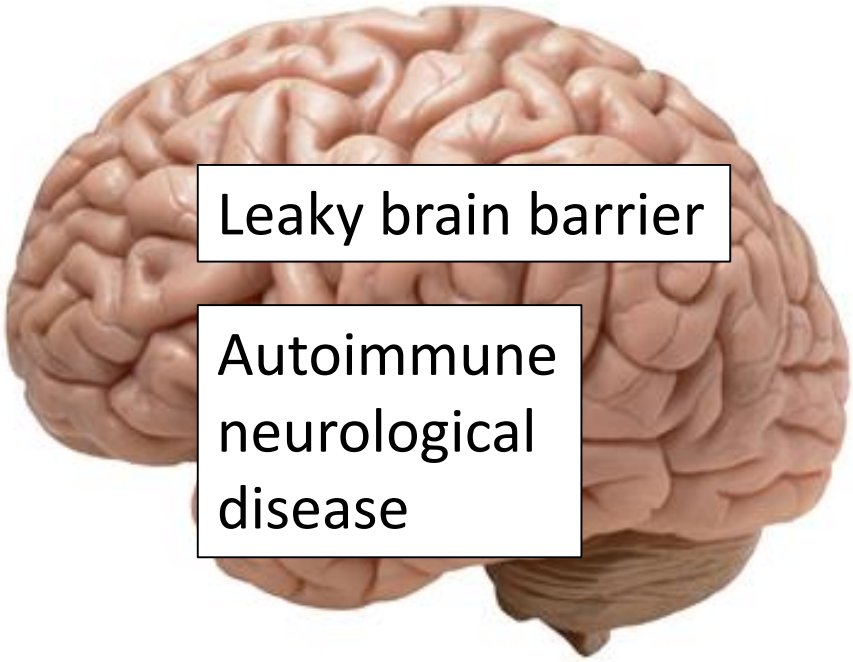


*A Samsel and S Seneff. Journal of Biological Physics and Chemistry 2017;17: 8-32

A Scenario for Gluten Intolerance



Glyphosate in wheat

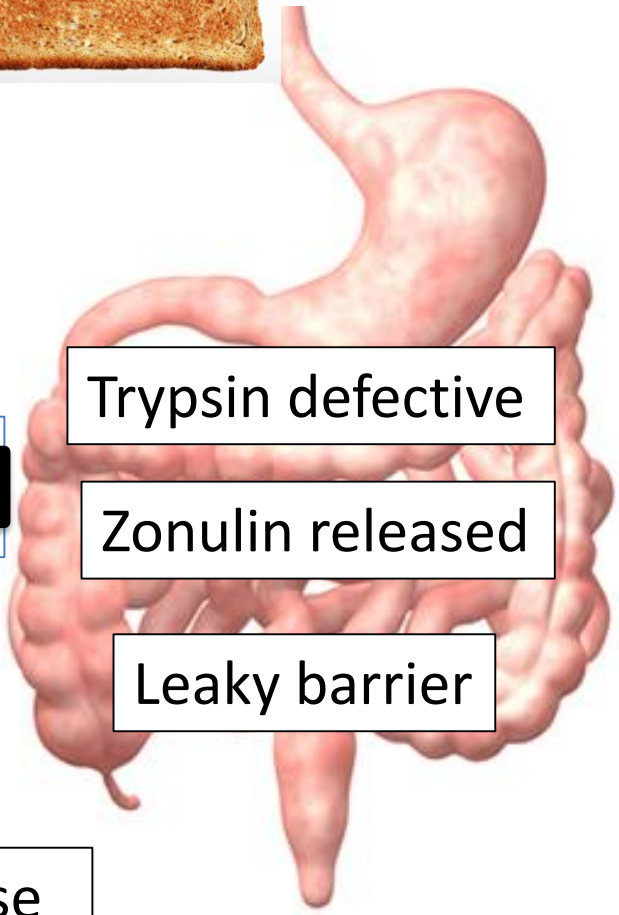


Leaky brain barrier

Autoimmune neurological disease

Zonulin

Gliadin



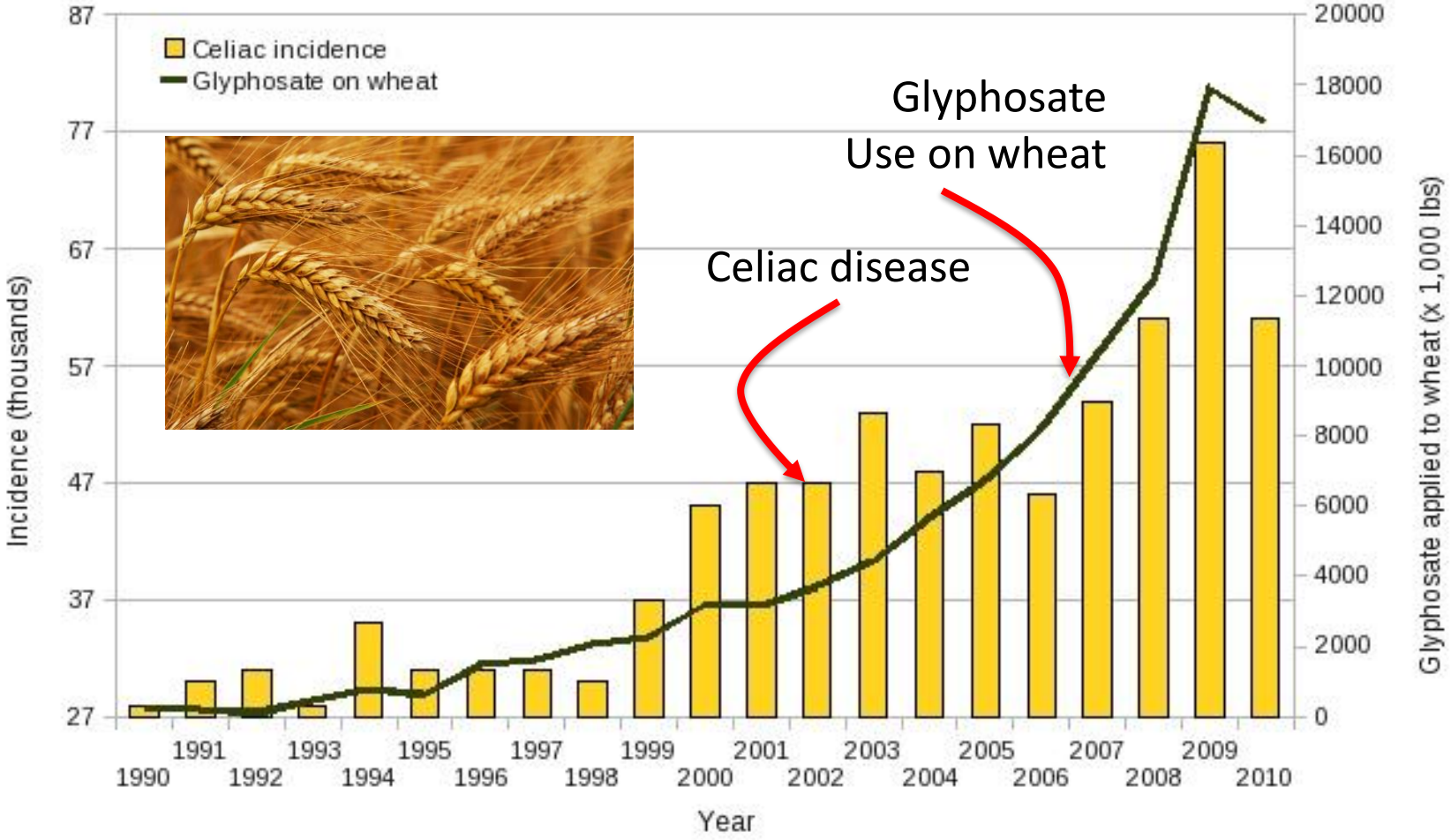
Trypsin defective

Zonulin released

Leaky barrier

Systemic immune response induces multiple complex symptoms

Glyphosate and Celiac Disease*



*Samsel and Seneff, Interdiscip Toxicol. 2013;**6**(4): 159–184.

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****

*A.A. Shehata et al., Curr Microbiol. 2013 Apr;66(4):350-8.

** M. Velasquez-Manoff, NY Times Sunday Review, Feb. 23, 2013.

*** C. Catassi et all, JAMA. 2002 Mar 20;287(11):1413-9.

****M. Eriksson et al., Int J Cancer. 2008 Oct 1;123(7):1657-63.

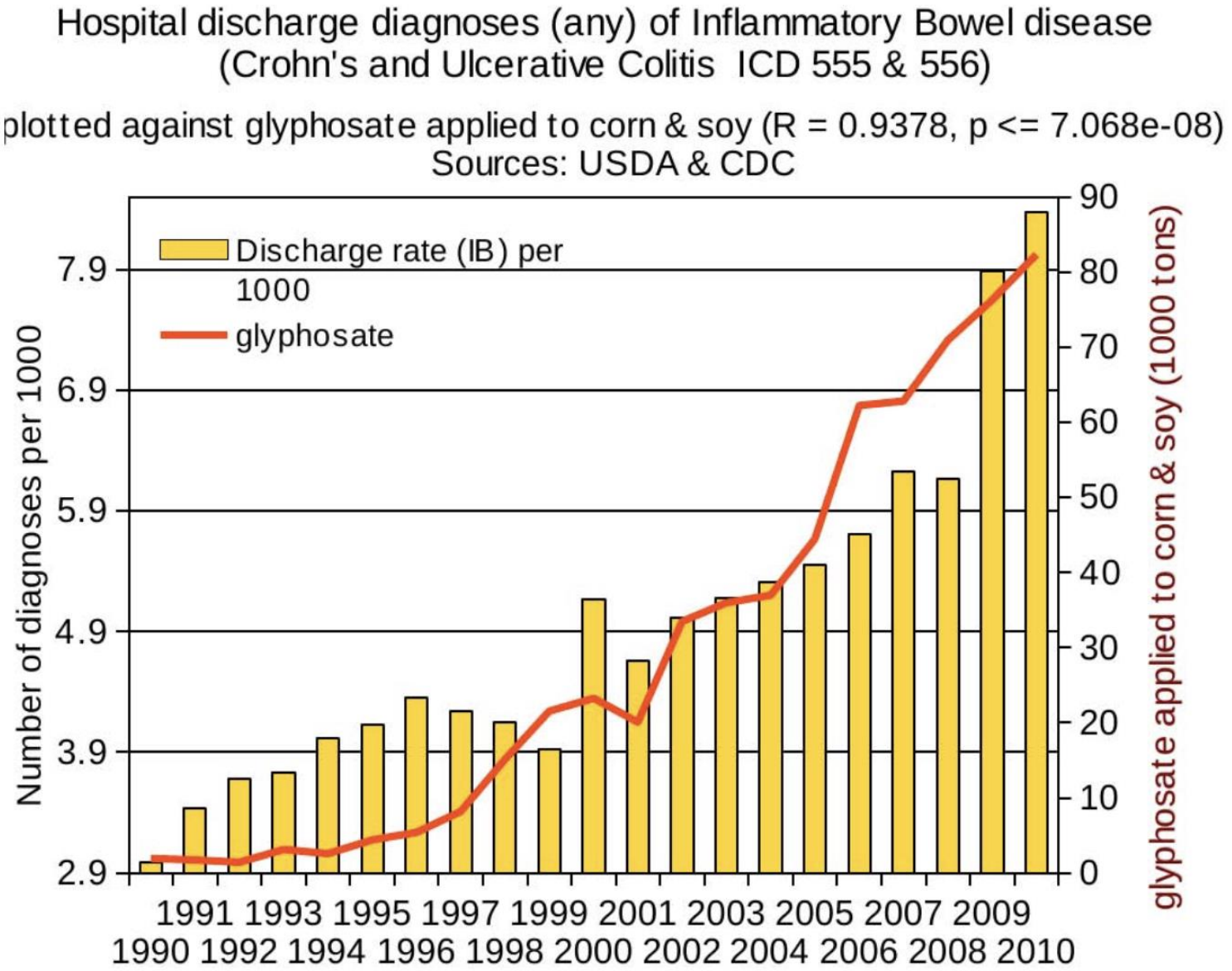
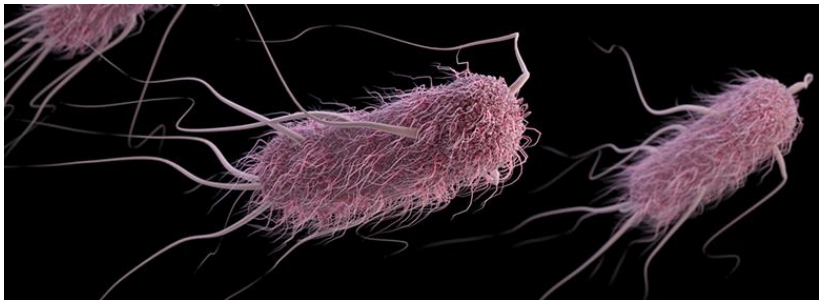


*Figure 20, NL Swanson et al. Journal of Organic Systems 9(2), 2014, p. 25.

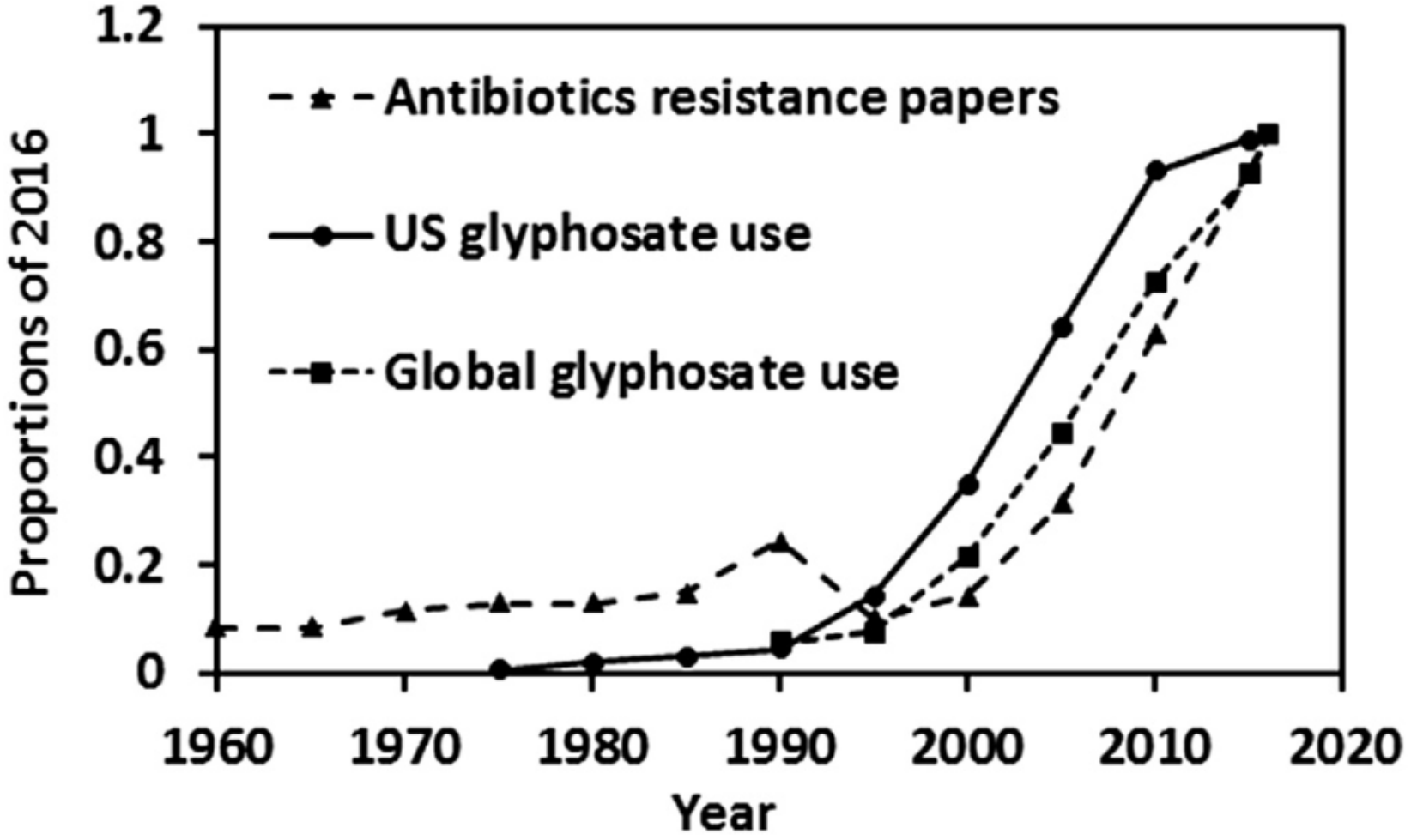
Glyphosate Induces Antibiotic Resistance*



- Actinobacteria produce a free radical scavenger in response to glyphosate that provides resistance to a wide range of antibiotics, including penicillin
- E. coli exposed to glyphosate develop an "efflux pump" that increases resistance to the fluoroquinolone Ciprofloxacin and the aminoglycoside Kanamycin.
  - Same effect observed in Salmonella exposed to glyphosate

*AHC Van Bruggen et al. Science of the Total Environment 2018;616-617: 255–268.

Glyphosate Usage and Papers on Antibiotic Resistance*



*AHC Van Bruggen et al. Science of the Total Environment 2018;616-617: 255–268.

A BTBR Mouse Model of Autism*

These mice had all the mouse features of autism

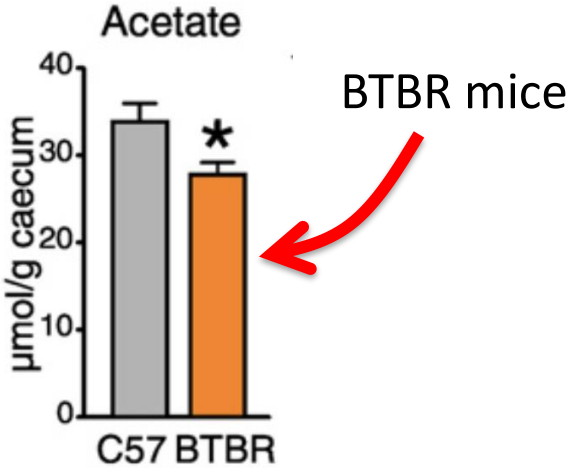
They were fed "standard rodent chow" – glyphosate contaminated?

Some features in the gut:

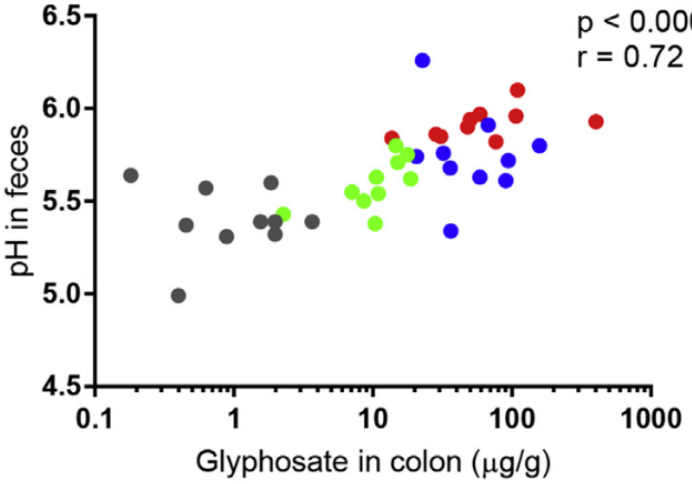
- Reduced levels of bile acids
  - Due to impaired CYP7A1 activity in the liver
- Further reduced levels of secondary bile acids
  - Impaired metabolism by gut microbes
- Reduced levels of Lactobacillus and Bifidobacteria
  - Microbes that metabolize bile acids
  - These microbes are preferentially killed by glyphosate
- Serotonin deficiency
  - Serotonin is derived from tryptophan, a product of the shikimate pathway which glyphosate disrupts

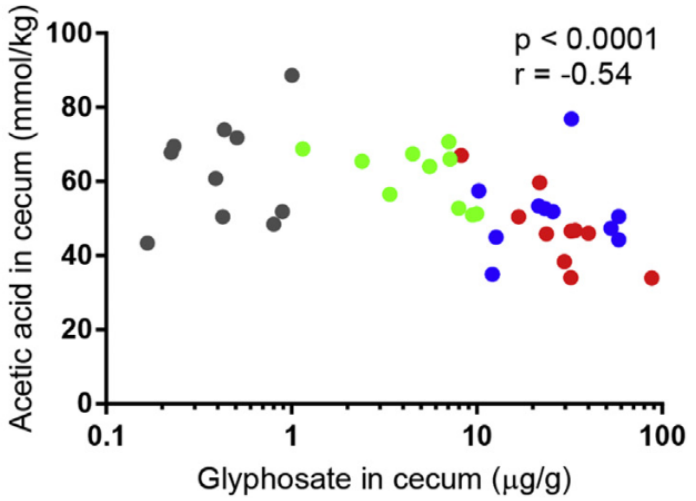
*AV Glubeva et al. EBioMedicine. 2017 Oct;24:166-178.

BTBR mice have low acetate, and glyphosate disrupts acetate synthesis in gut*



Children with autism had only 3.5 mg/ml acetate in stool samples compared to 5.1 in controls.**





*LN Nielsen et al. Environmental Pollution 2018;233:364e376.

**Adams et al. BMC Gastroenterology 2011; 11:22.

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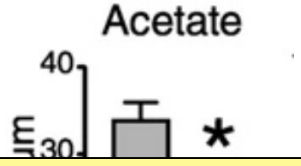
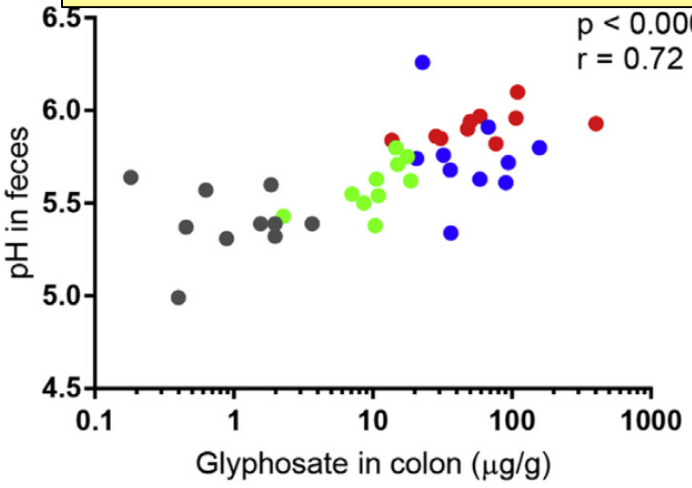
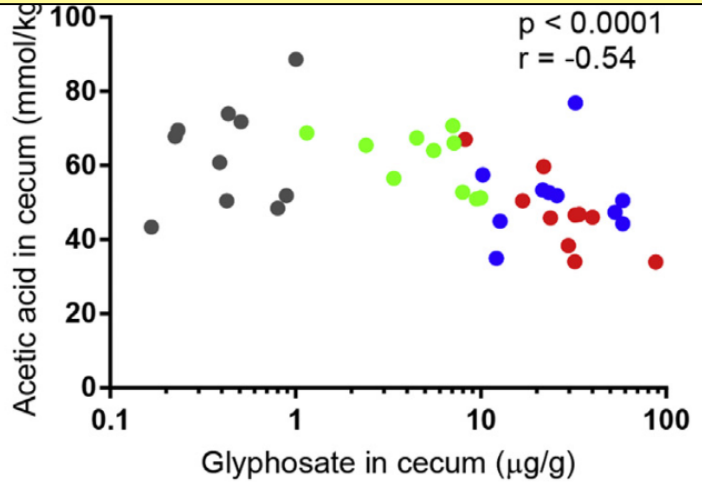


BTBR mice

Children with autism had

Elevated pH linked to glyphosate exposure results in small intestinal bacterial overgrowth (SIBO)





*LN Nielsen et al. Environmental Pollution 2018;233:364e376.

**Adams et al. BMC Gastroenterology 2011; 11:22.

Glyphosate, Pathogens, Autism*

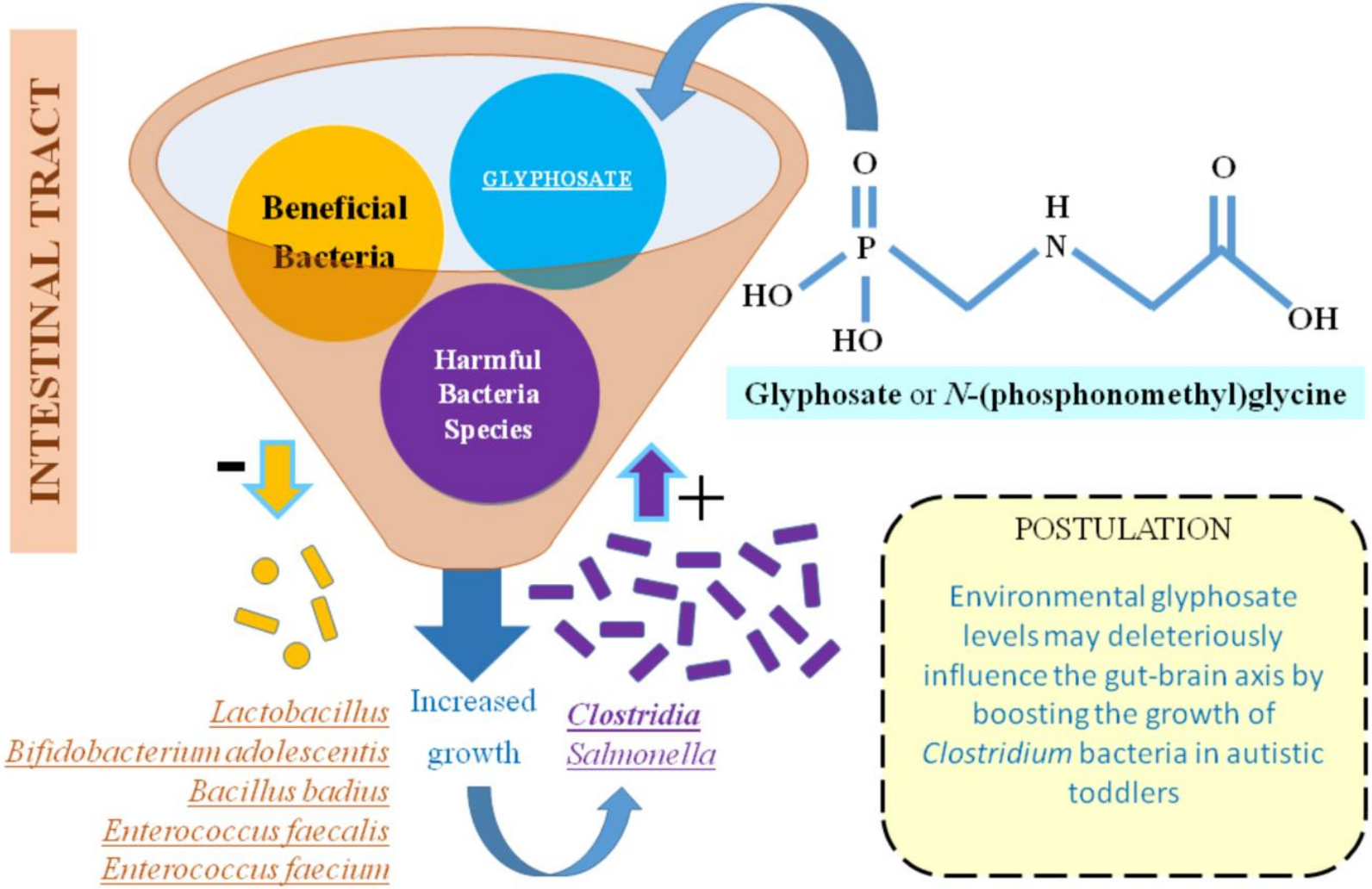


*Figure 2. I Argou-Cardozo and F Zeidán-Chuliá. Med. Sci. 2018; 6: 29.

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

CASE REPORT

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 HPHPA and p-cresol, 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.

Recapitulation

- Glyphosate contamination in food proteins makes them hard to break down
  - This leads to autoimmune disease
- Digestive enzymes are contaminated with glyphosate
  - Undigested proteins induce Celiac disease and leaky gut
- Glyphosate is a key factor in the emergence of antibiotic resistant pathogens
- The BTBR mouse model of autism is consistent with glyphosate damage in the gut
- Glyphosate promotes Clostridia overgrowth
  - This induces inflammatory bowel disease, an epidemic today
  - Autism has been linked to Clostridia overgrowth
  - Clostridia release toxins that induce an inflammatory response

Glyphosate and Manganese

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

Dr. Arden Andersen, D.O.,

Food Plague Primer: Glyphosate and Genetically Engineered Crops

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

Glyphosate Depletes Iron, Manganese and Zinc in Plants*

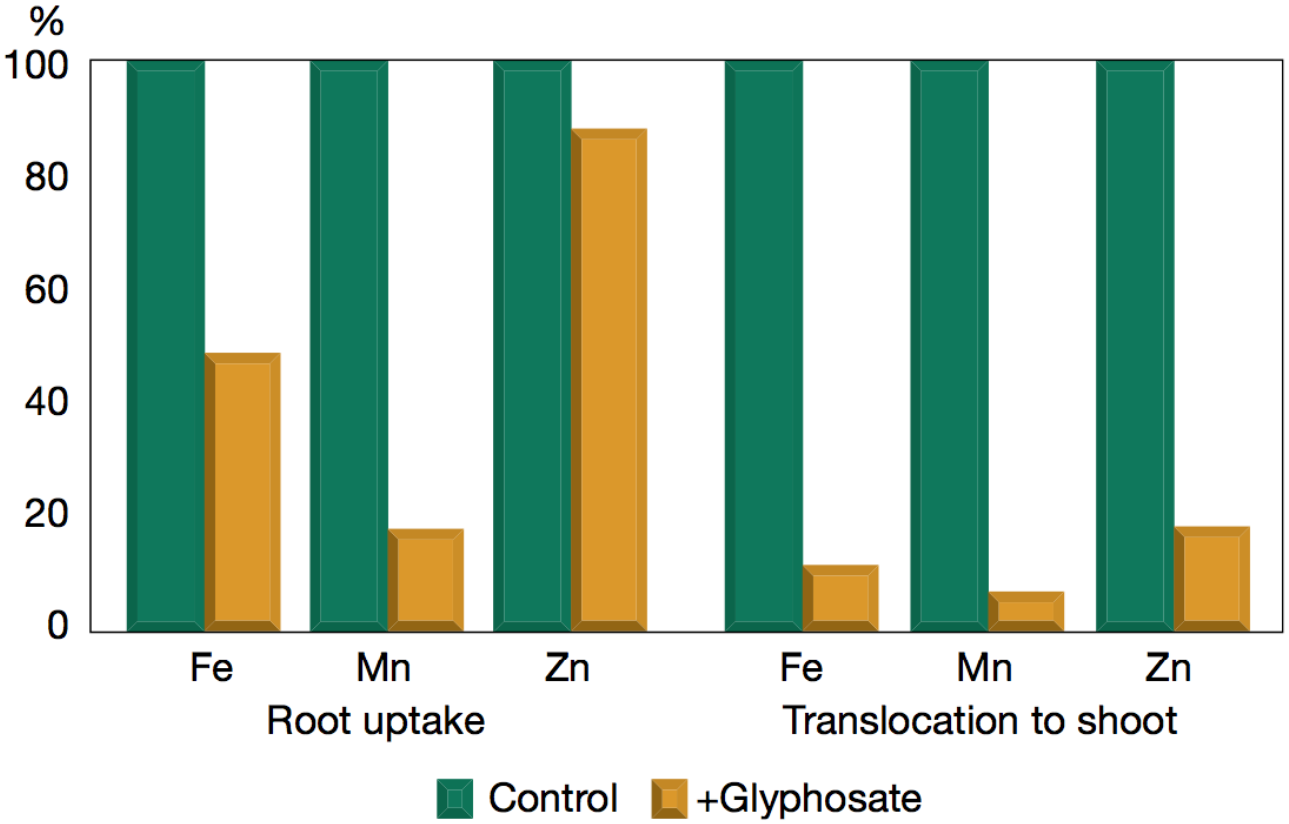
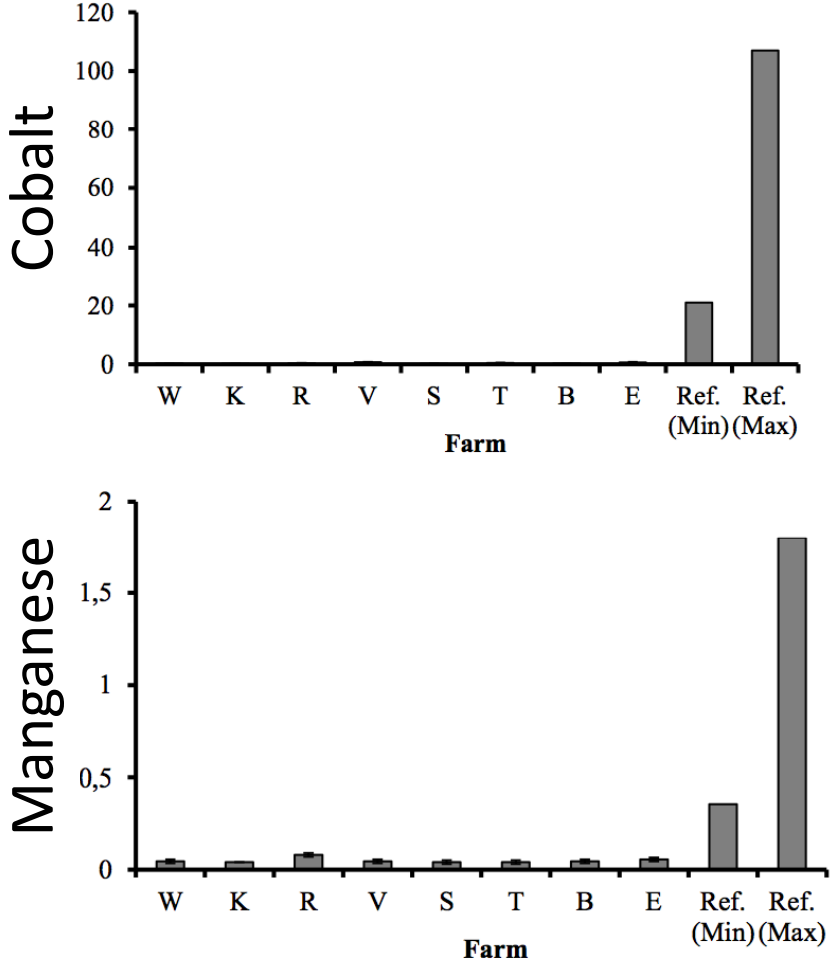


Figure 1. Effect of glyphosate* on nutrient uptake and translocation by "non-target" plants, Eker, et al. 2006. (* 2.5% of recommended herbicidal rate of glyphosate.)

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

Severe Deficiency in Serum Manganese and Cobalt in Cows*



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

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

Low Manganese in Teeth Linked to Autism*

- Studied lead, mercury and manganese levels in tooth enamel of shed primary teeth in 84 children
- Manganese accumulated after birth was down by 60% in autistic children
- *No other result was statistically significant*

*MM Abdullah *et al., J Autism Dev Disord*. 2012 Jun;42(6):929-36.

Some Consequences of Manganese Deficiency

- Lactobacillus critically depend on manganese
- Manganese superoxide dismutase protects mitochondria from oxidative damage
- Manganese is essential for detoxing glutamate (neurotoxin)
- Pituitary depends on manganese to release thyroid stimulating hormone
- Chondroitin sulfate synthesis in bones

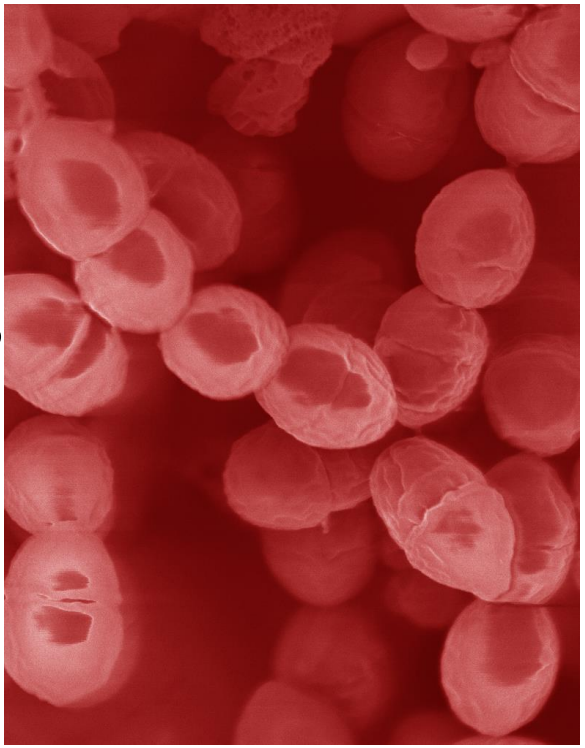
Glyphosate Kills Beneficial Bacteria*

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

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

Lactobacillus Depends on Manganese!*

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



Lactobacillus levels are low in the gut in association with autism

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

Lactobacillus Alleviate Anxiety*

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

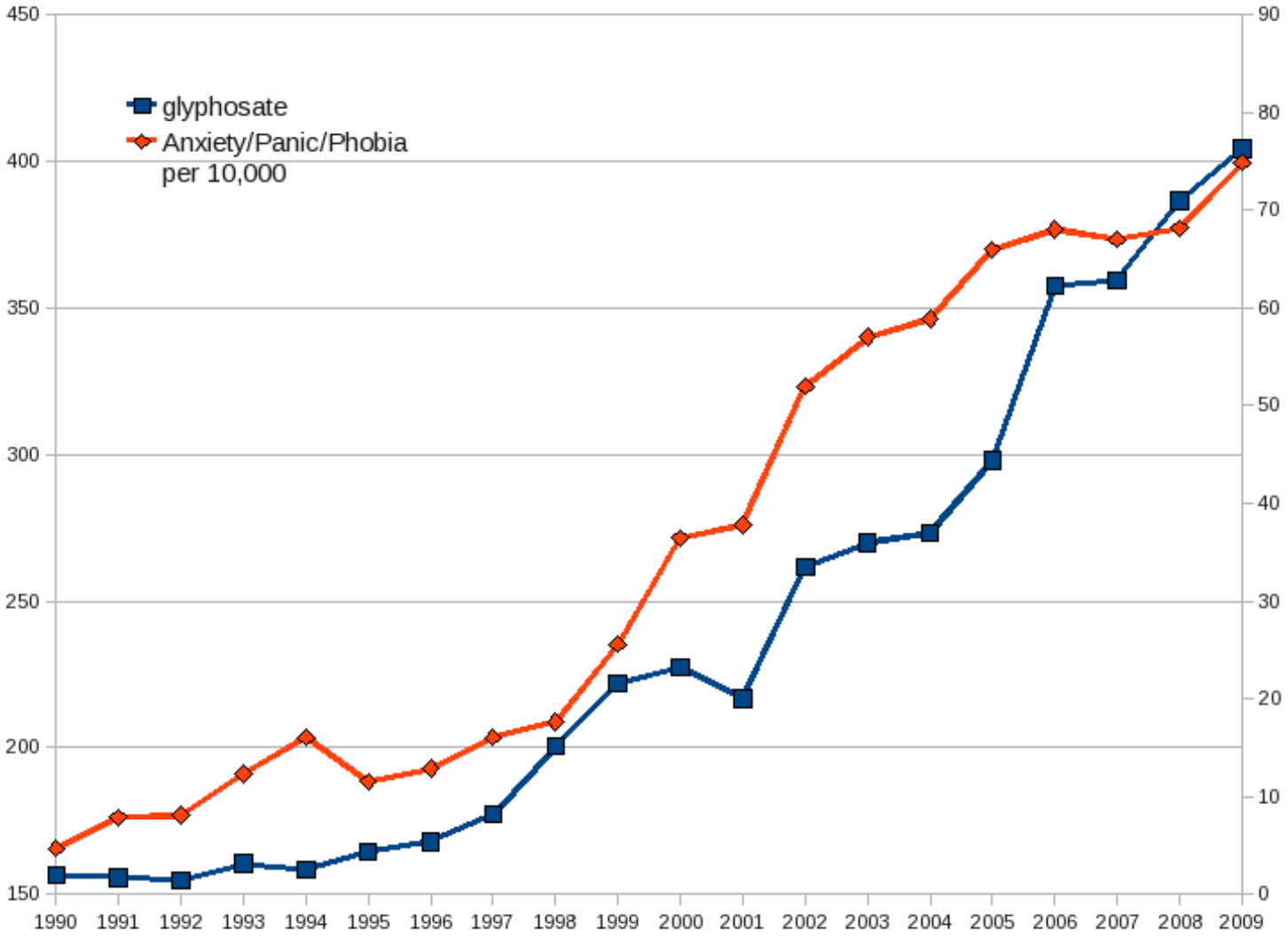
*R Av et al. Gut Pathog. 2009 Mar 19;1(1):6. doi: 10.1186/1757-4749-1-6.

Anxiety and Autism*

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

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

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

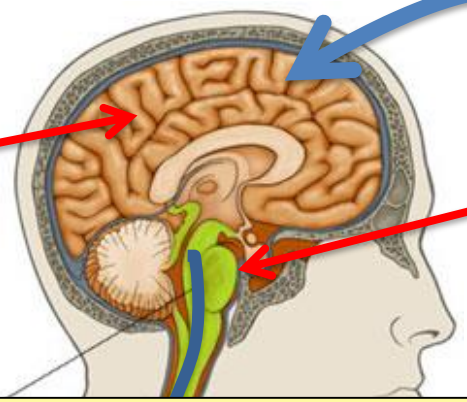


*Plots provided by Dr. Nancy Swanson

It’s not just deficiency!

Too little manganese in the cortex

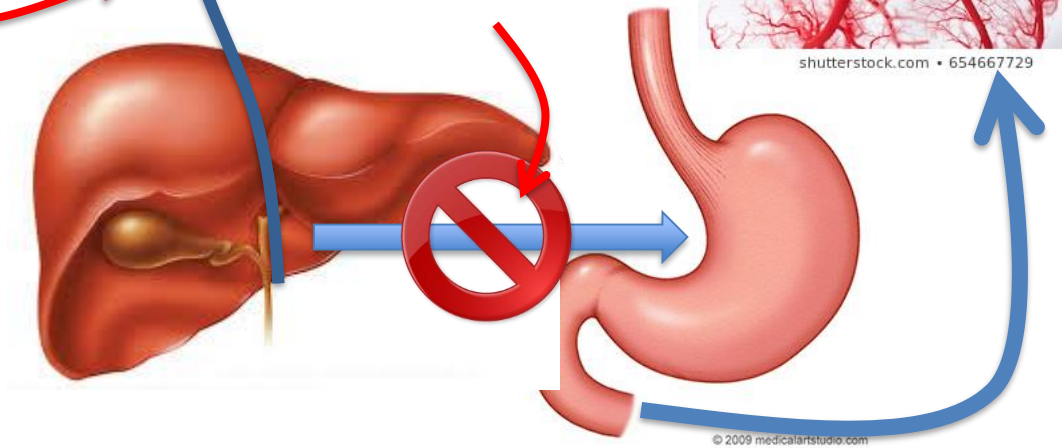
Too much manganese in the brain stem



Excessive manganese in the brain stem is linked to ADHD*

Vagus N

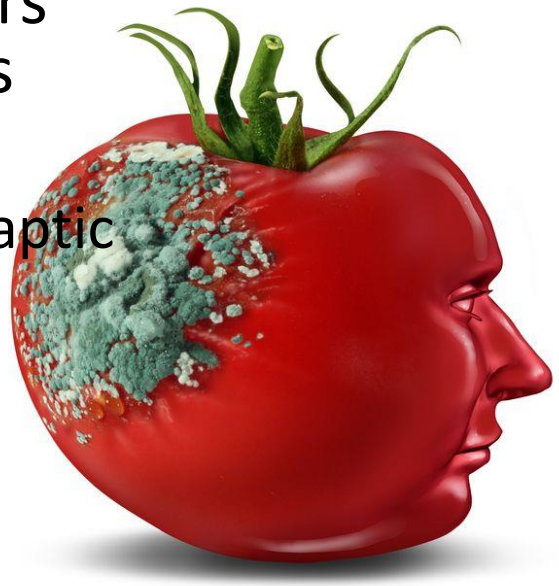
Bile acids



*JJ-H Shih et al. Neuropsychiatr Dis Treat. 2018; 14: 1831-1842.

Glyphosate and Glutamate*

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

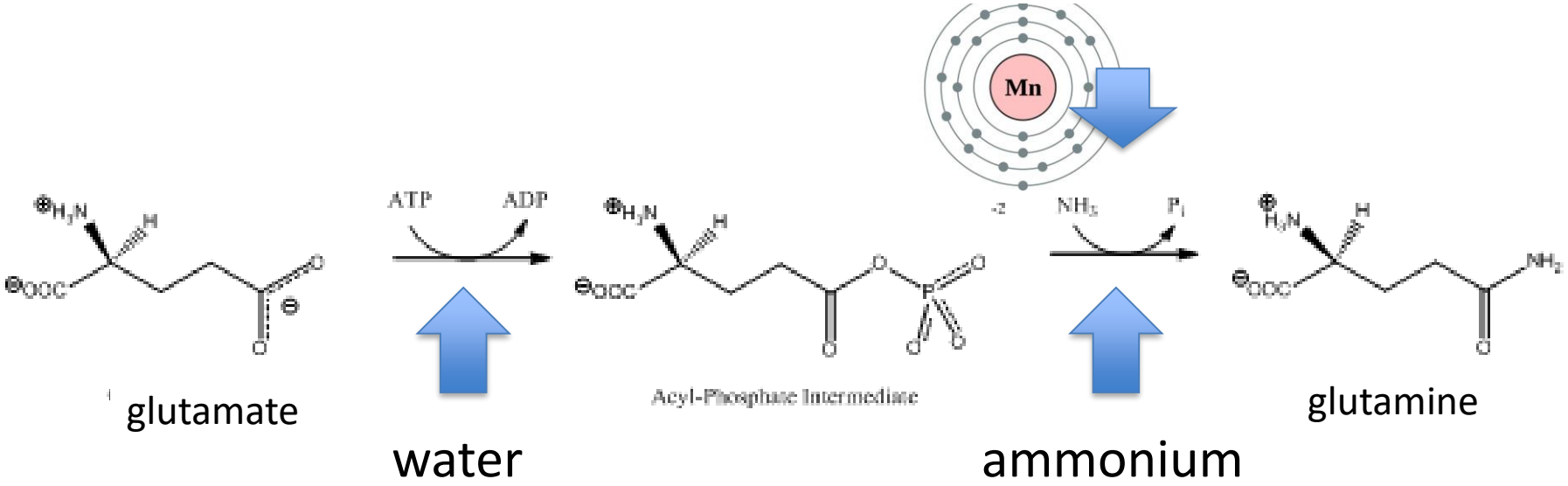


- Chronic exposure:
  - Decreased glutamate uptake and metabolism
  - Induced calcium uptake
  - Induced oxidative stress

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

Glutamine Synthesis Depends on Manganese!

Glutamine synthetase



glutamate

water

ammonium

glutamine

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

"Alteration of Plasma Glutamate and Glutamine Levels in Children with High-Functioning Autism"*

Amino acid	Control	HFA	*p*-value
Alanine	326.1±61.6	300.3±55.0	0.145
α-Aminobutyric acid	18.8±3.8	18.7±5.4	0.971
Arginine	89.1±19.0	95.3±18.5	0.279
Asparagine	40.8±8.3	43.1±7.0	0.311
Glutamate	20.9±4.5	27.9±7.4	<0.002*
Glutamine	513.1±48.5	445.8±50.6	<0.0004**
Isoleucine	53.6±11.5	62.2±14.5	0.033
Leucine	99.0±16.1	106.4±22.4	0.210
Lysine	155.3±28.5	164.2±32.5	0.332
Methionine	23.7±5.1	25.8±5.6	0.203
Ornithine	43.9±11.3	51.9±10.8	0.021
Phenylalanine	51.7±6.8	55.1±8.4	0.146
Proline	153.7±56.4	131.7±47.6	0.165
Serine	105.4±15.6	115.8±14.7	0.027
Taurine	33.4±5.5	37.8±7.9	0.036
Threonine	100.8±19.7	112.0±24.3	0.097
Tryptophan	44.8±5.6	47.3±6.4	0.167
Tyrosine	60.9±10.5	58.4±10.1	0.425
Urea	3976.3±818.7	3759.9±773.3	0.367
Valine	200.2±29.4	217.1±29.7	0.062

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

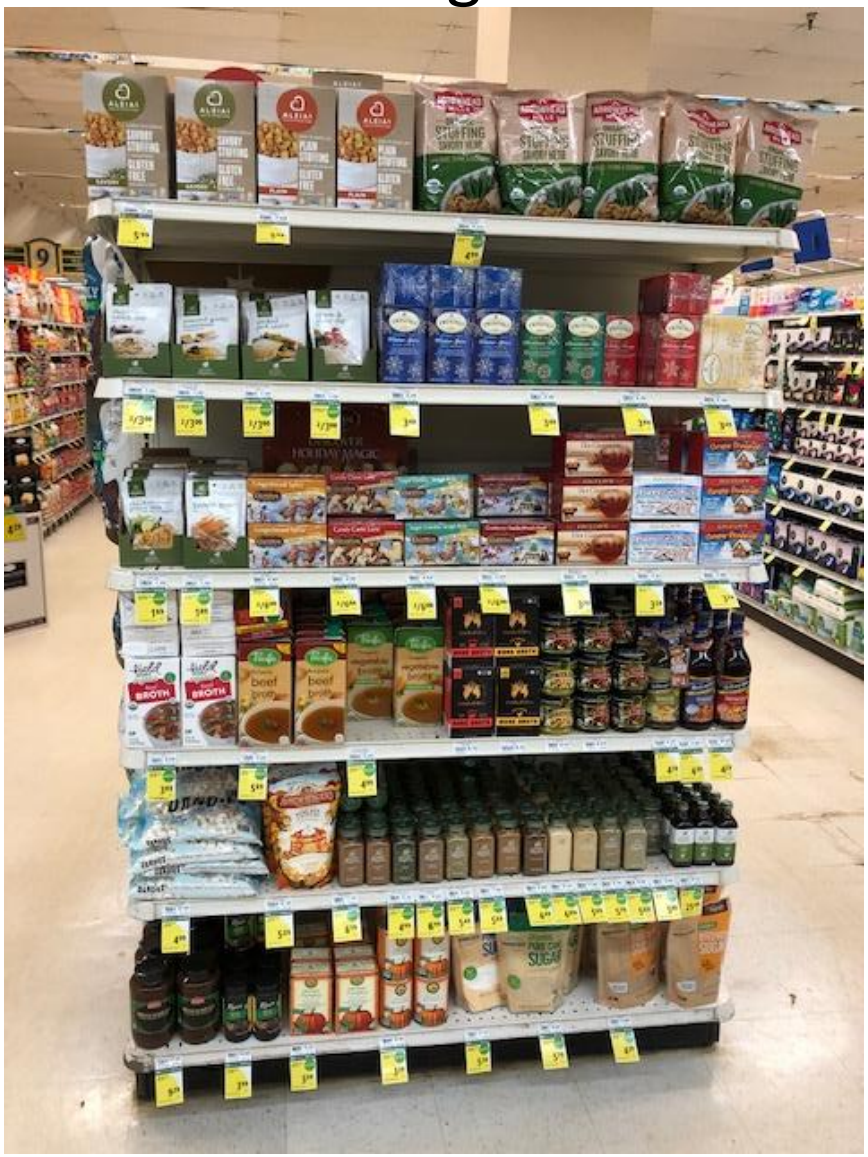
What you can do!

Go Organic!

Wholefoods:
Sign at Entrance

USDA ORGANIC

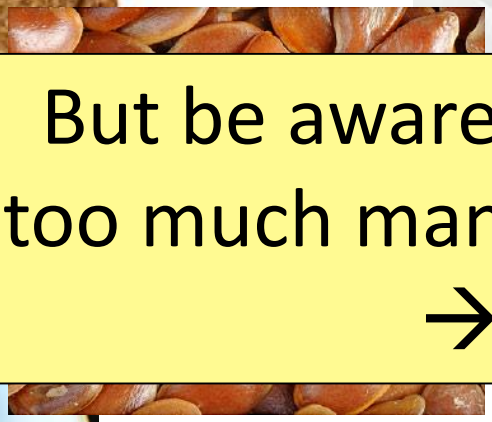
Foodland: organic shelf



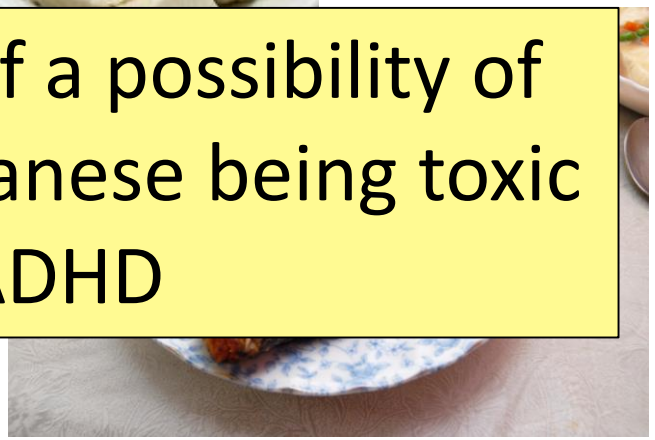
Eat Natural Probiotic Foods

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

Eat Foods Containing Manganese



But be aware of a possibility of too much manganese being toxic → ADHD



Summary

- Glyphosate (from Roundup) is pervasive in our environment
  - I believe it is the primary cause of the autism epidemic
- Glyphosate blocks the shikimate pathway in gut microbes, causing deficiencies in amino acids, neurotransmitters and folate
- Glyphosate induces leaky gut and inflammatory gut, and disrupts digestive enzymes, causing Celiac disease
- Glyphosate causes Clostridia overgrowth leading to neurotoxins that cause excess dopamine
- Glyphosate is a chelator and it binds tightly to manganese, disrupting the liver's distribution of manganese to the tissues
  - Results in simultaneous manganese deficiency and manganese toxicity, as well as glutamate toxicity
  - Lactobacillus depend on manganese to thrive and they alleviate anxiety
- Organic diet and probiotic foods are strategies to heal