Glycine - The Amino Acid Under Attack & Its Relevance in Chronic Disease
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Amino acids are organic compounds containing amine ($-NH_2$) and carboxyl (-COOH) functional groups, along with a side chain (R group) specific to each amino acid. About 500 naturally occurring amino acids are known but only 20 appear in the genetic code and can be classified in many ways - one of the most important amino acids is called glycine. Amino acids are the building blocks of proteins. In the form of proteins, amino acid residues form the second-largest component, second only to water, of human muscles and other tissues.[1] Their vast roles in the human body include catalyzing metabolic reactions (i.e. enzymatic function), providing structure, DNA replication, cell signaling, immune responses, cell adhesion and transporting molecules from one location to another. Proteins differ from one another primarily in their sequence of amino acids, which is dictated by the nucleotide sequence of their genes, and which usually results in protein folding into a specific three-dimensional structure that determines its activity. **If the sequence of the amino acid is changed within a protein the result can be a dramatic decrease in function** of that particular protein. In nature, structure determines function.

The research of Dr. Stephanie Seneff from MIT & Dr. Anthony Semsel has suggested that the herbicide known as ***glyphosate*** may have the ability to **substitute itself as glycine** within amino acid sequences, which can then change the function of the end product. Typically, this substitution can cause a decrease in function, as noted in a recent scientific experiment where the glycine in a muscle protein was substituted with alanine - the protein's function decreased dramatically with just one substitution. Many proteins have residues that are "conserved" which means that they are very important and when substituted or mutated can have grave consequences. Proteins that

have what are known as **"conserved glycine residues" (CGR)** are the most at risk and when "mutated" long-term may be linked to many chronic diseases including cancers, diabetes, neuropathies, obesity, asthma, infections, osteoporosis, infertility, and birth defects.

There are many proteins in the body that contain CGRs - one of clinical interest is the protein known as myosin. Myosin has fourteen CGRs in its amino acid sequence. A recent study showed that when just one of these residues was substituted with alanine, the function was decreased drastically. Myosin functions in muscle contraction of skeletal muscles, smooth muscles such as in the gut wall and bile canaliculi. If a substitution is made from glycine to glyphosate negative downstream physiological effects may ensue such as gut motility dysfunction, cholestasis, muscle fatigue among other far-reaching negative effects.

Another protein of clinical relevance is cytochrome C oxidase - the last enzyme in the respiratory electron transport chain of cells located in the membrane. It receives an electron from each of four cytochrome c molecules, and transfers them to one dioxygen molecule, converting the molecular oxygen to two molecules of water. In this process it binds four protons from the inner aqueous phase to make two water molecules, and translocates another four protons across the membrane, increasing the transmembrane difference of proton electrochemical potential which the ATP synthase then uses to synthesize ATP. Cytochrome c oxidases' CGRs are found where oxygen binds to it awaiting the transfer of electrons. The substitution with glyphosate may in effect render this most important enzyme less functional, thereby affecting the very foundation of human energy production physiology. A recent study done on zebrafish reported after exposure to physiological levels of glyphosate "brain decrease in cell viability, inhibited mitochondrial complex enzymatic activity, modulated gene expression related to mitochondrial complexes, induced an increase in RS production, promoted

hyperpolarization of mitochondrial membrane, and induced behavioral impairments." This data further contributed to the knowledge of the neurotoxic effects of glyphosate. Moreover, this study revealed mitochondrial dysfunction and as an important target of glyphosate.

Ceruloplasmin is an important protein in our body that belongs to the feroxidase enzyme family. It functions to carries more than 95% of the total copper in healthy human plasma.The rest is accounted for by macroglobulins. Ceruloplasmin exhibits a copper-dependent oxidase activity, which is associated with oxidation of Fe^{2+} (ferrous iron) into Fe^{3+} (ferric iron), therefore assisting in its transport in the plasma in association with transferrin, which can carry iron only in the ferric state.[5] When ceruloplasmin is not functioning properly many downstream negative effects, again involving the body's ability to carry out cellular respiration, can take place. Normal iron and copper metabolism as well as ATP production can be compromised, as well as increased levels of oxidative stress.

An issue aside from glyphosate substituting for glycine causing grave dysfunction in protein function, this pervasive chemical has also been shown to chelate the mineral manganese (Mn) in plants. This often overlooked but important nutrient is required for multiple essential functions in the body. A recent study on cows fed a feed that contained glyphosate revealed a severe depletion of serum Mn. Mn has important roles in physiology, and its depletion is associated with gut dysbiosis as well as neuropathologies such as autism, Alzheimer's disease (AD), depression, anxiety syndrome, Parkinson's disease (PD), and prion diseases. Glutamate overexpression in the brain in association with autism, AD, and other neurological diseases can be explained by Mn deficiency. Mn superoxide dismutase protects mitochondria from oxidative damage, and mitochondrial dysfunction is a key feature of autism and Alzheimer's. Chondroitin sulfate synthesis depends on Mn, and its deficiency leads to osteoporosis and osteomalacia. Lactobacillus, depleted in

autism, depend critically on Mn for antioxidant protection. Lactobacillus probiotics can treat anxiety, which is a comorbidity of autism and chronic fatigue syndrome. Sperm motility depends on Mn, and this may partially explain increased rates of infertility and birth defects. As noted in the scientific research, conditions of adequate Mn in the diet, glyphosate, through its disruption of bile acid homeostasis, ironically can promote toxic accumulation of Mn in the brainstem, leading to conditions such as PD and prion diseases.

Avoidance of glyphosate is the best strategy, which can be best attempted by eating organically grown food. Yet as pervasive as this chemical is, it is important to implement strategies for protection and detoxification, especially in those with chronic diseases such as Lyme disease, autism or any neurological disease. Testing for glyphosate levels can be done using *Great Plains* laboratories urinary assessment. Also, *The Detox Project*, is working alongside Pennsylvania-based Abraxis, Inc., to provide the global public with a uniquely developed and packaged home test kit for glyphosate: *The GlyphoCheck™ Home Test for Glyphosate in Food and Water*. This company uses immunoassay lateral flow device test kits that laboratories and governmental agencies have used for glyphosate analysis. *The Detox Project* is also working alongside Kudzu Science, is enabling the public to find out their long-term exposure to a range of the most used pesticides at home and in agriculture, such as glyphosate. Their website is www.detoxproject.org It is important to keep in mind that the body typically uses adipose to store toxins; keeping them sequestered instead of being in circulation where they can be damaging. Therefore, both serum and urine testing can be misleading. Indirect monitoring of physiological stress from toxins can be done by using blood levels of gamma-glutamyltransferase (GGT). GGT's predictive utility applies well beyond liver disease: elevated GGT is linked to "increased risk to a multitude of diseases and conditions, including cardiovascular disease, diabetes, metabolic syndrome (MetS), and all-cause mortality."[2] Low levels of

manganese are also associated with glyphosate toxicity as is decreased lactobacillus on stool analysis, which can lead to vitamin K2 deficiency. Some practitioners will use nutraceuticals to try induce the body to expel glyphosate, then do before and after levels. This type of challenge has both risks and benefits to discuss with a health care provider.

Strategies to help protect the body from glyphosate include avoidance, as mentioned as well as using foods high in *Acetobacter*, which can help the body rid itself of this toxin. A food that is high in *Acetobacter* is apple cider vinegar. Glyphosate is also known for suppression of proper gut bacteria function. Research by *Biomic Sciences* shows that glyphosate is ten times more potent than gluten in its ability to degrade tight junctions in the gut membrane wall. With the help of Dr. Zach Bush this company has recently proven that the supplement RESTORE can increase and strengthen tight junctions and can protect against ongoing everyday exposure to herbicides such as glyphosate. RESTORE is a soil-derived, lignite extract dietary supplement.[9] A recent study done by researcher at the NutriGenetic Research Institute found upon survey that those who sweat the most (physical activity, regular sauna use) were those with the lowest amounts of glyphosate in their urine. Although this study is unpublished it remains to be possible evidence as to the use of sweating as an excretion pathway for glyphosate.

Glyphosate is the most widely used herbicide in the world despite the large number of "tumorigenic effects on biological systems, including direct damage to DNA in sensitive cells, disruption of glycine homeostasis, succinate dehydrogenase inhibition, chelation of manganese, modification to more carcinogenic molecules such as N-nitrosoglyphosate and glyoxylate, disruption of fructose metabolism, etc." Glyphosate has the ability to substitute itself for glycine residues in many important proteins in the human body. This, among other detrimental effects, has massive implications in terms of impairing basic physiology, therefore resulting in a plethora of

phenotypic expressions of disease. Effort must be made to avoid this toxic substance as well as measures to help the body detoxify from it, especially in those with compromised systems fighting such diseases as Lyme disease.

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