#### Glyphosphate- Killing Us Softly, Monsanto Style

Glyphosate is assumed to be safe for humans. As a result, it's become the world's best-selling herbicide. However, a groundbreaking study documents that it may actually be fueling the plague of chronic & immune diseases, including cancer and autism. This study documents the underlying systemic damage produced by glyphosate, then discusses how that damage leads to specific diseases.

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# GLYPHOSATE

by Heidi Stevenson

This article is split into three parts. This is Part 1, <u>Glyphosate: Chronic Disease Degeneration</u>. It gives an overview and then goes on to discuss the primary findings of a new study about the human effects of Monsanto's herbicide, glyphosate. Part 2, titled <u>Glyphosate: Disease Creator</u>, discusses specific diseases, applying the basic harms produced by glyphosate and showing how they lead to each disease. Part 3, titled <u>Glyphosate: A Trajectory of Human Misery</u>, discusses glyphosate's use throughout the world and then draws conclusions.

Monsanto's herbicide, glyphosate, has become virtually ubiquitous based on a presumption of harmlessness in humans. In spite of noxious and aggressive superweeds that have developed in response and a host of reports citing harm and potential harm to the environment and farm animals, this premise of innocence has resulted in its use nearly everywhere. Because of that same image of innocence, its use has multiplied astronomically.

However, a new report from the journal *Entropy* turns the proposition of glyphosate's innocence in human health upside down. An exhaustive review of existing research in which 287 studies were reviewed, coupled with irrefutable logic, produces a frightening picture of the reality: Glyphosate may be the single most devastating substance ever introduced into agribusiness. As the authors, Anthony Samsel and Stephanie Seneff, concluded:

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. The range of diseases that can be associated with glyphosate is frightening. Its biological effects are so primary that virtually every bodily system—if not every one—is adversely affected. The authors state:

Our systematic search of the literature has led us to the realization that many of the health problems that appear to be associated with a Western diet could be explained by biological disruptions that have already been attributed to glyphosate. These include digestive issues, obesity, autism, Alzheimer's disease, depression, Parkinson's disease, liver diseases, and cancer, among others. While many other environmental toxins obviously also contribute to these diseases and conditions, we believe that glyphosate may be the most significant environmental toxin ...

#### **Glyphosate's Metabolic Disruptions**

The study documents that glyphosate disrupts several significant basic biological processes in humans with devastating results. Certain primary functions at the most basic levels are disrupted or diverted. These include:

- Disruption of the shikimate pathway in gut biota.
- Disruption of sulphate transport
- Increase in Flavonoid Synthesis
- Disruption of cytochrome P-450 enzymes

This section will explain and discuss each of these.

#### Shikimate Pathway Disruption

Glyphosate is believed to operate by disrupting the shikimate (pronounced shə **kih** mut) pathway in plants, a process for manufacturing a group of amino acids called aromatic (though the term has nothing to do with odor). These include phenylalanine, tyrosine, and tryptophan. Aromatic amino acids are required for a plant's survival.

It's been assumed that glyphosate is harmless in humans because the shikimate pathway does not exist in any animal. However, the shikimate pathway does exist in bacteria, including those in the mammalian gut. Until fairly recently, the importance of gut biota in health has largely been ignored. However, it's now understood to be key in many aspects of the body's function.

Gut bacteria are in a symbiotic relationship with the body. They digest food, synthesize vitamins, detoxify foreign substances, and are key in immune system function and gut permeability. Thus, anything that interferes with the shikimate pathway has the potential of causing severe harm.

#### Disruption of Sulphate Transport

Sulphate transport, the method by which sulphate is moved into and out of cells, is a delicate balance. When glyphosate is present, this balance becomes a tightrope walk. The problem is that both sulphate and glyphosate are kosmotropes, which can have a devastating impact on the blood.

A kosmotrope is a substance that can cause water to become gelled. Too much sulphate in blood can turn it into sludge, so it cannot circulate and bring nutrients and oxygen to cells or remove waste. Therefore, transport of sulphate is always a balancing act between cellular requirements and blood viscosity.

However, when glyphosate is added to the picture, the risk is even greater. Glyphosate is also a kosmotrope, which makes it significantly more difficult for sulphate to be transported where it's needed. As a result, sulphate transport is disrupted in the presence of glyphosate.

#### Increase in Flavonoid Synthesis

Glyphosate interferes with synthesis of the aromatic amino acid, tryptophan, instead favoring the production of flavonoids by as much as 20 times normal. While flavonoids are generally believed to be health-inducing, Samsel & Seneff's paper presents the likelihood that the picture is far more complex, and they propose a role for them in sulphate transport in the presence of glyphosate.

It's known that, in both plants and microbes, glyphosate induces synthesis of two kinds of phenols: monophenolic compounds and polyphenolic flavonoids. Although monophenols are known to be toxic, flavonoids are generally thought to be beneficial for heath. However, their metabolic mechanisms are unknown.

Carbon rings are part of the molecular structure of phenols. Molecules with carbon rings have a special capability. They can diffuse the effects of kosmotropes. Therefore, phenols, including monophenols and flavonoids, are able to diffuse the effects of sulphate by binding to it and escorting it through the bloodstream.

Sulphate transport comes under pressure in the face of glysophate's kosmotropic gelling effect on the blood. Therefore, aromatic amino acids may be oxidized into phenolic compounds to compensate, that is, to provide more phenols for sulphate transport.

However, once a phenol has delivered its sulphate, it becomes highly toxic. Sulphate-free phenols are destructive to phospholipids and DNA.

Therefore, to fulfill the more pressing need of sulphate transport, authors Samsel & Seneff propose that flavonoids are synthesized instead of tryptophan. That is, because of flavonoids' ability to counter the kosmotropic effects of glyphosate, they are produced at the expense of tryptophan.

They propose that, in the presence of glyphosate, flavonoids and phenols can transport sulphur from the gut to the liver, and then return to the gut by way of the hepatic portal vein to repeat the process. However, once a phenol has given up the sulphate anion in the liver, it becomes toxic, over time causing damage to the liver and the digestive system.

While the immediate problem of sulphate transport is resolved by overproducing flavonoids, there's a distinct downside in the long term. First, of course, is underproduction of tryptophan, with resultant harmful effects on tryptophan-associated processes. It also results in loss of sulphates from the gut, resulting in development of chronic disorders.

#### Disruption of Cytochrome P450 Enzymes

Glyphosate causes an excess build-up of shikimate by inhibiting EPSP synthase, a critical enzyme in the process that leads to the aromatic amino acids. As a consequence, the precursors are sent down other pathways that produce toxic compounds. For example, activity of the enzyme PAL is substantially increased, leading to the release of ammonia.

This appears to be a significant factor in glyphosate's damaging effects.

At the same time that PAL activity is increased, a side branch of the tryptophan synthesis pathway is opened to synthesize flavonoids. As noted before, flavonoids' metabolic function is not yet understood, so their benefits may not be the whole story.

Cytochrome P450 (CYP) is a large family of enzymes that catalyze the oxidation of organic substances and is critical for detoxing xenobiotics. It's been established since 1998 that glyphosate inhibits CYP in plants. Therefore, it follows that their detoxing function is disrupted.

Retinoic acid is catabolized (destroyed) by a CYP enzyme called CYP26A1. Though retinoic acid is required for the process of developing neural differentiation, the neuron cannot mature until retinoic acid is removed by CYP26A1. Therefore, glyphosate's inhibition of the CYP enzyme prevents the neuron from maturing.

CYP enzymes function throughout the body, both inside cells and through the bloodstream. Glyphosate is also carried in the blood. Thus, by inhibiting their function, glyphosate can disrupt any activity in which CYP enzymes are active. This is of particular concern in blood clotting, where two CYP enzymes are involved. Thromboxane A2 synthase (CYP5A1) regulates clotting and prostacyclin synthase (CYP8A1) regulates hemorraging. Glyphosate in the blood can inhibit these enzymes, thus disturbing the delicate balance of blood clotting and dissolution.

Endothelial nitric oxide synthase (eNOS) is a member of the CYP family. It's important for production of nitric oxide (NO), which is needed to relax blood vessels to ease blood flow.

Though not yet documented, it's predicted that glyphosate disrupts the production of sulphate by eNOS in the endothelium, further exacerbating the sulphate transport concern.

#### Evidence of CYP Enzyme Inhibition

Multiple evidence from several areas demonstrates that glyphosate inhibits CYP enzyme activity. It inhibits aromatase, which is a CYP enzyme that's key in converting testosterone to estrogen. Retinoic acid activity is enhanced, which can be explained by suppression of the CYP enzyme that breaks it down. Studies document that glyphosate suppresses certain detoxifyng CYP enzymes.

Two studies demonstrate that activity of CYP19, aromatase, is inhibited by glyphosate. It takes only 10 parts per thousand to disrupt aromatase's activity in a human liver cell line. At concentrations just one-hundredth the recommended agricultural use, aromatase is inhibited in human placental cells. Worse, when glyphosate is combined with chemicals in RoundUp, these effects happen with just 1/20 as much glyphosate.

In another study, a 15 micromoles concentration of glyphosate resulted in cutting the activity of benzenedetoxing CYP enzymes to one-fourth of normal. When the concentration was increased to 35 micromoles of glyphosate, the CYP activity was completely stopped.

A compelling study documented that rats given glyphosate intragastrically for two weeks suffer a reduction of CYP activity in the liver. This result is not surprising, since glyphosate is an organophosphate, and it's well established that this class of pesticides inhibits CYP enzyme function in human liver cells. Therefore, it would be unsurprising to find that glyphosate's inhibition of CYP liver enzymes that detox benzene could lead to severe adverse effects, since it's known to cause cancer.

Glyphosate may also be an indirect factor in the ongoing die-off of bees. The class of insecticides called neonicotinoids is known to kill bees. One study has found reduced pollination in genetically modified Roundup-Ready canola compared to organic canola. The authors suspect that a synergistic effect between glyphosate and neonicotinoids is worsening bee die-off.

### Pathology Induction by Glyphosate

Gyphosate causes disruption of the shikimate pathway in gut bacteria, which results in a domino effect of pathology. It causes formation of excess shikimate, along with deficiencies of aromatic amino acids in plants.

Aromatic amino acids include phenylalanine, tryptophan, and tyrosine, among others. All three can be in short supply as a result of glyphosate's enzymatic suppression. Phenylalanine cannot be synthesized in the body and is required for synthesis of tyrosine. Its suppression results in a cascade of adverse effects, including of course, reduction in tyrosine.

Excess ammonia is observed in the cells of plants treated with glyphosate. This is true for both natural and Roundup Ready plants. A likely cause of the excess ammonia is glyphosate-induced increase in the activity of phenylalanine ammonia lyase (PAL), an enzyme found in both plants and microbes that catalyzes release of ammonia. Most of glyphosate's ability to retard plant growth is probably a result of PAL activity, which produces both toxic ammonia and phenolic compounds.

# **Glyphosate Effects on Gut Bacteria**

Evidence of glyphosate's disruption of gut bacteria is found in cattle and poultry. Over the last ten to fifteen years, *Clostridium botulinum* infection has increased in German cattle. Glyphosate is toxic to *Enterococcus*, a friendly bacterium. This leads to a gut imbalance that favors overgrowth of *Clostridium*.

Research documents that glyphosate reduces beneficial bacteria and increases pathological bacteria in the gut. Particularly pathogenic strains of drug-resistant *Salmonella* and *Clostridium* were found, while beneficial *Enterococcus*, *Bacillus*, and *Lactobacillus* are susceptible to glyphosate. The result is overgrowth of pathogenic bacteria at the expense of beneficial bacteria.

In one instance, pathogenic bacteria do a good turn—but in the end, negate it with a particularly nasty byproduct. Antibiotic-resistant *Pseudomonas* are opportunistic pathogens that can break glyphosate down into metabolically-safe and usable phosphate and carbon. Unfortunately, a by-product of the process is neurotoxic formaldehyde, which can cause amyloid-like misfolding of tau protein in neurons, much like those found in Alzheimer's brains, among other mischief.

*Escherichia coli* (*E. coli*) suffers starvation, energy drain, and shut-down of the shikimate pathway in the presence of glyphosate. A switch to anaerobic fermentation occurs instead of oxidizing glucose (sugar), which is a less efficient method of producing energy. It is reminiscent of changes in soil microbes with glyphosate application.

#### **Frogs and Embryonic Development**

In research comparing the effects of pesticides on frogs, glyphosate was unique in being able to destroy tadpoles. Out of four species, two had no survivors, one had almost none, and the overall survival of the four species was 70 percent.

Glyphosate had a synergistic effect with a fungal pathogen, *Batrachochotrium dendrobatidis*, which reduced survival of tadpoles.

It is probable that glyphosate is a factor in the worldwide disappearance of frogs, and also that embryonic development is disrupted.

#### **Slow Effects in Mammals**

Samsel & Seneff state:

An insidious issue with glyphosate is that its toxic effects on mammals take considerable time to be overtly manifested.

Nonetheless, evidence is building in mammalian studies. Research on rats given glyphosate in quantities equivalent to the highest legally-allowed doses demonstrated that they suffered oxidative stress in only 30-90 days.

A long term study examined rats fed genetically modified (GM) maize, nonGM maize without glyphosate, or GM maize with glyphosate. The experiment ran for the rats' lifetimes, about two years. Unlike previous short-term research that had ended at 3 months. The results were dramatic. Rats fed the genetically-modified glyphosate-treated maize suffered multiple pathologies, including enormous mammary tumors in females, and gastrointestinal, liver, and kidney pathologies in males, which also developed skin and liver carcinomas. Male rats tended to die prematurely of liver and kidney deficiencies.

Roundup is a compound that includes both glyphosate and a surfactant called TN-20. Studies have found that the combination greatly increases glyphosate's toxicity, resulting in mitochondrial damage, and both apoptic and necrotic cell death. It's suspected that TN-10 disrupts the integrity of the cell barrier, which allows entry by glyphosate.

The synergistic effects of TN-20 with glyphosate were demonstrated in a study showing that dairy product starter microorganisms were inhibited by Roundup, but not by glyphosate alone. That study's authors wondered if a recent loss in the biodiversity of raw milk might be caused by Roundup.

Part 1, Glyphosate: Chronic Disease Degeneration Part 2, <u>Glyphosate: Disease Creator</u> Part 3, <u>Glyphosate: A Trajectory of Human Misery</u>

#### Source:

Samsel, Anthony; Seneff, Stephanie. 2013. "Glyphosate's Suppression of Cytochrome P450 Enzymes and Amino Acid Biosynthesis by the Gut Microbiome: Pathways to Modern Diseases." *Entropy* 15, no. 4: 1416-1463; doi:10.3390/e15041416

A new study has demonstrated glyphosate's ability to interfere with gut biota and underlying metabolic functions. The conclusion that glyphosate is a major factor in nearly all modern chronic diseases is inescapable. Here's how those disturbed metabolic functions are associated with conditions like autism, cancer, and Alzheimer's disease.

by Heidi Stevenson

This is Part 2 of a three-part series:

Part 1, <u>Glyphosate: Chronic Disease Degeneration</u> Part 2, Glyphosate: Disease Creator Part 3, <u>Glyphosate: A Trajectory of Human Misery</u>

With the damage done to primary cellular function, it should not be a surprise that glyphosate is implicated in the modern health plague, chronic diseases. It seems likely that virtually all are, at the least, exacerbated by it. Following are discussions of a wide array of these conditions and likely associations with glyphosate.

Please note that the interrelationships among glyphosate's effects are very complex. Therefore, as much as possible, health conditions are arranged so that associations with glyphosate's effects can be best understood and repetition is minimized. Nonetheless, some points may seem a bit out of context, while others may appear to be repetitious—though I've attempted to reduce such irritations. It should also be noted that this is not a complete listing of diseases and conditions discussed by Samsel & Seneff's report.

Most important of all, though, are the chilling effects that glyphosate and its symbiotic partner, Roundup, have on the human body.

#### **Cholesterol and Vitamin D Deficiencies**

Synthesis and breakdown of both cholesterol and vitamin D (which refers solely to vitamin D3 here) are affected by glyphosate's effects on CYP enzymes. Though there's certainly an association between sun avoidance and sunscreen use, it's likely that part of this epidemic is associated with glyphosate.

The importance of glyphosate's interference in synthesis of cholesterol cannot be overestimated. Cholesterol provides a wide array of functions throughout the body:

- Cholesterol is a precursor for synthesis of vitamin D, bile acids, and every steroid.
- Cholesterol is required to build and maintain membranes and membrane fluidity.
- Cholesterol is involved in cellular transport.
- Cholesterol is involved in cell signalling.
- Cholesterol is involved in nerve conduction.
- Cholesterol is part of the myelin sheath around nerves.
- Cholesterol may act as an antioxident.

It's not difficult to see that glyphosate's interruption in cholesterol synthesis can have domino effects throughout the body.

#### Obesity

Obesity is at the base of much modern ill health. However, a strong argument can be made that the obesity epidemic itself is caused by Agribusiness use of glyphosate. It's already been proposed that synthetic chemicals in general are behind the obesity epidemic. However, high levels of them are better noted for causing anorexia. Samsel & Seneff, though, argue that glyphosate can be behind both problems.

Tryptophan supply is curtailed by glyphosate. Serotonin is derived from tryptophan. Therefore, it follows that depletion of tryptophan leads to deficiency in serotonin.

But the tryptophan tale is even worse. When inflammation is present, after glyphosate redirects production to flavonoids, the limited tryptophan that is produced faces another glyphosate-induced problem. Gut inflammation causes tryptophan to be converted to kynurenine by lymphoid tissues at the inflamed site. So it's engulfed by two types of white blood cells, macrophages and neutrophils, for self-protection. Immune cells hoard kynurenine so they can defend themselves against DNA damage.

Although the popular press ties serotonin only to depression, it's highly significant in obesity. It is the hormone that indicates satiety so that hunger stops. Confirmation of the tryptophan-serotonin connection is confirmed by studies documenting low tryptophan and serotonin levels in obese people.

Sadly, trytophan levels remain low after weight reduction, so it should not be surprising that maintaining weight loss can be so difficult. Obesity is a genuinely pathological condition—a genuine disease, not a character defect.

In an experiment, a strain of endotoxin-producing bacteria was transferred from a human gut to the guts of mice with neither beneficial nor harmful bacteria. During a 16-week period, these mice became obese on a high-fat diet. Lest you think that it was the high-fat aspect that made them obese, the same diet was also fed to normal mice, which didn't gain weight.

Glyphosate changes the balance of gut bacteria to endotoxin-producers. That fact, in conjunction with the fact that the obesity epidemic has increased along with glyphosate's increased use, provides a strong prima facie case for glyphosate as a factor in obesity. This same trajectory of obesity has also happened in conjunction with glyphosate introduction in other areas of the world. South Africa, which started using glyphosate in the 1970s, along with Roundup Ready genetically modified crops, has the highest obesity rate in Africa.

#### **Inflammatory Bowel Disease**

C. difficile is a known causative agent of inflammatory bowel diseases (IBDs), including Crohn's disease and ulcerative colitis. The incidence of *C. difficile* has increased a great deal in North America over the last

few years. A study in Wisconsin showed that, although *C. difficile* was almost unknown in people with IBDs prior to 2003, it was found in 3% of cases in 2003, 7% in 2004, and 16% in 2005.

It is likely that glyphosate is fueling the growth in people with IBDs infected with C. difficile.

Glyphosate can also lead to IBD through its disturbances of tryptophan production. Normally, tryptophan is taken up by the liver primarily for production of adenosine triphosphate (ATP), which is the chemical produced by cells for energy. Any that isn't taken up circulates in the blood, making it available to cross the blood-brain barrier (BBB) into the brain, where it's used to make serotonin and melatonin. As already noted, low serotonin levels can lead to obesity.

Obesity does provide some limited protection against inflammatory disease in the gut. There are two factors providing such protection. One is that adipose (fat storing) tissues can store endotoxin produced by gut bacteria, so the lining is spared inflammatory damage. The other reason may be even more significant. Adipose tissue can supply sulphated steroids.

Unfortunately, though, obesity's protection against inflammation can be overcome by the disturbance in tryptophan creation and processing. The process is not yet well understood. However, experiments on mice have shown the protective effect of obesity does break down, leading to severe inflammatory bowel disease, bleeding, and diarrhea.

#### Anorexia/Cachexia

The term anorexia nervosa in this study is better understood to mean simply anorexia, which does not involve the psychological condition of refusing to eat. Anorexia, in this context, refers to an inability to eat instead of refusal, and is more closely related to cachexia, which refers to weakness and wasting of the body. It is an end stage of much disease, including tuberculosis, cancer, and aids.

A typical aspect of IBS is weight loss that results from loss of ability to transport nutrients across a damaged gut barrier. Thus, the processes that can lead to obesity are, paradoxically, the same ones that, when taken to greater extremes, can also lead to anorexia and cachexia.

Glyphosate triggers inflammation in a variety of ways, including tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), which promotes muscle breakdown, thus likely being a factor in the cachexia of some chronic diseases.

#### Autism

It's now well accepted that gut disease is associated with autism.

As noted earlier, glyphosate's interference with the shikimate pathway results in overactivity of the enzyme PAL, which leads to excessive ammonia, which plays a toxic role in autistic brains.

The synthesis of ammonia is a byproduct of anaerobic fermentation, and anaerobic *Clostridia* bacteria are found in excess in the feces of children with autism. In general, by-products of anaerobic bacteria, which include phenols, amines, ammonia, and hydrogen sulphide, are toxic to the bowel.

Hepatic encephalitis—confusion, personality changes, reduced consciousness, and coma resulting from liver failure—is related to autism. The connection is ammonia. Impaired liver function prevents detoxification of ammonia, leading to symptoms of both autism and hepatic encephalitis.

Reduction of serotonin in the brain, which is indirectly caused by glyphosate's redirection of tryptophan synthesis into flavonoids, is associated with autism:

- One study comparing 40 autistic children with normal controls found that 35% of the autistic children had a far lower serum ratio of tryptophan to large neutral amino acids.
- Inadequate dietary tryptophan is known to exacerbate autistic children's anxiety and repetitive behaviors.
- Mice genetically designed with a defective gene that reduces availability of serotonin in the brain exhibited autistic-like behaviors.

Methylation impairment is seen in both autism and Alzheimer's disease. It's caused by an inadequate supply of methionine. An experiment on carrot cell lines demonstrated several pathologies resulting from glyphosate exposure. They were short of phenylalanine, tryptophan, and tyrosine. On top of that, levels of three other amino acids, serine, glycine, and methionine, are cut by 50-65 percent.

Glyphosate interferes with synthesis of methionine, which is necessary for methylation, clearly indicating a link between glyphosate and both autism and Alzheimer's disease.

#### **Alzheimer's Disease**

Ammonia, which is synthesized by gut bacteria as a result of glyphosate, plays a toxic role in Alzheimer brains.

Glyphosate fuels the growth of antibiotic-resistant *Pseudomonas*, which breaks it down into safe chemicals. Unfortunately, a byproduct of the process is formaldehyde, which can induce amyloid-like misfolding of proteins in the brain, a key trait of Alzheimer's disease.

Lysosomes, structures in cells that break down waste materials, depend on sulphate—but glyphosate disrupts sulphate transfer. Liposomal dysfunction is a major factor in Alzheimer's disease.

Excess ammonia, already demonstrated to be a problem caused by glyphosate, is a known issue in Alzheimer's disease.

Glyphosate is a potent chelator of divalent cations, and zinc is one of them. Therefore, it's likely that zinc is chelated and removed from the system, leading to zinc deficiency, which is noted for causing diarrhea and increasing risk of pneumonia and malaria. Glyphosate also reduces the number of friendly gut bacteria that help absorption of minerals, including iron and zinc.

Zinc is used in the brain in the process of degrading amyloid- $\beta$  plaques. However, as a result of glyphosate, zinc can be in short order, so these plaques don't get removed. The result is continued buildup of Alzheimer's characteristic plaques, thus worsening, or possibly even causing, the condition.

Deficiencies of zinc and copper have been noted as likely factors in Alzheimer's disease. A South Africa study found that supplementing zinc in Alzheimer's patients known to be low in zinc did not help. However, when vitamins D and A were also supplemented at the same time, improvements were noted. This ties back to glyphosate's impairment of CYP enzymes, which are required to synthesize vitamin D.

#### **Parkinson's Disease**

Dopamine is synthesized from tyrosine, which is synthesized from phenylalanine—and phenylalanine is inhibited by glyphosate. Reducing tyrosine and phenylalanine in the diet reduces dopamine concentrations in the brain, so it's reasonable to assume that reduction of tyrosine by glyphosate's inhibition of phenylalanine will result in reduction of dopamine.

Parkinson's disease is characterized by impaired dopamine signaling in the brain, and it has also been associated with several pesticides. Though glyphosate has not been named as one, that may be a result of preconceptions about its safety.

Sulphate deficiency has been noted in the brains of people with Parkinson's disease, as well as Alzheimer's and amytrophic lateral sclerosis, which though generally considered hereditary, has been increasing over the last few years. Thus, there is good reason to suspect glyphosate's complicity in all three of these devastating brain conditions.

# **Multiple Sclerosis**

Molecular mimicry is a theory of some autoimmune disorders. It suggests that abnormal entry into the body of a molecule that is similar to ones found in the body can result in an immune response that identifies normal tissues for attack and destruction because of the resemblance.

Multiple sclerosis (MS) is a disease in which the myelin sheath around nerves is attacked and destroyed by the immune system. MS sufferers often have inflammatory bowel disease. A search of the scientific literature found matching mimics in gut bacteria. Coupled with glyphosate's ability to cause gut inflammation and leaky gut syndrome, a case can be made that the increasing rate of MS is related to the herbicide.

#### **Liver Disease**

Fatty liver disease is a growing threat to health. Nonalcoholic fatty liver disease leads to cirrhosis and liver failure. Several glyphosate-related factors may be involved.

TNF- $\alpha$  and other cytokines, which are triggered by glyphosate, induce liver-damaging inflammation. TNF- $\alpha$  inhibits insulin signaling, which is a factor in metabolic syndrome. Cytokines can induce fibrosis and lipid overloading in the liver.

Of course, obesity is associated with liver disease, and glyphosate can induce obesity.

#### **Sleep Disorders**

Typtophan is a precursor of melatonin, which is excreted from the pineal gland, and it's a major factor in sleep cycle regulation. Glysophate's disruption of tryptophan production may be a factor in sleep disorders.

# Fertility

Zinc, which has been shown in the discussion on Alzheimer's disease to be diminished by glyphosate, is necessary for male reproduction.

Cholesterol sulphate is essential in fertilization, so glyphosate-induced CYP inhibition, which can interfere with cholesterol production, can interfere with fertilization, helping to explain falling fertility rates.

In 1978, Argentina's birthrate peaked, and has been in decline since then, but the rate of decline accelerated in the last five years of the 20th century. Roundup Ready soybeans were introduced there in 1996 and spread at an unprecedented rate. Argentina is now the leading soybean producer in the world.

The second largest soybean producer is Brazil, where the fertility rate has dropped from more than 6 per woman to under 2. Like Argentina, in the mid-90s they took to to Roundup Ready soybeans with the

associated use of glyphosate. A plague of glyphosate-resistant superweeds has developed, which has resulted in massively increased usage of the herbicide. Since starting to grow genetically modified crops, both a rapid decrease in the birth rate and increase in still births have been noted.

The birth rates in both western Europe and the US have declined for several years. While other factors are certainly at play, it seems probable that glyphosate is also a culprit.

Glyphosate has been shown to interfere with testosterone production. In men, the steroidogenic acute regulatory protein (StAR) is required in the process to synthesize the hormone testosterone. A study on a rat cell line found that very low doses of Roundup interfere with StAR function, and higher doses cause necrosis and apoptosis of rat testicular cells. StAR protein levels were reduced by 90 percent.

Aside from StAR, another enzyme called the side chain cleavage enzyme (P450scc) is required to produce steroids. The research just described also found that Roundup inhibits P450scc activity by 71%.

Interestingly, glyphosate alone did not have this effect. Samsel & Seneff surmise that it was a combination of glyphosate and surfactants acting in synergy that had the effect. Significantly, StAR and P450scc are involved in producing several hormones, not only testosterone. Therefore, Roundup is also likely to have adverse effects not only on fertility, but also on the adrenal glands, which produce the glucocorticoids and mineralocorticoids steroids.

An in vitro study on synthesis of progesterone in testicular Leydig cells compared the effects of several pesticides: Ammo, Banvel, Cotoran, Cyclone, Dual, Fusilade, and Roundup. Only Roundup had an effect, and that effect was significant. It reduced progesterone synthesis as much as 94% in a dose-dependent manner.

#### **Birth Defects**

Glyphosate is known to cross the placental barrier, and it has been associated with birth defects. A study of a farming population in Ontario, Canada showed a statistically significant increase in spontaneous late-term abortions associated with exposure to glyphosate at any time during pregnancy.

Glyphosate's inhibition of CYP enzymes causes an increase in retinoic acid. African clawed frog and chick embryos were exposed to low doses of glyphosate, 1/5,000 of the standard. The result was frog embryos that developed into tadpoles with cranial deformities and chick embryos with microcephaly, abnormally small heads. These defects were traced back to an increase in retinoic acid.

Glyphosate leads to inflammation and inflammation leads to excess reactive oxygen species (ROS) and reactive nitrogen species (RNS). Both ROS and RNS can damage DNA during replication, thus disrupting embryo development.

Cell cycle checkpoints exist in the life cycle of cells to verify whether there is any DNA damage before allowing progression to the next stage. This is of great importance in mitosis (cell division) to assure that defects are not passed on. Sea urchins, a very simple form of animal life, are used to study mitosis. Cyclin dependent protein kinases (CDKs) help verify whether cells should progress past checkpoints. A live sea urchin study found that Roundup delays activation of a CDK by dephosphorylation of tyrosine. This indicates a means by which glyphosate can cause birth defects and stillbirths.

Preeclampsia, a life threatening condition of pregnancy, may be caused by inadequate sulphate supply, which is caused by glyphosate. Preeclampsia is becoming a much more common problem in pregnant women.

#### Cancer

The last thing that glyphosate is generally accused of causing is cancer. That, though, may be far from true. Glysophate's association with breast cancer is implicated as a result of glyphosate-exposed mice that developed massive breast tumors in a recent study. Breast cancer has recently skyrocketed in the US, with one in three women now expected to develop it.

The fact is that professional pesticide operators who are exposed to glyphosate through their jobs have been found to suffer an increased risk of myeloma, bone marrow tumors known to be associated with disease-causing agents. Glyphosate causes chronic inflammation, which is known to damage DNA. Depleted tryptophan is also linked to DNA impairment.

Multiple myeloma accounts for 15% of all lymphatohematopoietic cancers (cancers of blood and lymph production) and 2% of all cancer deaths in the United States. Glyphosate's ability to trigger obesity is a likely factor in myeloma incidents.

Impaired sulphation is suggested as a cause of breast cancer because it could lead to slower metabolization of sex hormones, leading to increased breast density, which is associated with cancer. The CYP enzyme, CYP1A2, could be a factor as a result of inhibition by glyphosate, as well as its interference with sulphate transport.

Obesity is associated with breast cancer, which again leads to culpability of glyphosate. Inflammation has also been linked to it, so glyphosate's ability to trigger inflammation implicates it again.

With so many aspects of glyphosate's effects coming into play, it certainly shouldn't be surprising that we're seeing enormous increases in cancer rates.

Part 1, <u>Glyphosate: Chronic Disease Degeneration</u> Part 2, Glyphosate: Disease Creator Part 3, <u>Glyphosate: A Trajectory of Human Misery</u>

#### Source:

Samsel, Anthony; Seneff, Stephanie. 2013. "Glyphosate's Suppression of Cytochrome P450 Enzymes and Amino Acid Biosynthesis by the Gut Microbiome: Pathways to Modern Diseases." *Entropy* 15, no. 4: 1416-1463; doi:10.3390/e15041416

Glyphosate has likely caused more damage to human health than any other chemical ever produced. Indeed, it is probably a cause of the explosion in chronic diseases. Surely civilization cannot be maintained when the average person is irrevocably ill. This trajectory of human misery must come to an end. by Heidi Stevenson

This is Part 3 of a three-part series:

Part 1, <u>Glyphosate: Chronic Disease Degeneration</u> Part 2, <u>Glyphosate: Disease Creator</u> Part 3, Glyphosate: A Trajectory of Human Misery

#### **Ubiquity of Glyphosate**

Glyphosate was first introduced in 1974 and has become the world's most dominant herbicide. It's now generic, so there are many brands and formulations. As a result, it's virtually ubiquitous, found nearly everywhere on earth. Further driving its use are genetically modified (GM) crops, which were first developed for the purpose of creating glyphosate-tolerant plants, usually known as Roundup Ready. These have resulted in ever-more blatant and free use, especially in the wake of glyphosate-resistant superweeds. Estimates put glyphosate-tolerant GM crops at 90% of all transgene crops.

In the United States alone, the amount and increase in glyphosate's use is stunning. The following table gives estimated figures in millions of pounds of glyphosate for one year:

Year	2001	2003	2005	2007
Range	85-90	128-133	155-160	180-185

Notice that the amount of use has doubled in just six years.

#### **Exposure to Glyphosate**

Samsel & Seneff state:

The Western diet is a delivery system for toxic chemicals used in industrial agriculture. It consists primarily of processed foods based on corn, wheat, soy and sugar, and they're consumed in high quantities. Chemical residues of insecticides, fungicides and herbicides like glyphosate contaminate the entire diet.

Roundup Ready GM crops have become the mainstay of Agribusiness. These include soy, beet sugar, and corn—which supply the bulk of the processed food industry. High fructose corn syrup, implicated in the diabetes epidemic, is produced mostly with GM corn. Cotton is genetically engineered and its oil has entered the food supply.

Glyphosate is systemic in plants, so it cannot be washed off. If it's used on a crop, it will be in the food produced from it. All the soy, sugar, cotton, and corn that ends up in packaged foods is carrying glyphosate into our bodies.

Food and dairy animals are raised in concentrated animal feed operations (CAFOs). The bulk of their diets consists of GM grain crops. Grain and sugar crops take up higher levels of glyphosate than other crops. Therefore, the flesh, eggs, and milk of CAFO-raised animals are contaminated with glyphosate, which enters the food pipeline.

Glyphosate is used not only on Roundup Ready crops, but also on glyphosate-sensitive sugar cane and wheat shortly before harvest, when it acts as a dessicant. It's also used as a dessicant on Roundup Ready sugar beets, canola, and cottonseed for oils, among others.

The perception that glyphosate is not toxic in humans results in difficulty obtaining figures on how much glyphosate ends up in the food supply. The United States Department of Agriculture's (USDA's) Pesticide Data Program is voluntary. Searching for information on residues for the year 2010, the most recent year for which data is provided, shows residue levels for all pesticides except glyphosate and another organophosphate, glufosinate. The USDA has simply not monitored residue levels for either of these herbicides, though they will this year (2013), but only for a small sampling of glyphosate residues in soy.

#### **Increasing Limits on Glyphosate Use**

Governments have failed to control use of glyphosate. The precautionary principle has not been in evidence anywhere. The drive to use it has increased as the use of glyphosate on Roundup Ready crops, which has driven development of noxious superweeds. Therefore, Agribusiness in the forms of chemical and biotech industries have demanded increased limits on glyphosate residue.

In 1999, the EU and UK, where no GM crops are currently grown for human consumption, increased the limit for soy from 0.1 parts per million to 20 ppm—a 200-fold increase! The US limit for soy is currently the same.

Pressure is now on to increase levels even more. In the EU, industry is pressing for an increase of at least 100 times current residue levels in lentils from 0.1 ppm to 10 ppm, or even 15 ppm. Safety isn't factored in. Approval levels are based solely on anticipated use, and glyphosate use is being driven massively higher by the noxious superweeds that exist only because of it.

The residue limits for food animals are even worse, and by a huge amount. Animal-feed grass is allowed glyphosate residues of 300 ppm, and animal-feed corn can have glyphosate residues of 400 ppm!

#### **Glyphosate's Toxicity**

It should come as no surprise that sickness is becoming the normal state of health. Chronic diseases, once fairly rare, are now how we live and die. Diseases once seen almost exclusively in the elderly are now being seen in children. Autoimmune and neurological disorders are becoming common.

There are many potentially causative and contributory factors, but glyphosate has generally gotten a pass because it was considered "generally recognized as safe"—GRAS—for its apparently low toxicity. Indeed, short term studies appeared to confirm its innocence. However, long term studies of its effects on health weren't done until recently. The most insidious factor in glyphosate's toxicity has been the slow expression of harmful effects. Because of it, studies demonstrating glyphosate's insidious action inside the body—like those Samsel & Seneff reviewed—have been systematically ignored.

So glyphosate is now the most popular herbicide on earth, and that factor is driving the extent of harm it produces. It isn't just the fact of its toxicity that's at issue, it's the sheer volume of usage.

Samsel & Seneff's research is blowing away the smokescreen around the harmful effects of this monstrous product. They have provided specifics for how glyphosate can destroy health and produce the modern plague of chronic diseases.

#### **Glyphosate: A Trajectory of Human Misery**

The proven and probable effects of glyphosate are manifold. The meteoric rise in chronic diseases and metabolic disorders has occurred during the same time period that glyphosate was introduced, and has followed a trajectory much like that of the herbicide's massive increase in use.

At some point, officials in power must take their heads out of the sand and address the evidence that ties glyphosate to the epidemic of chronic diseases. Samsel and Seneff have now collected, sorted, and logicially extrapolated on evidence from studies, and they leave little question that there must be an association between the herbicide and the phenomenom of mass ill health.

Samsel and Seneff do not oversell their findings. They clarify that glyphosate is not the only toxin in today's world. Nonetheless, its known effects on some of the human body's most basic functions—disruption of gut bacteria, impairment of sulphate transport, and interference with CYP enzyme activity—indicate that, at the very least, glyphosate must have a synergistic effect with other environmental toxins.

It is, therefore, imperative that—at the very least—a moratorium be declared on the use of glyphosate until and unless it can be demonstrated to be safe. Surely it's long past time to apply the precautionary principle to glyphosate and its partner in synergy, Roundup. The toll in human suffering, not to mention costs to society and economic losses, cannot be allowed to continue.

Surely civilization cannot be maintained when the average person is irrevocably ill. This trajectory of human misery must come to an end.

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