

## **Glyphosate's Suppression of Cytochrome P450 Enzymes and Amino Acid Biosynthesis by the Gut Microbiome: Pathways to Modern Diseases**

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Anthony Samsel and Stephanie Seneff, from the Massachusetts Institute of Technology (MIT).

This article is 48 pages long with 286 references. KEY POINTS FROM THIS ARTICLE:

- 1) "Glyphosate, the active ingredient in Roundup®, is the most popular herbicide used worldwide," it is extensively used in agriculture and lawn maintenance.
- 2) Glyphosate residues are found in the main foods of the Western diet, especially sugar, corn, soy and wheat.
- 3) "Glyphosate is toxic because it inhibits the cytochrome P450 (CYP) enzymes." CYP enzymes play crucial roles in the detoxification of xenobiotics. [Xenobiotics are chemicals found in an organism that are not suppose to be there]
- 4) "Glyphosate enhances the damaging effects of other food borne chemical residues and environmental toxins. Negative impact on the body is insidious and manifests slowly over time as inflammation damages cellular systems throughout the body."
- 5) Most of the diseases and conditions associated with a Western diet (gastrointestinal disorders, obesity, diabetes, heart disease, depression, autism, infertility, cancer and Alzheimer's disease) are linked to Roundup (glyphosate).
- 6) "80% of genetically modified crops, particularly corn, soy, canola, cotton, sugar beets and most recently alfalfa, are specifically targeted towards the introduction of genes resistant to glyphosate." [Roundup Ready® crops]
- 7) Studies show life-long exposure to glyphosate in animals cause liver and kidney dysfunction, greatly increases risk of cancer and shortened lifespan.
- 8) Glyphosate's mechanism of action is the disruption of the pathway involved in the synthesis of the essential aromatic amino acids (phenylalanine, tyrosine, tryptophan), a pathway that is absent in all animals (the shikimate pathway). "However, this pathway is present in gut bacteria, which play an important and heretofore largely overlooked role in human physiology." These gut flora are critical for synthesizing vitamins, detoxifying xenobiotics, and they participate in immune system homeostasis and gastrointestinal tract permeability.

9) The incidence of inflammatory bowel diseases (Crohn's disease) has increased substantially in the last decade in Western Europe and the US, and glyphosate's impact on gut bacteria may be responsible.

10) Many of the health problems associated with a Western diet could be explained by biological disruptions attributed to glyphosate. "These include digestive issues, obesity, autism, Alzheimer's disease, depression, Parkinson's disease, liver diseases, and cancer, among others."

11) "We believe that glyphosate may be the most significant environmental toxin, mainly because it is pervasive and it is often handled carelessly due to its perceived nontoxicity."

12) Glyphosate "disrupts gut bacteria and suppresses the CYP enzyme class," causing a combination of gut dysbiosis and impaired sulfate transport, resulting in the "recent alarming increase in all of these health issues."

13) Glyphosate is contaminating our food supplies; glyphosate: \* Causes gut dysbiosis leading to inflammatory bowel disease and its relationship to autism. \* Impairs the transport of free sulfate. \* Inhibits CYP enzymes. \* Depletes serum tryptophan, leading to obesity. \* Can cause extreme tryptophan depletion leading to impaired nutrient absorption and anorexia nervosa. \* Can lead to brain-related disorders such as autism, dementia, depression, and Parkinson's disease. \* Can be linked to reproductive issues and cancer.

14) Glyphosate reduces levels of the amino acids serine, glycine and methionine by 50 to 65%. "The reduction in methionine can have many adverse consequences, as methionine is an essential sulfur-containing amino acid that has to be supplied from the diet."

15) In plant seeds, glyphosate decreases levels of calcium, magnesium, iron and manganese, "leading to deficiencies in these nutrients in humans who consume foods derived from glyphosate-exposed crops."

16) Glyphosate disrupts gut bacteria.

17) Autism is associated with dysbiosis in the gut.

18) An increase in short chain fatty acids and ammonia in the gut increases autism, and these are by-products of anaerobic fermentation secondary to an overgrowth of anaerobic bacteria caused by glyphosate.

19) Children with autism are significantly more likely to have been formula-fed rather than breast-fed, and non-organic soy formula might be contaminated with glyphosate, contributing to autism development.

20) Low levels of serum sulfate are associated with autism. Glyphosate disrupts the transport of free sulfate.

- 21) Autism is associated with gut dysbiosis, causing impaired sulfate metabolism and a significantly reduced level of free sulfate in the blood.
- 22) "Autism is also associated with a decreased ability to sulfate and hence detoxify acetaminophen." [Important]
- 23) Both colitis and Crohn's disease are associated with sulfate depletion which can be caused by glyphosate exposure.
- 24) The alarming die-off of honeybees is linked to record levels of glyphosate use.
- 25) Glyphosate's effects on gut bacteria leads to depleted sulfate supplies resulting in inflammatory bowel disease and "leaky gut syndrome."
- 26) Low serum tryptophan drives weight gain due to suppressed serotonin signaling. Glyphosate wipes out the gut bacteria that produce tryptophan.
- 27) Tryptophan is an essential amino acid. Tryptophan depletion leads to serotonin and melatonin depletion in the brain. Serotonin is a potent appetite suppressant. Serotonin deficiency leads to overeating and obesity.
- 28) Tryptophan is transported across the blood brain barrier and becomes the sole precursor to the synthesis of the neurotransmitter serotonin and the hormone melatonin. "Impairment in the homeostasis of serotonin, an important neurotransmitter that regulates mood, appetite and sleep, has been linked to depression, autism, and Alzheimer's disease, as well as obesity." Reduced serotonin is linked to impulsive aggression, violence, and criminal behavior. "There has been a marked increase in the rate of irrational school associated violent deaths in the United States since 1990, and glyphosate may play a role in this pattern through depletion of serotonin bioavailability."
- 29) "The obesity epidemic began in the United States in 1975, simultaneous with the introduction of glyphosate into the food chain, and it has steadily escalated in step with increased usage of glyphosate in agriculture."
- 30) Farmers in India have anomalously high suicide rates following adoption of Western agricultural methods based on the extensive use of Roundup®, and this can be explained by glyphosate depletion of tryptophan and subsequent serotonin suppression.
- 31) Glyphosate depletes tryptophan. Serotonin is reduced because it is made from tryptophan. Melatonin is reduced because it is made from serotonin. Melatonin is a potent antioxidant, neuroprotective against aging and many neurodegenerative conditions such as Alzheimer's and Parkinson's. Glyphosate impairs antioxidant protection due to the suppression of melatonin synthesis. Reduced melatonin will also lead to sleep disorders.

32) "South Africa arguably has the highest obesity rates in all of Africa, and it is also the African country that has most heavily embraced glyphosate usage since the 1970's."

33) Glyphosate interferes with CYP proteins that play a role in producing vitamin D in the liver. Vitamin D3 deficiency can contribute to mood disorders and may be a key factor in Seasonal Affective Disorder.

34) "Excess ammonia and zinc deficiency are also implicated in neuronal disorders, particularly Alzheimer's disease, attention deficit hyperactivity disorder (ADHD), and autism."

35) "DNA methylation impairment is a factor in neuronal diseases, and glyphosate's depletion of methionine could contribute to this defect."

36) Glyphosate causes these effects on the brain: \* Serotonin depletion \* Excess ammonia \* Zinc depletion \* Methylation impairments

37) Glyphosate enhances ammonia synthesis which increases autism, hepatic encephalitis, and Alzheimer's disease. Ammonia plays a critical role in the etiology of Alzheimer's. "Excess ammonia synthesis by gut bacteria under the influence of glyphosate could be a factor in both autism and Alzheimer's disease."

38) Zinc deficiency is a major problem worldwide. Phytates, found in many nuts and grains, bind to dietary minerals (like zinc) and interfere with their absorption. Lactobacilli and other beneficial gut bacteria produce the enzyme phytase, which improves the intestinal absorption of important minerals like zinc. Glyphosate reduces the number of these types of beneficial gut bacteria, thereby enhancing the poor absorption of these vital minerals.

38) "Zinc deficiency increases the risk of diarrhea, pneumonia and malaria in infants and young children." "Zinc is the most abundant trace metal in the brain."

39) Zinc deficiency is implicated in autism, ADHD, and Alzheimer's. Zinc is required for memory function and the maintenance of synaptic health as we age. Zinc sulfate supplements improve ADHD symptoms, an "effect that could be attributed to the supply of sulfate as well as zinc."

40) "Zinc deficiency along with excess exposure to copper may be a key factor in Alzheimer's disease."

41) "Methylation impairment has been observed in association with autism and Alzheimer's disease, and this is caused by an inadequate supply of the substrate, methionine." Gut bacteria can synthesize methionine and thereby improve methylation, but glyphosate can significantly reduce methionine synthesis. Methionine is the source of methyl groups in methylation pathways.

42) Glyphosate enhances inflammatory bowel disease. Inflammatory bowel disease allows gut bacteria to leak into the vascular system, leading to an autoimmune disorder resulting in destruction of the myelin sheath. "The recent increase in the incidence of MS may be traced to inflammatory bowel disease, and, hence, to glyphosate."

43) Tyrosine is synthesized from phenylalanine. Dopamine is synthesized from tyrosine. Both tyrosine and phenylalanine are depleted by glyphosate in both plants and microbes, reducing their bioavailability in the diet, reducing dopamine concentrations in the brain. Impaired dopamine signaling is a key feature of Parkinson's disease.

44) "Sulfate deficiency in the brain has been associated with Parkinson's disease, as well as Alzheimer's disease and Amyotrophic Lateral Sclerosis." Glyphosate disrupts sulfate transport from the gut to the liver, leading to "severe sulfate deficiency throughout all the tissues."

44A) Glyphosate may play a role in liver disease, cancer, cachexia, and developmental and fertility problems.

45) "Cholesterol sulfate plays an essential role in fertilization and zinc is essential to the male reproductive system, with a high concentration found in semen. Thus, the likely reduction in the bioavailability of these two nutrients due to effects of glyphosate could be contributory to infertility problems."

46) "Glyphosate is capable of crossing the placental barrier. Preeclampsia, a life-threatening condition for both the mother and the fetus that develops during the third trimester, is on the rise in America, and it has been proposed that this may be due to impaired sulfate supply, directly attributable to glyphosate exposure. For all of these reasons, glyphosate exposure would lead to infertility problems."

47) Countries that most rapidly and substantially use Roundup Ready® soybeans (Argentina, Brazil) experience significant declines in fertility rates.

48) Increased use of glyphosate selects for a "rapidly evolving glyphosate resistant weed population," leading to increased use of glyphosate and a further rapid drop in birth rates. The declining birth rates in Western Europe and in the US may be linked to glyphosate exposure.

49) Glyphosate exposure any time during pregnancy has been associated with a statistically significant increased risk of a late-pregnancy spontaneous abortion.

50) "Roundup® interferes with testosterone synthesis at very low concentrations."

51) Glyphosate exposure may lead to a substantial increased risk of multiple myeloma.

52) "The incidence of breast cancer has skyrocketed recently in the United States, to the point where now one in three women is expected to develop breast cancer in their lifetime," and glyphosate may be implicated in this effect.

53) Cachexia (muscle wasting) is a frequent debilitating complication of cancer, AIDS, and other chronic inflammatory diseases. The loss of muscle mass arises from accelerated protein degradation via (the ubiquitin-proteasome pathway), which is related to glyphosate exposure.

54) Commercially introduced in the US in 1974, glyphosate is now the dominant herbicide worldwide. Becoming generic in 2000, the dramatic drop in cost has encouraged glyphosate's global use. About 90% of the transgenic crops grown worldwide are glyphosate resistant.

55) "The rapidly growing problem of glyphosate-resistant weeds is reflected in steady increases in the use of glyphosate on crops." Today, Americans use 180 to 185 million pounds of Roundup®, on their yards and farms every year.

56) "The Western diet is a delivery system for toxic chemicals used in industrial agriculture." [Key Point] "The diet consists primarily of processed foods based on corn, wheat, soy and sugar, consumed in high quantities." "Chemical residues of insecticides, fungicides and herbicides like glyphosate contaminate the entire diet."

57) "The recent alarming rise in type-2 diabetes has been attributed to excess intake of high fructose corn syrup, which has increased to unprecedented levels in the last decade. This refined sugar is now usually derived from glyphosate-exposed GM corn."

58) "GM cotton is also increasingly being used as a source for cottonseed oil, widely present in processed foods such as potato chips, due to its low cost."

59) "The highest levels of glyphosate are found in grain and sugar crops."

60) "Cows, pigs, sheep, goats, chickens and even farm-raised fish and shrimp are fed a diet primarily of genetically engineered grains and forage materials laced with herbicide. As a consequence, animal products like, eggs, butter, cheese and milk are also contaminated with these residues."

61) "The notion that glyphosate has minimal toxicity in humans, widely popularized by Monsanto, has prevented farmers from using caution in their application of this chemical to their crops."

62) The recent rise in the rates of autism can be characterized as a chronic lowgrade encephalopathy, secondary to severely depleted sulfate supplies to the brain. Glyphosate might be responsible for the dysbiosis and sulfate depletion.

63) "Glyphosate may be the most significant environmental toxin contributing to autism." [WOW!] "The key pathological biological effects of glyphosate: disruption of the gut bacteria, impairment of sulfate transport, and interference with CYP enzyme activity-can easily explain the features that are characteristic of autism."

64) Developmental immunotoxicity is the permanent modifications to immune function that takes place early in life, leading to later development of allergies, asthma, and autoimmune diseases. Prenatal and/or early life exposure to environmental toxins may contribute to the increased incidence of these conditions.

65) Glyphosate may be the "most important factor in the development of multiple chronic diseases and conditions that have become prevalent in Westernized societies." These chronic diseases include autism, inflammatory bowel disease, chronic diarrhea, colitis and Crohn's disease, obesity, cardiovascular disease, depression, cancer, cachexia, Alzheimer's disease, Parkinson's disease, multiple sclerosis, and ALS, among others.

66) "Glyphosate's disruption of the body's ability to detoxify other environmental toxins leads to synergistic enhancement of toxicity."

67) Glyphosate's depletion of sulfate can lead to a multitude of pathologies in the brain, including autism, Alzheimer's disease, ADHD, Parkinson's disease, multiple sclerosis and ALS.

68) "Most critical in our view are the vegetable oils derived from GM crops, canola oil, soybean oil, corn oil, and cottonseed oil, as well as soy-derived protein, beet sugar, and high fructose corn syrup - ingredients that are pervasive in processed foods."

69) "Glyphosate is likely also present in meat, eggs, cheese, and other dairy products derived from animals fed glyphosate-contaminated grass, alfalfa, corn, and soy."

70) The pathologies to which glyphosate could contribute, "include inflammatory bowel disease, obesity, depression, ADHD, autism, Alzheimer's disease, Parkinson's disease, ALS, multiple sclerosis, cancer, cachexia, infertility, and developmental malformations. Glyphosate works synergistically with other factors, such as insufficient sun exposure, dietary deficiencies in critical nutrients such as sulfur and zinc, and synergistic exposure to other xenobiotics whose detoxification is impaired by glyphosate."

71) Glyphosate has known toxic effects that are probably "negatively impacting health worldwide."

72) "Glyphosate is likely to be pervasive in our food supply, and, contrary to being essentially nontoxic, it may in fact be the most biologically disruptive chemical in our environment."

### **COMMENTS FROM DR DAN MURPHY**

Roundup® is the most used herbicide worldwide. Roundup's® active ingredient is glyphosate. Monsanto originally commercially released it in 1974. Its global use has skyrocketed for three reasons:

1) Monsanto genetically modified plants so that they are resistant to the effects of Roundup®, thus allowing more Roundup®, to be used on crops, including, corn, soy, cotton, sugar beets,

wheat, alfalfa, canola, cows, pigs, sheep, goats, chickens, farm-raised fish and shrimp, eggs, butter, cheese and milk, canola oil, soybean oil, corn oil, cottonseed oil, soy-derived protein, and high fructose corn syrup.

2) Weeds that Roundup® are designed to kill have been adapting, becoming resistant to Roundup®, thus requiring more Roundup®, to be used on crops.

3) Roundup® lost its patent in 2000, allowing for cheap generic competition. Becoming more affordable has significantly increased its utilization on crops.

Roundup® causes intestinal dysbiosis from several mechanism.

Roundup® exposure has been linked to liver and kidney dysfunction, greatly increased risk of cancer, shortened lifespan, inflammatory bowel diseases, Crohn's disease, chronic diarrhea, colitis, digestive issues, obesity, autism, Alzheimer's disease, depression, Parkinson's disease, leaky gut syndrome, multiple sclerosis, ADHD, violent impulsive behavior, suicide, infertility, preeclampsia, late-pregnancy spontaneous abortion, multiple myeloma, cardiovascular disease, cachexia, and ALS.

Glyphosate, the active ingredient in Roundup® "may in fact be the most biologically disruptive chemical in our environment."

This is one of the most over-the-top articles I have ever reviewed.