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Review • **Survey** • Nutrition • Dietary Intervention • Public Health • Clinical Care • Pesticides

Survey Reports Improved Health After Avoiding Genetically Modified Foods

Part 1: Health Concerns—GMOs, Bt-toxin, and Roundup®
Part 2: Survey Results
Part 3: Focus on Digestive Disorders

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Abstract: A survey of 3,256 respondents, primarily residing in the United States, reveal improvements in a wide range of health symptoms following the removal or reduced consumption of genetically engineered foods, also called genetically modified organisms or GMOs. The changes are consistent with reports by physicians and others about improvements accompanying a switch to largely non-GMO and organic diets. The conditions that were most frequently reported as showing improvement include: Digestive: 85.2%, Fatigue, low energy: 60.4%, Overweight or obesity: 54.6%, Clouding of consciousness, "brain fog": 51.7%, Food allergies or sensitivities: 50.2%, Mood problems, such as anxiety or depression: 51.1%, Memory, concentration: 48.1%, Joint pain: 47.5%, Seasonal allergies: 46.6%, Gluten sensitivities: 42.2%, Insomnia: 33.2%, Other skin conditions (not eczema): 30.9%, Hormonal problems: 30.4%, Musculoskeletal pain: 25.2%, Autoimmune disease: 21.4%, Eczema: 20.8%, and Cardiovascular problems, including high blood pressure: 19.8%. Mechanisms by which GMOs may contribute to digestive disorders—the most frequently reported symptoms improved by GMO avoidance—is discussed. Three possible modes of action by GMOs are evaluated: 1) the disruptive and unpredictable nature of the process of genetic modification itself, which can introduce or elevate allergens, toxins, and anti-nutrients; 2) possible allergenic and toxic effects of *Bt* toxin, the insecticide produced within most genetically engineered corn varieties grown in the United States (US); and 3) the health impacts of glyphosate-based herbicides, such as Roundup®, which are sprayed on and absorbed into most genetically engineered food crops. The studies in these areas support several potential causative pathways leading to digestive disorders and may help explain why these and other related diseases have been rising in parallel with the increased acreage of GMOs and the application of Roundup® on these crop acres.

Part 1: Introduction—Discussion of Health Concerns—GMOs, Bt-toxin, and Roundup®

Widespread Use of Untested GM Foods and Related Pesticide Chemicals

The process of genetic modification (GM) involves the transfer or rearrangement of genetic material within or between species' DNA using laboratory techniques. These laboratory techniques are distinct from natural methods, such as hybridization, that alter the genome through sexual reproduction.

Most of the currently commercialized crops known as genetically modified organisms (GMOs) have had non-plant genes inserted into their DNA. Such genes are usually taken from bacteria or viruses, to confer a

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particular trait. Eleven genetically modified (GM) food crops are currently grown for commercial consumption. The six major GM crops are soy, corn, cotton, canola, sugar beets, and alfalfa, all of which are used as food for humans and animals. Cottonseed and canola are also processed into food-grade oils and sugar beets are refined to make sugar.

All six major GMOs are engineered to be herbicide tolerant (HT), i.e. to survive spray applications of herbicide (vernacular: "weed killer"). HT crops comprise 89% of all GMOs grown in the US. By far, the most widely grown HT variety of crops is called "Roundup® Ready" (RR), produced by Monsanto Company to withstand field treatments of Roundup® herbicide with glyphosate as the active ingredient, which is absorbed into the crop.[1] The food portion of RR crops contains high residue levels of glyphosate.[2] As of 2016, 94% of soybeans grown in the US were RR.[3] Other varieties of GMOs are engineered to withstand the herbicide glufosinate, and more recently, Dicamba and 2,4-D.

See associated Editorial and Comments attached with this article

Some varieties of corn and cotton have genes from *Bacillus thuringiensis*, a soil bacteria variety, inserted into their cells, which produce a toxic insecticide called *Bt* toxin. As of 2016, 76% of corn grown in the US is both *Bt*-producing (*Bt*) and HT. Corn with only the *Bt* trait comprises just 3% of the US corn acreage, while HT-only corn comprises 13%. For cotton, 80% are both *Bt* and HT, 4% are *Bt* only, and 9% are HT only.[4]

Varieties of GMO zucchini, yellow squash, and papaya varieties have virus genes inserted into them, which are designed to provide resistance to infections from specific plant viruses. Two newly approved crops, apples and potatoes, were engineered using double stranded RNA technology, which suppresses expression of the gene that causes the food to oxidize and discolor (i.e. turn brown when sliced). A small amount of GMO apples was commercially released for the first time in 2016 and according to the potatoes' developer, J. R. Simplot, GMO potatoes have been sold via supermarkets.[5] Numerous other types of GMO crops have been developed and many have been subject to field trials.

Background

The US Food and Drug Administration (FDA) policy regarding GMOs, implemented in 1992 and still in force, allows GMO makers to determine on their own if their foods are "Generally Recognized as Safe" (GRAS). If they are deemed to be GRAS, the FDA does not require any safety studies or labels.

The FDA also does not require that companies submit any data to the agency, but offers companies a voluntary pre-market consultation. There are no requirements or safety testing standards. Documentation provided by the GMO makers is typically summary in nature with no raw data.[6]

At the end of the consultation, the FDA releases a letter to the company acknowledging that it is the responsibility of the GMO maker to determine that their foods are safe, and that the voluntary consultation process simply confirms that the company made that determination. In one letter to Monsanto regarding their MON810 *Bt* corn, the FDA Regulatory Affairs Manager wrote, "Based on the safety and nutritional assessment *you* have conducted, it is our understanding that *Monsanto* has concluded that corn products derived from this new variety are not materially different in composition, safety, and other relevant parameters from corn currently on the market, and that the genetically modified corn does not raise issues that would require premarket review or approval by FDA." (Emphasis added.) *The letter does not state that the FDA declares that the GMO is safe*.[7]

The agency justified this hands-off approach in the policy document by declaring that it "wasn't aware of any information" showing that GMOs were different "in any meaningful or uniform way"[8] — a direct contradiction to the opinions voiced in the memos from their scientists.

In 1998 the FDA was forced to turn over tens of thousands of pages of internal memos related to GMOs due to a lawsuit filed by the Alliance for Bio-integrity. The memos[9] revealed that agency scientists who were tasked to help create the FDA policy on GMOs had repeatedly warned their superiors that GMO foods were quite different than foods created from traditional breeding. The technology, they said, could create serious side effects, such as allergies, toxins, antibiotic-resistant diseases, and nutritional problems. They urged their superiors to require rigorous long-term tests.

The same set of FDA documents also revealed that the White House had instructed the agency to promote biotechnology.[10] Then Vice-President Dan Quayle said it was necessary to "resist the spread of unnecessary regulation" in order to keep America the "world leader in biotechnology."[11]

The person who oversaw the GMO policy for the FDA was a political appointee, Michael Taylor, the former outside attorney for Monsanto, later the company's vice president of government and regulatory affairs, and later the Deputy Commissioner for Foods at the FDA.

Although several other nations require some limited safety data, even those requirements are widely criticized as inadequate, obsolete, and inappropriately reliant on unpublished research provided by the GMO producers themselves. There are very few safety studies that would be rigorous enough to be called "academic." Although proponents of GMOs often point to compilations of hundreds of studies, the vast majority of

these are considered commercial in nature. They look at data for market considerations, but rarely have relevant designs for safety evaluations. Furthermore, analysis of industry "safety" studies has revealed research protocols apparently designed to hide evidence of harm.[12]

No human clinical trials and no post-market surveillance on health outcomes related to GMO consumption have been conducted. In 2002, Health Canada announced that it would monitor the health of Canadians to see if GMOs adversely affected health, but by the next year, according to CBC TV news, they "abandoned that research less than a year later saying it was 'too difficult to put an effective surveillance system in place.'" The reporter added, "So at this point, there is little research into the health effects of genetically modified food. So will we ever know for sure if it's safe?" [13] In 1998, it was discovered that the United Kingdom's Food Standards Agency had asked supermarket executives for the purchasing data from the 30 million consumers using loyalty cards, so they could see if those eating GMOs had higher rates of cancer, birth defects, childhood allergies, or hospital admissions. When the data collection plans were made public, the government, which had told the public that GMOs were safe, withdrew the program.[14]

In the face of insufficient pre- and post-marketing safety studies, extra attention must be paid to reports from individuals and/or their healthcare providers about potential reactions to the inclusion or exclusion of GMOs from their diet. Although correlation does not equal causation, any correlations between national health statistics and GMO consumption should be carefully investigated. Otherwise, even a significant rise in disease rates related to GMOs will easily go unnoticed.

Survey design informed by physician and personal reports

On May 8, 2009, the American Academy of Environmental Medicine (AAEM) published their policy paper on GMOs, which included a review of several peer-reviewed safety studies. Several animal studies, according to their policy paper, reveal a long list of disorders, including "infertility, immune dysregulation, accelerated aging, dysregulation of genes associated with cholesterol synthesis, [faulty] insulin regulation, cell signaling, and protein formation, and changes in the liver, kidney, spleen and gastrointestinal system." The policy concludes, "There is more than a casual association between GM foods and adverse health effects. There is causation as defined by Hill's Criteria in the areas of strength of association, consistency, specificity, biological gradient, and biological plausibility."[15] The AAEM called on the US government to implement an immediate moratorium on all GM foods and urged physicians to prescribe non-GMO diets for all patients.

"Physicians are probably seeing the effects in their patients," said AAEM past-president Jennifer Armstrong, MD, "but need to know how to ask the right questions."[16] According to David Schubert, PhD, of the Salk Institute, the patients at greatest risk from consuming GMOs are the very young. "Children are the most likely to be adversely affected by toxins and other dietary problems."[17]

Starting in November 2009, the author of this paper (JMS) began interviewing physicians and other healthcare providers who advise their patients to switch to a non-GMO and/or organic diet, asking what outcomes they observed. Audiences at numerous medical and healthcare conferences, as well as at more than 100 public lectures, were informally surveyed from the stage. Audience members shared which symptoms or conditions improved after the dietary changes. Commonly, after individual audience members shared their stories, numerous others raised their hands to indicate that they too experienced similar improvements.

The selection of health conditions used in the formal survey reported herein was based primarily on the thousands of responses by audience members, as well as numerous private conversations and email exchanges with individuals and healthcare practitioners.

Three mechanisms by which GMOs may cause health problems

Reviewed herein are three main mechanisms by which GMOs might produce or exacerbate the conditions listed in the survey: 1) the generic side-effects of the GMO transformation process, 2) the *Bt* toxin found in GMO corn and cotton plants and 3) the herbicides—particularly glyphosate-based herbicides (GBHs)—that are sprayed on most GMOs.

Collateral effects of genetic engineering

The process of creating a GMO crop results in significant damage to the host organism, with hundreds or thousands of mutations possible throughout the plants' genome.[18] A GM plant's total DNA can be 2-4% different from that of its natural parent.[19] In addition, up to 5% of its natural genes can alter their levels of protein expression because of a single insertion.[20]

These changes in the genetic sequence and expression can impact numerous other compounds and phytochemicals that make up a plant. For example, Monsanto's data on cooked GM soybeans shows as much as seven times the level of trypsin inhibitor, a natural soy allergen, and a doubling of soy lectin, an anti-nutrient that can potentially block nutrient absorption.[21] Monsanto's MON810 *Bt* corn has 43 genes that are significantly altered in their expression levels. One of these, which produces an allergenic protein called gamma zein, is normally switched off in corn. In Monsanto's GMO variety, however, the allergenic protein is expressed.[22] In

addition, GM corn and soy produce higher amounts of lignin.[23]

The most comprehensive comparison of a GMO crop and its non-GMO equivalent to date, conducted by Antoniou et al., showed that Monsanto's RR corn has 117 proteins and 91 small molecule biochemicals that are significantly different from natural corn. For example, there was an increase of several polyamines in the GMO corn, including putrescine and cadaverine. In addition to being responsible for the foul odor of rotting flesh, these two substances, according to co-author Dr. Michael Antoniou, "enhance the effects of histamine, thus heightening allergic reactions, and both have been implicated in the formation of carcinogenic substances called nitrosamines with nitrite in meat products."[24]

Unanticipated changes in proteins

1. Amino acid sequence

Side-effects from the process of genetic engineering can result in unexpected changes in the amino acid sequence of the transgene product. For example, the transgene construct inserted into RR soybeans was designed to create a fixed length of RNA transcript. Instead, the portion of the transgene that was supposed to determine the length of the transgene (NOS terminator) failed to function correctly. This resulted in overly long RNA transcripts *that do not exist in nature* with some potentially able to produce proteins that are different from the intended/targeted result. Most GMOs use the same inefficient NOS terminator.

2. Glycosylation

Proteins produced in transgenic organisms may be modified by addition of materials, such as sugars, in unpredicted ways. The binding of sugar (glycosylation) to proteins can convert a benign protein, such as naturally produced by beans, into an immunoreactive and potentially allergenic protein, when produced in transgenic peas.[25]

3. Misshaped proteins

The shape of a protein is critical to its function. The process of genetic engineering may result in unpredicted alterations of protein shape and size, with potentially dangerous effects. In a proteomics analysis of MON810, for example, researchers discovered that seed storage proteins in the Bt corn were truncated, which they described "as a major concern."[26]

One reason proteins can be misshaped is if they are folded improperly. When the polypeptides produced from inserted foreign genes fold after synthesis in the potentially different cellular environment of the GMO, that new environment may have characteristics (e.g. altered pH or a lack of needed "chaperone" proteins) that affects folding in ways different from their native context. Likewise, the new cellular context may cause them to denature more frequently.

Unanticipated effects from altered RNA

It is now understood that certain types of small RNA molecules can have a direct and significant impact on gene expression through a process known as RNA interference (RNAi). RNAi usually results in reducing expression of certain genes, which in turn can lead to decreases or increases in expression of others. This may impact an organism's function and health. The process of engineering small RNA molecules into GMOs also has the potential of unintentionally producing additional small RNAs that can interfere with the function of genes that are not being targeted. Since small RNAs in food have been found to survive digestion and enter the body of the consumer, [27] ingestion of the intended and unintended small RNA molecules in the GMO can alter gene function with unknown consequences.

Gene transfer from GMOs

Transgenes may horizontally transfer to humans or other organisms. While GMO DNA has been identified in various organs and the blood of animals fed GMOs, the studies were unable to determine if they were integrated into the host cells' genome. Netherwood et al[28] confirmed that part of the RR soybean transgene transferred and integrated into bacteria living inside human intestines. It is not known whether the transformed bacteria actively expressed the transgenic protein. If it is expressed, then our gut flora may be compromised by GMOs and forced to produce GMO proteins continuously inside our digestive tract.

Evidence of adverse effects from GMO process

A striking example of the damage caused by the generic GMO process was highlighted in experiments by Arpad Pusztai. Commissioned by the United Kingdom (UK) government to design testing protocols for GMO food safety, Pusztai and his team came up with a system to better identify the impacts of the inserted transgene as well as the unintended consequences due to the process of genetic engineering.[29] To demonstrate the protocol, they used a GM potato engineered with a gene from the snowdrop plant that produces a protein with insecticidal properties called galanthus nivalis lectin (GNA). Pusztai and his colleagues conducted extensive research on GNA for nearly seven years and found it to be harmless to rats.

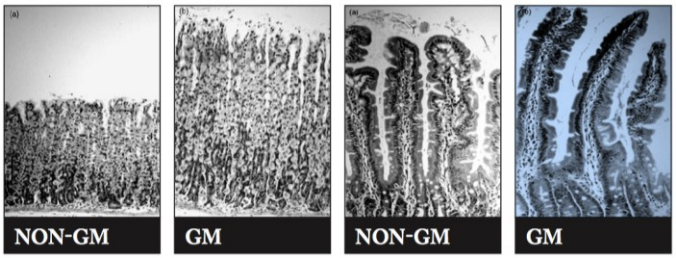
As part of their feeding trial, groups of rats were fed diets with GMO potatoes, natural potatoes of the same type, or natural potatoes spiked with added GNA in the same amount produced by the GMO potato.[30]

The GMO potatoes adversely affected virtually every organ system of young rats—with most changes found after just 10 days. The diet with added non-GMO GNA, however, did not produce such harm. This

demonstrated that effects from the GMO process—other than the lectin itself—were toxic to the animals. The impacts of the GMO potato included the following:[31]

- The young rats' brains, livers, and testicles were generally smaller, suggesting disruption of normal growth processes due to either malabsorption of nutrients or unknown toxins.
- White blood cells responded to a challenge more slowly, indicating immune system damage; organs related to the immune system, including the thymus and the spleen showed changes.
- The animals had enlarged pancreases and intestines, and partial atrophy of the liver.[4]
- In all cases, the GM potato created proliferative cell growth in the stomach and in both the small and large intestines; the lining was significantly thicker than controls (see Figure 1). Although no tumors were detected, such growth may indicate a precancerous condition.

Figure 1. *The digestive tract of rats fed GM potatoes engineered to produce GNA lectin showed excessive cell growth compared to rats fed non-GMO potatoes. Another group of rats fed non-GMO potatoes plus the GNA lectin did not exhibit the cell growth. This suggests that the process of genetically engineering the potato, and* not *the lectin, was the cause.*



Stomach
The stomach lining of GM-fed rats showed proliferative cell growth.

Intestines
The excessive cell growth was also found in the wall of the small intestines (crypts) in rats fed GM potatoes.

Photos provided by Stanley Ewen.

The studies conducted by the makers of GMOs have not used the same rigorous approach as Pusztai. His approach includes the third feeding group in which animals consume non-GMO crops spiked with just the protein produced in the GMO. Thus, their studies cannot evaluate which of the side-effects are due to the specific gene product and which are due to the generic transformation process itself. Industry studies do not generally test for the type of health effects found in Pusztai's rats, leaving us without valuable and necessary information regarding the biochemical products, physiological effects, and clinical consequences of GMO foods.

Consumption of the Bt Toxin insecticide

Two types of commercialized crops, corn and cotton, are engineered to produce an insecticide called *Bt* toxin. The only product from cotton that we consume directly is cottonseed oil, which is generally void of proteins and would therefore not be a source of dietary *Bt* toxin. *Bt* corn, however, can expose us to the toxin via fresh corn and corn products, such as corn chips, polenta, and tortillas.

Bt toxin is produced from *Bacillus thuringiensis* soil bacteria. In its natural state, the toxin creates small holes in insects' gut walls, killing them. It is believed that the gut bacteria within the insect move through the "leaky gut" and then kill the insect.[32]

Genetic engineers have inserted various altered *Bt* toxin genes directly into the DNA of corn and cotton plants so the crops produce the toxin in every cell. To justify this addition to our food supply, biotech companies and the US Environmental Protection Agency (EPA) claimed that *Bt* toxin and *Bacillus thuringiensis* in their natural forms were used as natural methods of pest control for years, with no impact on humans or mammals of any type and were therefore only dangerous to certain insects.[33] However, several peer-reviewed published studies contradict this assertion.

Studies in mice showed that natural *Bt* toxin provoked systemic and mucosal immune system responses as powerful as cholera toxin. Furthermore, exposure to *Bt* toxin sensitized the mice so that their immune system responded to formerly harmless substances.[34]

A 2008 Italian government study found that *Bt* corn provoked profound immune responses in mice.[35] Monsanto's own rat studies with *Bt* corn also showed toxicity and immune responses.[36] Another mouse study confirmed that *Bt* toxin is cytotoxic.[37]

A 2012 article in *Journal of Applied Toxicology*[38] "documented that modified *Bt* toxins [from GM plants] are not inert on human cells, but can exert toxicity." In vitro and in generally higher concentrations than that which is expected to be produced in average *Bt* corn, researchers found that *Bt* toxin disrupts the cell membrane of human cells in just 24 hours, causing fluid to leak through the cell walls.

In the US, farmworkers exhibited antibody responses to *Bt* toxin and hundreds of people in the Pacific Northwest, who were inadvertently sprayed with *Bt* when it was used to kill gypsy moths, exhibited allergic and flu-like symptoms. Some workers had to go to the hospital.[39]

Numerous reports, including medical investigations and hospital records, show that thousands of agricultural workers in India exposed to *Bt* cotton varieties reported skin rashes and other health symptoms.[40,41]

US EPA regulators assumed that *Bt* toxin would be broken down in the stomach. However, in a 2011 Canadian study conducted at Sherbrooke Hospital, researchers discovered *Bt* toxin in the blood of 93% of the

pregnant women and 69% of non-pregnant women.[42] A mouse study confirmed that *Bt* toxin is cytotoxic;[43] it therefore might also damage human blood cells. Since fetuses do not have fully developed blood brain barriers, it is possible that the toxin reaches the fetal brain.

In 2001, the EPA's Scientific Advisory Panel, which included leading experts in the US, pointed to these early mouse and farmworker studies and stated that they "suggest that Bt proteins could act as antigenic and allergenic sources."[44] The EPA disregarded the warning, reregistered the *Bt* crops, and continues to claim that *Bt* toxin has no impact on humans or mammals.

They also claim that the *Bt* toxin engineered into plants is the same as that which was sprayed. However, industry submissions and published papers establish that the genetically engineered *Bt* toxin in plants is structurally different [45] from the natural *Bt* toxin used in spray applications to crops. Whereas the spray version creates a protoxin that is fully activated after entering the alkaline environment of the insect's gut, the plant version is designed to be immediately toxic. The genetically engineered *Bt* toxin (the plant version) has properties of known allergens, fails the World Health Organization's allergenicity decision tree criteria[46] and is produced in concentrations thousands of times higher than the spray version. Most notably, while the spray version can be washed off the plant and biodegrades quickly in sunlight, the plant version is encapsulated within the plant cells, remains intact, and cannot be removed by washing.

Increased herbicide use and residues on food

Herbicide-tolerant crops comprise 89% of all US grown GMOs. These plants are engineered to allow specific herbicides to be sprayed in high amounts without damaging the GM plant. Although GMO companies had publicly predicted GMOs would reduce herbicide use, the opposite has occurred—pesticide chemical use has increased as a result of GMO crop use. In fact, overuse of these herbicides has resulted in "superweeds," which have developed resistance to the herbicide. Farmers often spray higher quantities of the herbicides to kill these "superweeds." According to Benbrook, statistics from the United States Department of Agriculture (USDA) reveal that herbicide tolerant crops led to an increase in herbicide use of 527 million pounds over the first 16 years.[47] Use of Roundup® and other GBHs has increased 100-fold since the late 1970s.[48,49] The allowable glyphosate residues on GMO crops have also increased substantially, as government regulations have been relaxed to allow higher use of pesticides to accommodate industry goals.[50]

A 2013 paper in the journal *Entropy* examined the potential effects of glyphosate ingestion. Examining the biochemical impacts on two key metabolic pathways, as well as its broad-spectrum chelating effects, the authors speculate potential causal mechanisms that link it to *"most of the diseases and conditions associated with a Western diet, which include gastrointestinal disorders, obesity, diabetes, heart disease, depression, autism, infertility, cancer and Alzheimer's disease."*[51] (Emphasis added.) Although interesting, it remains to be demonstrated whether the suggested association between glyphosate ingestion and this very wide range of human disease takes place at real-world levels of exposure.

Numerous studies in the past several years, ranging from in vivo and in vitro, to occupational exposure analyses, have implicated Roundup®, or its active ingredient glyphosate, in cancer, birth defects, endocrine disorders, Parkinson's, and damage to beneficial gut bacteria.[52]

In order to postulate how applications of Roundup® or other GBHs and residues on GMO crops might cause or exacerbate specific disorders, it is necessary to identify glyphosate's possible modes of action in the body.

Glyphosate as carcinogen

The International Agency for Research on Cancer (IARC) of the World Health Organization, which is responsible for classifying chemicals as carcinogens, classified glyphosate and glyphosate-based herbicides as class 2A carcinogens—"Probably carcinogenic." They confirmed that glyphosate causes cancer in animals, it creates mutations in human DNA, and where it is sprayed, there have been spikes in cancer among the exposed populations. IARC also determined that glyphosate is genotoxic and creates oxidative stress.[53]

Glyphosate as chelator

Glyphosate, the active ingredient in Roundup®, was patented as a powerful mineral chelator in 1964, a decade before Monsanto patented it as an herbicide. It binds with cations, including zinc, manganese, cobalt, aluminum, calcium, magnesium, arsenic, iron, selenium, cobalt, chromium and arsenic. Living organisms—plants and animals (including humans)—rely on minerals for numerous metabolic pathways to function. When bound with glyphosate, the minerals cannot be utilized. [54] Glyphosate applications may therefore result in symptoms of mineral deficiency, even though the minerals are present, because the bound ("chelated") mineral is not biologically available to perform its biochemical and physiological functions. Whether glyphosate disturbs nutrient mineral homeostasis at real world levels of ingestion that could then result in disease remains an urgent factor to be investigated.

Glyphosate inhibits critical metabolic pathways

Monsanto has long described glyphosate's herbicidal mode of action as its ability to block plants' shikimate pathway. They identify the mechanism as direct inhibition of excitatory postsynaptic currents (EPSPs) by binding to

the active site of that enzyme. Other researchers identify glyphosate's tendency to strongly bind with cobalt and manganese as the mechanism for inhibiting the shikimate pathway. In either case, this shikimate pathway produces the aromatic amino acids—tryptophan, tyrosine, and phenylalanine, which are needed for plant survival.[55]

Monsanto has claimed that glyphosate is safe for humans and other mammals because they lack the shikimate pathway. However, critical gut bacteria in humans and mammals also possess the shikimate pathway to produce these essential aromatic amino acids, which are the building blocks for producing proteins.

The production of serotonin, for example, requires tryptophan, which is a product of the shikimate pathway. There is insufficient research to determine whether the amount of tryptophan produced by gut bacteria contributes significantly to the production of serotonin. If so, when there is insufficient tryptophan in the food, glyphosate's suppression of the shikimate pathway may reduce overall serotonin levels.

Serotonin might also be impacted in other ways. Up to 90% of the serotonin in the human body is produced in the gut by enterochromaffin (EC) cells. It is now well established that a large proportion of the serotonin produced by EC cells is dependent on stimulation from certain gut bacteria.[56] Gut bacterial dysbiosis resulting from sufficient amounts of glyphosate ingestion could therefore give rise to inadequate amounts of serotonin production by EC cells. This could lead to health and behavioral problems.

No studies have evaluated the impact of glyphosate on gut-produced and microbe-produced serotonin.

Regardless, the safety determination must not ignore the fact that other metabolic pathways could also be disrupted by glyphosate's ability to bind with nutrient metals. Minerals are critical components in numerous pathways acting as vital elements of many enzymatic functions, and glyphosate's ability to chelate is potent and thus potentially damaging to health.

Glyphosate as antibiotic

Glyphosate was patented as a broad-spectrum biocide, which preferentially kills the types of bacteria that are considered beneficial in the gut of humans and animals. For example, *Lactobacillus* and *Bifidobacteria* are particularly sensitive to glyphosate and are killed in the presence of even low concentrations. Unfortunately, bacteria considered potentially pathogenic in the human gut are more resistant to glyphosate including *Clostridium difficile*, *Escherichia coli*, and *Salmonella*.[57] Studies are needed to evaluate the extent of antibiotic activity that occurs in the human gut due to real-world levels of glyphosate exposure.

Glyphosate as mitochondrial toxin

Glyphosate can disturb vital functions of the mitochondria. This may be due in part to its ability to bind with manganese, which is needed by the mitochondria for proper functioning. Further research is needed to establish whether the amount of glyphosate residues in food are sufficient to contribute to mitochondrial dysfunction in humans.[58]

Glyphosate as teratogen

Glyphosate and GBHs can interfere with the retinoic acid pathway in fetal development. Studies have shown teratogenic effects.[59] However, these studies used high, unrealistic doses, so further studies using realistic doses are needed.

Glyphosate as endocrine disruptor and estrogen mimicker

Several studies have shown that glyphosate influences hormones and can act as an endocrine disruptor. For the most part, these studies use animal models and human cells with levels of glyphosate that are higher than that which is expected to be consumed as residues on food. Of course, many endocrine disrupting chemicals can exert an influence—even a greater influence—at minute levels. There are no regulatory requirements to test these low levels because government policies have not kept pace with the body of research on low-dose impacts. Some research of note, using both small and high dosages, includes:

- Glyphosate can interfere with the action of aromatase, which determines the ratio of estrogen and testosterone.[60]
- Rats fed Roundup® (R) in the drinking water over 24 months, and also those fed GMO RR corn, showed changes in their sex hormones. "In females, the androgen/estrogen balance in serum was modified by GM maize and Roundup® treatments… For male animals at the highest R treatment dose, levels of estrogens were more than doubled."[61]
- Adjuvants or surfactants used with herbicides are generally considered inert, but the "inert" ingredient in the full formulation of Roundup® can also exert low dose hormonal effects. According to Defarge, et al., "Aromatase activity was decreased both by the co-formulants alone (polyethoxylated tallow amine-POEA and alkyl polyglucoside-APG) and by the formulations, from concentrations 800 times lower than the agricultural dilutions; while G [glyphosate] exerted an effect only at 1/3 of the agricultural dilution. *It was demonstrated for the first time that endocrine disruption by GBH could not only be due to the declared active ingredient but also to co-formulants*." (Emphasis added.)
- Seralini observed hormonal effects observed in rats fed GBHs, but it is unclear whether the impacts were due to the glyphosate, the adjuvants, the GMO

transformation process, or a combination of them all.[62]

- At parts per billion, glyphosate attached to estrogen receptors in human breast cancer cells and triggered growth,[63] although a follow-up study was unable to replicate this result.[64]

Overlapping and synergistic factors

A two-year feeding study highlights how negative impacts of GMOs may be due to both the GMO process and the added herbicide.[65] The researchers fed rats RR corn that had been sprayed with Roundup®, RR corn without Roundup®, or Roundup® without the corn. The Roundup® alone was tested at a range of doses, including a very low dose of a level that would be permitted in drinking water. Animals in all three treatment categories—GMO alone, Roundup® alone, and GMO corn with Roundup®—suffered organ damage, especially to the liver and kidney but also to the pituitary gland. Increased tumor incidence and mortality were observed in most treatment groups. In particular, a statistically significant increase in mammary tumor incidence occurred in the lowest dose Roundup® group. In this study, it was clear that compared to controls, rats fed GMO RR corn, Roundup®, and the combination of the two, were all harmed. Most animal studies that test GM crops do not include multiple feeding groups, making it unclear whether the causative factor is the GMO, the *Bt* toxin, or the Roundup®.

In the study above, a follow up molecular analysis (transcriptome – gene function profile) of liver and kidney tissues clearly confirmed the damage for the lowest dose Roundup®-fed group.[66] A further molecular analysis involving proteomics (protein type profile) and metabolomics (metabolite profile) found that this lowest-dose Roundup®-fed group suffered from non-alcoholic fatty liver disease (NAFLD),[67] an increasingly common condition that can lead to a more serious disease, non-alcoholic steatohepatosis, and ultimately to cirrhosis. NAFLD is also a risk factor for liver cancer. This study has identified long-term low-dose exposure to Roundup® as a previously unrecognized risk factor for NAFLD and its associated complications.

Several animal studies show health impacts

The online publication *GMO Myths and Truths* provides an excellent summary of the research results on GMOs, using laboratory and farm animals. The publication also counters several arguments proposed by GMO advocates that attempt to downplay the findings. The categories of problems discovered, as listed below, are from studies[68] conducted both by independent researchers and by GM industry employees or contractors.

- Severe organ damage and increased rates of large tumors and mortality[69]
- Altered blood biochemistry, multiple organ damage, and potential effects on male fertility[70]
- Stomach lesions and unexplained mortality[71]
- Immune response and allergic reaction[72]
- Immune disturbances[73]
- Enlarged lymph nodes and immune disturbances[74]
- Disturbed liver, pancreas and testes function[75]
- Liver aging[76]
- Disturbed enzyme functioning in kidney and heart[77]
- Higher density of uterine lining[78]
- Severe stomach inflammation and heavier uteri[79]
- Liver and kidney toxicity[80]
- Changed level of fats in blood and signs of liver and kidney toxicity[81]
- Toxic effects on liver and kidneys and altered blood biochemistry[82]
- Enlarged liver[83]
- Disturbances in digestive system and changes to liver and pancreas[84]
- Excessive growth in the lining of the gut[85]
- Intestinal abnormalities[86]
- Altered blood biochemistry and gut bacteria, and immune response[87]
- Altered gut bacteria and organ weights[88]
- Less efficient feed utilization and digestive disturbance[89]

Consumer exposure

Consumers are exposed to GM foods and GM DNA through consumption of the whole food crop, derivatives of the crop, and to a lesser extent through milk, meat, and eggs from animals that have been fed GM feed. GMO crops can be eaten raw (e.g. GMO papaya and zucchini) or cooked (e.g. edamame, corn, corn chips, tortillas, zucchini, squash, etc.). Therefore, any legitimate safety testing must include both raw and cooked samples, including samples cooked in a variety of real-world means including baking and frying.

GMO product derivatives include highly processed components, such as sugar, corn sweeteners, soy protein-based products and the oils from soy, corn, cottonseed, and canola. For these, the DNA and proteins derived from the transgene are often removed during processing. While processing may reduce the health risk, it does not ensure that GMO derivatives are always as safe as their non-GMO counterparts. The composition of these processed ingredients may be altered due to the changes that take place in the plant as a result of the disruptive GMO transformation process. This could result in the presence of novel toxins and allergenic substances.

GMO DNA has been detected in milk from animals fed GMOs.[90] It is not clear whether the *Bt* toxin consumed by the animals continues to be intact after consumption and digestion, and if it will be active in meat or dairy products. According to a study by Aris and Leblanc, "there may be a high risk of exposure through consumption of contaminated meat."[91] They cite studies showing that "trace amounts of the Cry1Ab toxin were

detected in the gastrointestinal contents of livestock fed on GM corn."[92]

Glyphosate residues are found in food from RR crops sprayed with a GBH. In 1999, Monsanto claimed that residue levels of up to 5.6 mg/kg in GM-soy represent "…extreme levels, and far higher than those typically found."[93] But authors of a 2014 study demonstrated that "Seven out of the 10 GM-soy samples we tested, however, surpassed this 'extreme level'" (of glyphosate [plus its derivative AMPA]).[94] Their average residue level was 9.0 mg/kg.

Glyphosate is water soluble; therefore it is unlikely that soybean *oil* (rather than whole soy) contains residues. According to a report from China, however, tests verified the presence of aminomethylphosphonic acid (AMPA), the primary breakdown derivative of glyphosate in soybean oil.[95] AMPA exhibits some toxic properties and has a similar structure and profile to glyphosate.[96] Another study by Bøhn et al., showed significant levels of glyphosate residues in GMO soybeans.[97]

According to Monsanto's radiolabel studies submitted to the EPA and later obtained by Anthony Samsel, glyphosate is found in animal tissues.[98] A study using an ELISA detection method found glyphosate residues in breast milk,[99] while two studies using mass spec did not.[100]

If GMOs and GBHs have detrimental effects, it is logical to conclude that animals fed a diet almost exclusively of GMOs would be measurably different than animals raised on diets free from GMOs. According to Heinemann's extensive review of the scientific literature, studies reveal the presence of "DNA and protein unique to GM plants within animals and animal products." Furthermore, "There is compelling evidence that animals provided with feed containing GM ingredients can react in a way that is unique to an exposure to GM plants. This is revealed through metabolic, physiological or immunological responses in exposed animals."[101] No studies have been conducted to determine how these differences could exert an influence on the health of humans consuming the animal products.

The consumption of residues of GBHs is not limited to RR crops. It is not uncommon for some non-GM crops, such as wheat, barley, rice, wine grapes, sunflowers, rye, oats, and sugarcane, to be given a pre-harvest application of GBH as a desiccant to dry the crop, accelerate ripening/maturation (as the plant dies), and/or kill weeds. To accommodate this practice, the EPA raised the allowable levels of glyphosate residues on more than 160 crops.[102] The actual amount of glyphosate residues in food, however, is not yet measured by the FDA, even though they monitor levels of all other commonly used pesticides. The FDA announced plans to monitor glyphosate residues, but the program was suspended and then later declared active once again. However, we do not yet have a measure of human glyphosate exposure in the US. According to independent food testing, common US foods ranged from a low of 8.02 ppb in Goldfish Crackers Colors by Pepperidge Farm, to 1,125.3 ppb in Original Cheerios by General Mills.[103] The EPA asserts that these levels are below permitted residue levels and thus pose no health concerns for consumers. However, others challenge that level as unscientific. For example, the amount of Roundup® consumed by rats in their drinking water that caused non-alcoholic fatty liver was 0.1 ppb containing 0.05ppb of glyphosate. On a per body weight basis the rats ingested 4 nanograms (4 thousand millionths of a gram) of glyphosate per kilogram body weight. This is 437,500 times lower than US permitted levels.[104] And based on glyphosate levels detected in US citizens, Americans probably consume about 1000-fold more glyphosate than the amount responsible for the liver disease in rats.[105] Thus it is possible that ingestion of glyphosate from foods at the residue levels detected could cause harm over the long term.

Organic crops are not allowed to be sprayed with GBH. Therefore, if GBH is one of the causative factors in the health problems reported, we would expect better outcomes for those who switch to organic, rather than those who switch to non-GMO foods that are still sprayed.

The main source of exposure to glyphosate is through food. However, secondary sources include air, rain, water, and drift from agricultural and homeowner use.[106]

Part 2: Survey Results

Methods

Survey participation was requested from November 2014 through August 2015. The questionnaire was emailed to 180,716 members of the database of the Institute for Responsible Technology (IRT). There were 3,256 responses—a response rate of 1.8%.

Reporting bias

This is a self-selecting survey of a non-representative sample of the population. IRT is a leading advocacy group that educates people on the health dangers of GMOs. The results of this survey are therefore limited to a population that is already aware of GM crops and has been exposed to information about the negative health impacts. Some percentage of the respondents may be biased towards attributing health improvements to the elimination of GMOs based on expectations. On the other hand, this population will have a higher percentage of people who have become educated about GM food risks, eliminated them, and may have noticed a change as a result.

There is also an expected bias on a per-disease basis. People will more likely identify an actual connection between their diet and a chronic condition if that condition is normally associated with a dietary response. Gastrointestinal disorders and food allergies are more likely to be considered and evaluated in terms of

reaction to diet compared to cancer, for example, or infertility. Furthermore, the more serious diseases, once discovered, are often treated with pharmaceuticals, surgery, and other treatments that might overshadow or mask the impact of the diet.

The Questionnaire

Based on the first question in the survey, respondents offered results from dietary changes for themselves (80%), their spouse (4.6%), their child (4.2%), and their patient (1%). In addition, 2.2% provided information on their pet, 3% on their livestock, and 7% on "other," but these were not tallied in the results below. Most respondents did not choose to indicate their zip code or location, but of the 1,870 who did, 1,620 were in the US and 98 in Canada. Thus, the vast majority of respondents were located in the US, which is consistent with the demographics of the email list used to solicit responses.

The survey was designed to identify the relative frequency of conditions that improved with a non-GMO diet, and the degree of reported improvement. It was not intended to identify what percentage of the population would improve on a non-GMO diet.

The survey was composed of six questions. The second question was, "What symptoms or conditions have you seen improve since switching to a non-GMO Diet?" Response choices for each of 28 symptoms or conditions were as follows:

1. Some Mild Improvement
2. Moderate Improvement
3. Significant Improvement
4. Nearly Gone
5. Complete Recovery
6. N/A Not Applicable*

*"Not applicable" was the pre-checked default response, required by the survey system used.

Table 1 shows the percentages of respondents who indicated any improvements, 1-5.

Competing co-factors

There are no laws requiring GMO foods to be labeled as such in the US. Avoiding them, therefore, usually involves a strategy that can introduce other possible co-factors that may be responsible for the reported improved health outcomes. Because organic foods are not allowed to intentionally contain GMOs, switching to organic foods is a popular strategy to avoid GMOs. However, numerous toxic chemicals are also considered prohibited substances according to the organic standards. Thus, improvements in health may be due in part or in full to the elimination of these other products.

Most GMOs are found in processed foods. This is because derivatives of soy, corn, cottonseed, canola, and sugar beets are common ingredients in processed foods. Many people choose to avoid GMOs by reducing consumption of processed foods. Therefore, health improvements may be related to the benefits of unprocessed foods.

Some healthcare practitioners recommend elimination of GMOs along with other dietary instructions at the same time, such as eliminating gluten or dairy, which may contribute to or account for the health improvements.

The questionnaire included the question: "In addition to eliminating GMOs from your diet, were there other changes that you made at the same time or thereafter? Check all that apply." The number and percentage of respondents that checked each change shown in Table 2.

Table 1. Survey Question #2 Responses

Health Condition Improved	% Reported
Digestive problems	85.2%
Fatigue	60.4%
Overweight or obesity	54.6%
Clouding of consciousness (brain fog)	51.7%
Mood problems/anxiety/depression	51.1%
Food allergies or sensitivities	50.2%
Memory and concentration	48.1%
Joint pain	47.5%
Seasonal allergies	46.6%
Gluten sensitivities	42.2%
Insomnia	33.2%
Other skin conditions	30.9%
Hormonal problems	30.4%
Musculoskeletal pain	25.2%
Autoimmune disease	21.4%
Eczema	20.8%
Cardiovascular problems and high blood pressure	19.8%
Asthma	14.8%
Menstrual problems	13.1%
Diabetes	10.6%
Other mental disorders	7.9%
Underweight	6.5%
Cancer	4.8%
Kidney disease	4.5%
Infertility	3.8%
Autism spectrum	2.6%
Alzheimer's disease	2.4%
Parkinson's disease	1.4%

Table 2. Survey Question #4 Responses

Dietary Change	Number	Percent
Organic diet	2,424	74.4%
Reduced processed foods	2,182	67.0%
Stopped drinking soda, or other sweetened beverages	1,503	46.2%
Gluten-free	1,099	33.8%

Eliminated dairy products	755	23.2%
Raw	381	11.7%
Vegetarian	372	11.4%
Vegan	228	7.0%
No other changes	226	6.9%

Without carefully controlled human clinical trials, it may be impossible to assess how much, if any, the GMO component of the diet is causing health problems. The following evidence does, however, support the notion that GMOs (and their associated pesticide content) are a contributor to health conditions:

1. Most of the reported improvements in humans correlate with the categories of health impacts of GMOs, glyphosate, and GBH on animals in carefully controlled feeding trials, which exclude other confounding dietary factors.
2. Based on informal surveys and conversations referred to above, farmers and veterinarians describe improvements in livestock that are switched to non-GMO soy, corn, or both. In livestock, there are generally no other dietary changes and the reported improvements, e.g. gastrointestinal, immune, irritable or aggressive behavior, fatigue level, skin health, etc. are similar or identical to those reported by individuals and their practitioners.
3. The categories of reported improvements also correlate with many of the diseases and conditions that increased in parallel with the expanded exposure of GMOs and their associated herbicides in the US population (See Figures 2 through 5).
4. The reporting of numerous health improvements was consistent across various dietary strategies. For example, gastrointestinal health improved for a large percentage of respondents, irrespective of whether their strategies were to switch to organic, reduce processed foods, or favor brands labeled non-GMO, etc. The non-GMO component was common to all.
5. The characteristics of GMOs, and the agricultural toxins found in the foods, can plausibly explain the conditions linked to their consumption.

***Part 3*: Focus on Digestive Disorders**

No survey can, on its own, demonstrate causality. This survey does, however, provide data that can be analyzed in conjunction with other evidence to support the argument that GMOs promote particular disorders. Below we examine additional data that may explain or highlight a causal relationship between GMO consumption and the most frequently cited health improvement in the survey—digestive problems.

With 85.2% of survey respondents reporting mild to total recovery, digestive issues are by far the number one category of self-reported benefits from a non-GMO diet. The breakdown of responses is as follows: Some Mild improvement (5.9%), Moderate Improvement (11.3%), Significant Improvement (29.1%), Nearly Gone (22.2%), Complete Recovery (16.6%).

Digestive disorders in general include inflammatory bowel, Crohn's disease, irritable bowel, acid reflux, diarrhea, constipation, ulcerative colitis, bloating, and gas.

According to CDC data, incidence of inflammatory bowel disease (IBD), Crohn's, and ulcerative colitis all rose in parallel with the percentage of GMO corn acreage planted in the US since 1996 and the amount of GBH sprayed on GMO corn and soy acreage. The corresponding graphs shown in Figures 2 through 5 are reproduced below with permission from Nancy Swanson.

Figure 2. *IBD diagnoses and acres of Bt corn*[107]

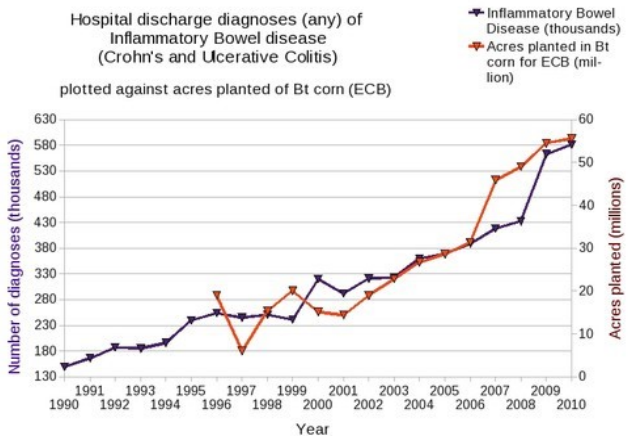


Figure 3*. Function Bowel disorders and acres of Bt corn*[108]

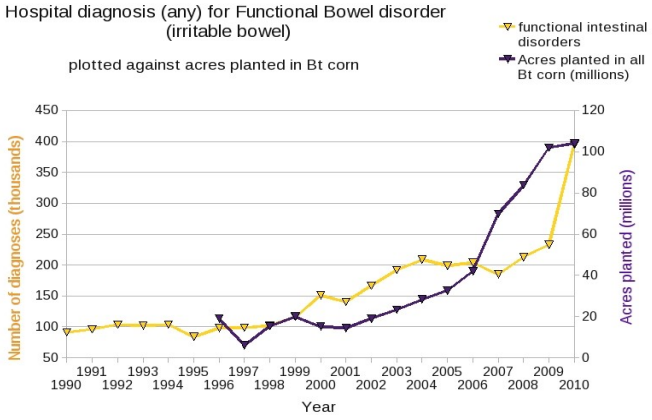


Figure 4. *IBD and glyphosate applied to corn and soy:* Correlation between inflammatory bowel disease and glyphosate applications to US corn and soy crops.[109]

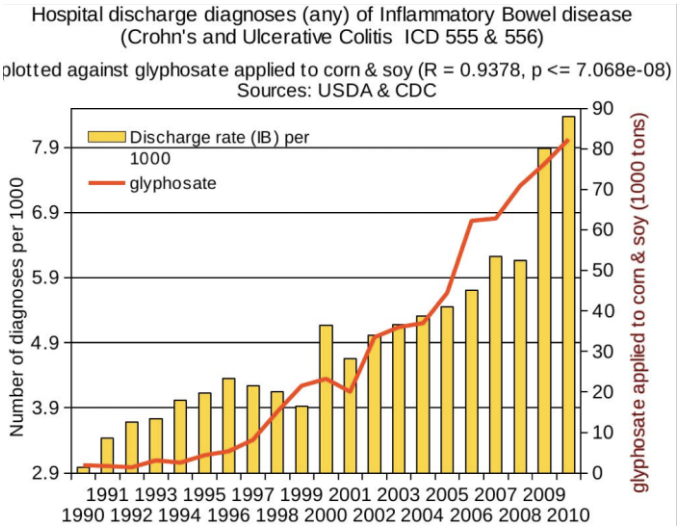
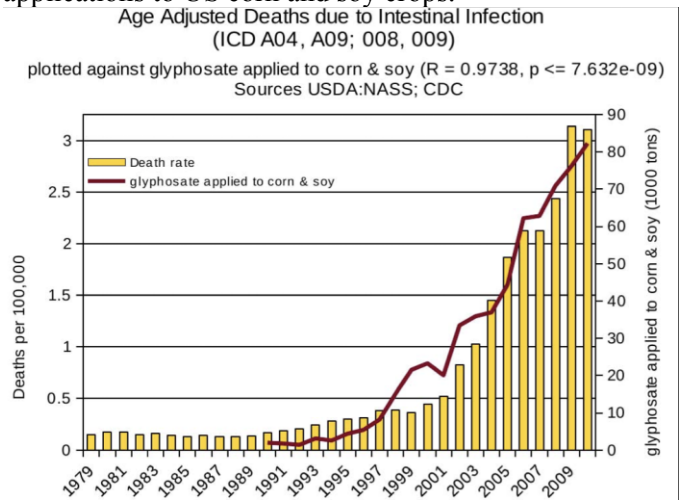


***Figure 5**. Deaths due to intestinal infection and glyphosate applied to corn and soy*: Correlation between age-adjusted intestinal infection deaths and glyphosate applications to US corn and soy crops.[110]



Digestion and GMOs

The digestive tract is the first and largest point of contact with food. According to Arpad Pusztai, who was commissioned by the UK government to create a protocol for testing the safety of GMOs, the digestive tract can reveal numerous reactions to consumed toxins and should therefore be the first subject of a GMO food risk assessment. In his research using rats, Dr. Pusztai discovered that the stomach and intestinal lining of these animals fed GMO potatoes showed altered architecture and potentially precancerous cell growth compared to controls. His study design further revealed that the changes were not due to the protein expressed from the transgene, implicating the generic process of the GMO transformation process as the cause.[111]

In another study on rats fed GMO peas, the rat intestines were heavier, possibly indicating excessive cell growth (a hallmark of cancer), but researchers ultimately failed to examine the intestines for cell growth.[112]

The FlavrSavr tomato, engineered for delayed ripening and rotting, was approved and marketed in the US in 1994 but quickly withdrawn by 1997. Scientists conducted rat feeding studies on two lines of the tomato. In the line that was not commercialized, 7 of 20 rats developed stomach lesions. According to Pusztai, the type of stomach lesions linked to the tomatoes "could lead to life-endangering hemorrhage, particularly in the elderly who use aspirin to prevent [blood clots]."[113] Studies on the FlavrSavr did not look beyond the stomach to evaluate other possible impact on the intestines.

A study by Carman and colleagues found that pigs fed typical transgenic corn and soy-containing feed in the US had significantly higher incidence of severe inflammation of the stomach than controls. In fact, compared to a non-GMO diet, the stomachs of 32% of the GMO-fed pigs were scored in a category of severe inflammation—a classification that was above and beyond any of the inflammation ratings for animal feds a non-GMO diet.[114]

With the exception of Pusztai's rat studies, it is difficult to tell whether the cause of the digestive problems seen in animal studies was due to the GMO transgene product itself, , the added herbicide, or the disruption of plant host gene function resulting in novel toxins or allergens.

In a study conducted by Monsanto, GMO soy was found to contain 27% more trypsin inhibitor than its natural isogenic counterpart.[115] Additional data from Monsanto's study that was not published, was later discovered by medical writer, Barbara Keeler, in the archives of the *Journal of Nutrition*. It demonstrated that the trypsin inhibitor in GMO soy was resistant to denaturing from heat. After cooking GMO soy meal twice, according to a review by Pusztai and Bardocz, "one of the soybean lines (61-67-1) appeared to have almost seven times as much trypsin inhibitor per mg sample dry weight as the parent. Indeed, the values of this GM soybean approached that found in untoasted seed samples. Even the other GM line (40- 3-2) contained three times as much trypsin inhibitor as the non-GM line." They concluded "heat treatment appeared to have a far lesser denaturing effect on the trypsin inhibitor content of the GM lines."[116]

Trypsin, a pancreatic protease, catalyzes the hydrolysis of proteins into smaller peptides for digestion and reduces the allergenicity of the proteins. By blocking the effects of trypsin, trypsin inhibitors can inhibit the digestion of proteins and enhance the allergenic properties of proteins.

In addition, the toasted GM soy meal contained nearly twice the amount of a lectin, which may interfere with assimilation of nutrients.[117]

The pancreas of mice fed RR soy exhibited profound changes.[118] Starting in month two, production of alpha-amylase, a major pancreatic enzyme that degrades carbohydrates, dropped by an average of 77%. In months

five and eight, it was 75% and 60% lower than controls. This reduced production of alpha-amylase was confirmed in the rough endoplasmic reticulum, the Golgi apparatus, and within zymogen granules.

One-month-old GMO-fed mice produced less zymogens than those fed a non-GMO diet, but the differences became negligible as they aged. The size of these granules was consistently smaller in GMO-fed mice, with the biggest difference being 39%, in month five. The pancreatic modifications disappear after removing the GMO soy from the diet.

Digestion and Bt toxin

The possible role of *Bt* toxin as a causative agent in digestive disorders is not difficult to extrapolate. Its mode of action as an insecticide is to kill insects by creating holes in the walls of their guts. Studies on human embryonic kidney cells demonstrate that *Bt* toxin creates similar micropores.[119] Increased intestinal permeability in humans is known to be causally associated with a variety of autoimmune, inflammatory, allergic and pain-related conditions.

While the amount of *Bt* toxin required to cause micropores in human cell cultures in dishes was higher than the amount of toxin that is supposed to be produced in *Bt* corn and thus ingested, we cannot discount the potential for *Bt* toxin to cause holes in the human digestive tract for a number of reasons:

1. The environment within the stomach may be quite different than the lab simulation and the type of cells used in the experiment are not those found in the gut. The quantity needed to disrupt the cell integrity may be less (or more) in vivo.
2. The amount of *Bt* toxin produced by corn can vary, depending on environmental and other factors. According to an investigation by Professor Terje Traavik on *Bt* corn in the Philippines, the expression of *Bt* toxin in one single corn cobb varied per kernel up to 64-fold. The range may have actually been larger, but the amount was measured at the limit of detection. This particular corn, however, may have also been atypically unstable. It was associated with a strong smell and health conditions that afflicted the nearly 100 people living adjacent to the cornfield.[120]
3. The *Bt* toxin gene may transfer to the DNA of bacteria living within the gut. Although this was never studied for *Bt* corn, research on RR soybeans confirmed that part of the RR gene, including its viral promoter, transferred and integrated into the DNA of gut bacteria of ileostomy subjects. Although the transformed bacteria survived exposure to glyphosate, it is not clear whether this was due to the intact functionality of the transgene or to the bacteria's natural immunity to this antibiotic. If the *Bt* toxin gene transferred and continued to function from within gut bacteria, the amount of the toxin produced by the gut flora could well exceed the level produced in corn. Further, the exposure could be constant, 24 hours per day. Unfortunately, this is hypothetical because no studies have investigated this potential risk.

As discussed above, numerous studies of *Bt* toxin elicit an immune response. Histamine is the major paracrine stimulant of gastric acid. Thus, elevated immune reactivity might contribute to digestive disorders through histamine production. For example, histamine is involved in the secretion of gastric acid.[121]

Mice fed potatoes engineered to produce the *Bt* toxin developed abnormal and damaged microvilli, as well as proliferative cell growth in the lower part of their small intestines (ileum).[122]

Digestion and Glyphosate

A study on fairly high levels of Roundup® exposure in carnivorous fish revealed remarkable adverse effects throughout the digestive system, including "disruption of mucosal folds and disarray of microvilli structure" in the intestinal wall, along with an exaggerated secretion of mucin throughout the alimentary tract. [123]

Reduced digestive enzymes

Although the relevance of fish model to human health is limited, it is remarkable that the activity of protease, lipase, and amylase, important enzymes involved in the digestion of proteins, fats, and carbohydrates, were all decreased in the esophagus, stomach, and intestine of these fish following exposure to glyphosate.[124]

Enzymes secreted by the pancreas are responsible for the breakdown of food so that it can be absorbed through the walls of the small intestine into the bloodstream. Any restriction of these enzymes may result in impaired digestion and a shortfall of nutrient assimilation. If carbohydrates are not properly degraded in the small intestine, (as may occur with reduced alpha-amylase), they may be broken down by bacteria in the large intestine, which can produce gas. If protein digestion is inhibited, which may occur with reduced zymogens, it can increase the chance of allergic reactions to protein fragments. The pancreas may also be forced to produce and excrete more protein digesting enzymes, possibly putting undue pressure on the organ.

Ultimately, if the digestive system is not functioning properly, then food particles are not broken down as quickly or as completely. This can create several problems:

- Nutritional deficiencies: If a person is not properly absorbing and gaining sufficient nutrition from the foods consumed, overall health, including the immune system, can suffer.
- Dysbiosis: With poor digestion, proteins can remain intact for longer than normal periods in the gastrointestinal (GI) tract. This can result in the larger, undigested food particles becoming the

"food" of pathogenic gut bacteria, leading to overgrowth, which can further compromise digestion and immunity.

- Inflammation: When proteins putrefy, they can also release excess hydrogen sulfide (as toxic as cyanide gas) which irritates and inflames the mucous membranes.
- Autoimmunity: Undigested proteins also have a greater likelihood of provoking autoimmune reactions, in which the immune system attacks parts of the body.

Intestinal inflammation also appears to reduce production of cholecystokinin (CCK) and this reduction in CCK, in turn, reduces the digestive enzymes produced by the pancreas, as well as the bile produced in the liver. Without sufficient enzyme levels, digestion is slowed down, particularly digestion of proteins; without sufficient bile, fat and fat-soluble vitamins cannot be digested and absorbed efficiently.

This can become a vicious cycle: Larger food particles can result in bacterial overgrowth, which in turn can further irritate the lining of the intestines, further lowering digestive capacity both directly and through reduced CCK levels. Lowered digestive capacity results in increased large food particles.

Glyphosate altering gut bacteria

Glyphosate has been shown to reduce the population of healthy bacterial varieties in the digestive tract and promote overgrowth of dangerous pathogenic bacteria, according to in vitro research with poultry[125] and cattle models.[126]

The implications for health may be quite profound and complex. For example, *Bifidobacterium* strains, which are often used as probiotics, reduce the cytokines that provoke inflammation. *Bifidobacterium* is one of the types of bacteria that are easily killed by glyphosate.[127] The result could be an increase in inflammation, which is now recognized as central to the disease process for numerous diseases.

On the other hand, "the highly pathogenic bacteria," such as those that produce *Salmonella* or *Clostridium botulinum* (the botulism toxin), "are highly resistant to glyphosate." Furthermore, some of the beneficial bacteria that are killed normally keep some of the pathogenic bacteria population in check. Researchers in Germany, for example, suggest that glyphosate use kills lactic-acid producing bacteria in the gut of cattle, allowing the bacteria that produce deadly botulism to flourish. This might explain the increase in chronic botulism in cattle.[128] Cases of Sudden Infant Death Syndrome have also been linked to the botulism toxin.[129]

Bacterial pathogens can activate zonulin, a protein that modulates the permeability of the tight junctions between cells of the wall of the digestive tract. Activation of zonulin can induce a breakdown of the tight junctions in cells lining the gut, leading to increased intestinal permeability or "leaky gut".[130] Indeed, some of the same bacteria whose growth is stimulated through glyphosate exposure, i.e. *Clostridium botulinum*,[131] *Clostridium perfringens*,[132] and *Salmonella*,[133] have been found to provoke diseases in humans; these are not benign bacteria.

An experimental study using two intestinal cell lines showed that glyphosate could adversely affect mucosal barrier integrity. The authors concluded that at higher doses "glyphosate significantly disrupts the barrier properties of cultured intestinal cells."[134]

By inhibiting the Shikimate pathway, glyphosate might reduce the production of tryptophan and serotonin. Because serotonin is important for intestinal motility, a deficiency could have consequences for digestive health. According to a review article by Sikander, et al., "Altered serotonin signaling may lead to both intestinal and extra intestinal systems in IBS [irritable bowel syndrome]."[135]

Digestive disorders as gateways to other conditions

Digestive disorders not only create symptoms themselves, they can act as causative factors for other conditions. Lack of proper breakdown and assimilation of nutrients can lead to nutritional deficiencies, which can result in a myriad of health problems. A hyperpermeable gut is linked to numerous inflammatory and metabolic disorders, ranging from allergy to depression and autoimmunity. Altered gut bacteria can impact detoxification, immune function, and the availability of key nutrients. Therefore, many of the other symptoms listed in the survey may have originated in the gut.

Conclusion

GMOs are pervasive in the diet of people living in the US and several other nations. Although presumed safe or GRAS by the US government and GMO producers, published studies point to numerous physiological responses in animals and cell lines that challenge this assumption. They demonstrate changes or even damage to the immune system, reproductive system, vital organs (especially liver and kidney), digestive system, and endocrine system.

Survey results of 3,256 people reporting improvements in at least some health conditions, after switching to a non-GMO, diet suggest GMOs may be contributing to health conditions. Many of the conditions that improved in the survey participants are similar to the health issues found in lab animals fed GMOs or the associated herbicide Roundup®. Other dietary factors, such as increased consumption of organic food, reduction of processed food, etc., may also play a role in the health improvements. Thus, future research should exclude confounding factors as much as possible.

Digestive issues were by far the most common problem reported by respondents as improved when

GMOs were removed from the diet. GMOs can negatively impact digestion through several possible modes of action and digestive disorders in turn, can lead to numerous other health issues.

Future research is also warranted to clarify if the generic GMO transformation process, *Bt* toxin, and/or the glyphosate/GBH residues are contributing to or causing health problems and to definitively determine the causative pathways of potential harm in the human body.

It is clear that more research needs to be done. However, given the prevalence of data correlating GMOs and glyphosate/Roundup® with health issues, and evidence that a switch to non-GMO organic diets contributes to recovery (improved health), the author believes the precautionary principle dictates that healthcare practitioners should advise patients to avoid exposure by switching to organic foods. Furthermore, practitioners are encouraged to document the impacts and publish case studies.

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- Stanley Ewen
- Tom O'Bryan DC
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See associated Editorial and Comments attached with this article

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