BULLETPROOF

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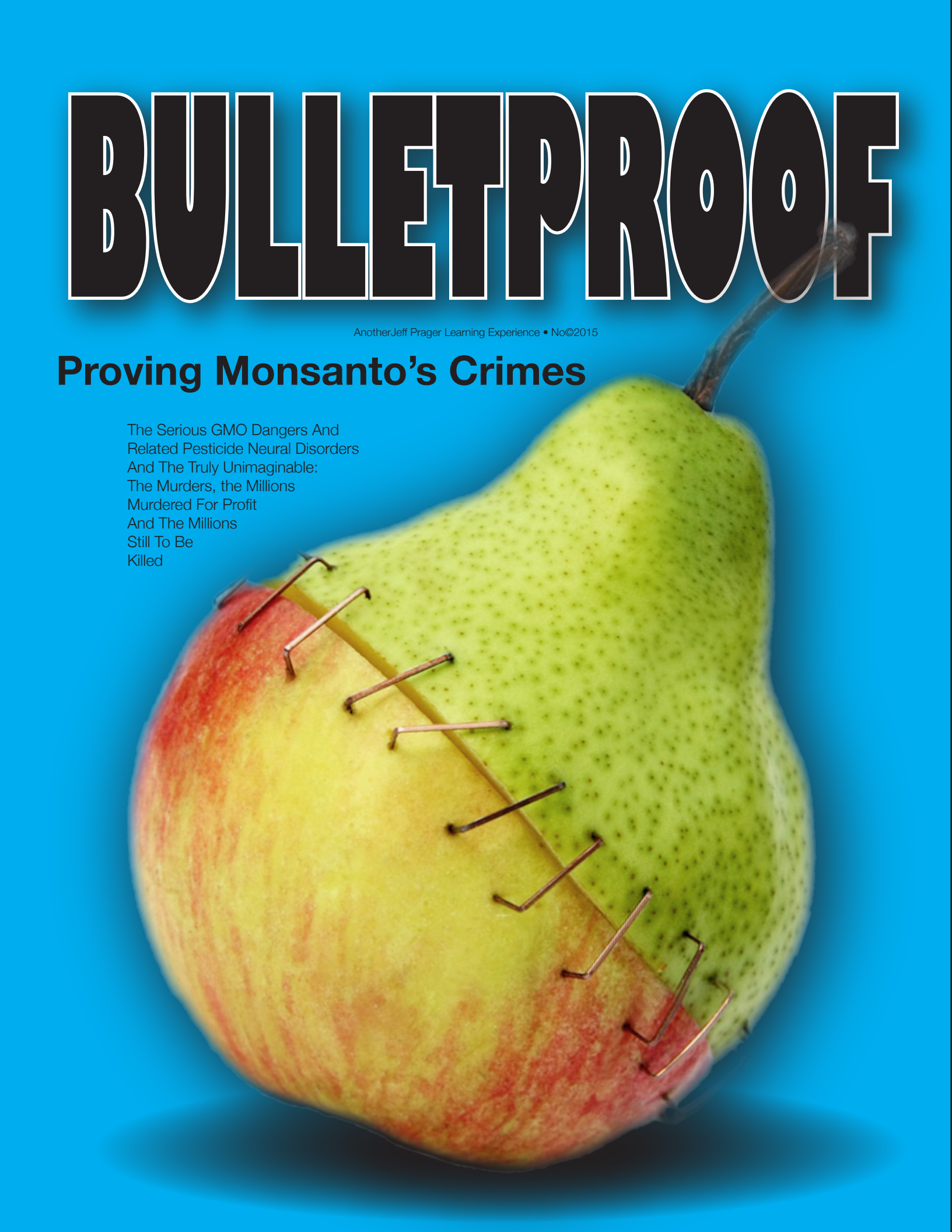
Proving Monsanto's Crimes

The Serious GMO Dangers And
Related Pesticide Neural Disorders
And The Truly Unimaginable:
The Murders, the Millions
Murdered For Profit
And The Millions
Still To Be
Killed



GMO FACTS: SETTLING THE GMO DISPUTE

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Another Jeff Prager Learning Experience Publication™

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A Cooperative Research Agency Of The Department Of GMO: Murder & Maim, Division 6
• Genocide Unit •

American National Institute Of GMO Crimes & Pesticide Pathology and Genetically Modified Offenses (ANIOGMOCPPGMO)
and the United States Non-Existent Enforcement And Compassion Division of the Federal Do-Good Administration (FDA)

~ ANARCHY DIVISION ~

Text Title Font Thanks To: ALL OVER AGAIN

This is a **Gimme Some Truth**™ Feature Length Commercial-Free Adult Film Rated 'R' for Reality

Brought to you by good fortune, late nights and sheer serendipity

"A library is a hospital
for the mind."

-Anonymous

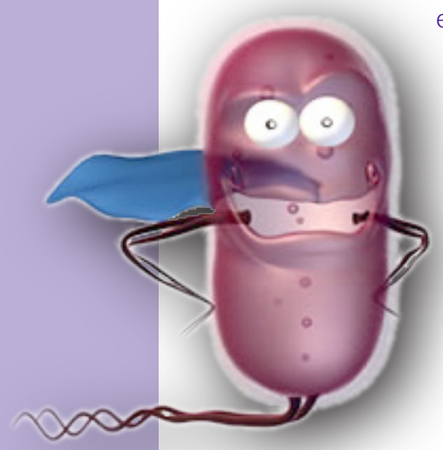
If you've been kind enough to trust me based on my previous research and you've downloaded this free PDF you'll also find that the data contained in this PDF is Bullet Proof and unimpeachable, just as I imagined and intended that it would be.

Thank you for reading

~ Jeff Prager

Researching
The Effects Of Glyphosate

by Jeff Prager



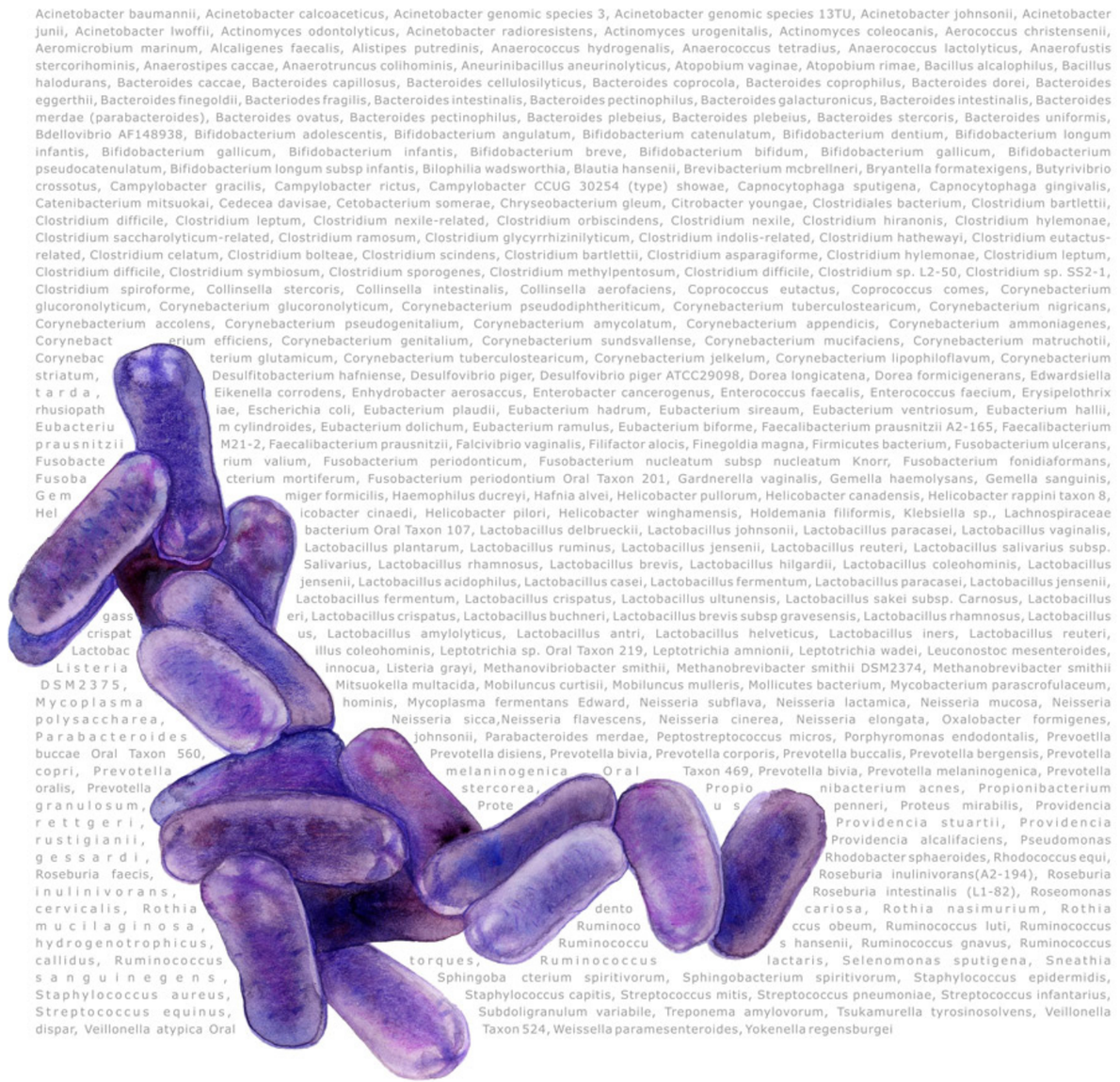
Researching the effects of glyphosate alone, as though it expressed a singular affect on the human species is a slight of hand, a three-card-monte, it's the grift. Synergy, when glyphosate reacts with aluminum, or with a neurotransmitter or when it reacts with a food coloring, a food additive or the many hundreds of varieties of gut bacteria is data that may never be known. Synergy generates extraordinary elaborateness even for those humans at the top of the intellectual food chain and the complexities may never be known. Yet to investigate the safety of glyphosate as a potential "lone purveyor of ill" using the currently standard scientific methods of drug safety approval is a tragic pretense responsible for millions and perhaps some day billions of injured and dead of our species, a farcical real-life genocide by any other name.

Within this body of work I've published which is a mere fraction of the available total you will find study after study that specifically addresses that chemicals that react with, or are added to, glyphosate and how these additives can increase the toxicity of glyphosate by more than 1000 times. We don't even know the names of some of these chemicals. Trade secret poisons.

This is just one of many different and varied methods employed by the greedy bastards to comply with safety standards. Test glyphosate alone and show that the effects are not so bad after all. Synergy notwithstanding.

It doesn't matter whether we're discussing vaccines, smoking, food additives, alcohol, the gasoline fumes we all despise when we pump gasoline, the red food coloring in the Maraschino cherry in your cocktail or the flame retardant you're breathing all night every time you buy new pillows or pillow cases. Or wear new clothes.

Synergy is an eternal mystery. But investigating glyphosate under current federal regulations that are looser than the poorly braided rope used in a failed lynching should be very serious federal crimes and very likely they are, as soon as someone locates the ever so slightly ambiguous legislation and case law from 6 decades ago.



each of us is broken


MONSANTO
• A Division Of Murder Incorporated •
Humanitarian Poisons Division

GMO?

Genetically Modified Organism

A GMO IS:

the direct human manipulation of an organism's DNA in a laboratory environment.

A GMO IS NOT:

Plants and animals that are traditionally bred to achieve specific characteristics such as breeding dogs or cross-pollination of plants

SCIENCE OF GMOS

Genetic modification may include the ADDITION OF DNA from species that would NOT BREED in nature.

Genetic modification may also involve REMOVING SPECIFIC STRANDS OF DNA.

Cross-species—or transgenic—genetic manipulation has gone so far as to **COMBINE FISH DNA WITH STRAWBERRIES** and tomatoes.

GMO foods have only existed in groceries since the *late 1990's.*

GMO life can be **patented**

GMO varieties of corn and potatoes are engineered to **PRODUCE THEIR OWN PESTICIDES.**

STUDIES OF GMOS

NO LONG-TERM TESTING.
It took decades for the dangers of Trans-Fats (another artificial food) to become understood.

Mice fed GM pesticide-producing corn over four generations showed **ABNORMAL** structural and chemical changes to various organs and significantly reduced fertility.

herbicide-resistant crops can cross-pollinate to create **HERBICIDE-RESISTANT WEEDS.**

Pesticide-producing GMO crops have led to RESISTANCE IN INSECTS.

TRANGENIC DNA HAS BEEN FOUND IN **80%** OF WILD CANOLA IN NORTH DAKOTA

PREVALENCE OF GMOS

You probably eat GMOs **EVERY DAY.**

30,000

different GMOs exist on grocery store shelves (largely because of how many processed foods contain soy.)

PERCENT OF GMOS IN TOTAL CROP PRODUCTION
2011 (USA)

PUBLIC OPINION OF GMOS

Polls consistently show that a significant majority of North Americans would **LIKE TO BE ABLE TO TELL** if the food they're purchasing contains GMOs.

OUT OF A CBS NEWS POLL:

87% want GMOs labelled

53% would not buy genetically modified food

NATIONAL OPINIONS OF GMOS:

The USA is the **largest** producer of GMO crops and **does not mandate** labels for GMO food.

In 30 other countries there are bans or restrictions on the production of GMOs, because they are **not considered proven safe.**

SOURCES: http://peeltheorange.com/pressroom/gmofactsheet.php

DESIGN BY MCKENZIE LONG AT CARDINAL INNOVATIVE

What are the CYP genes?

Because Dr. Stephanie Seneff and Dr. Anthony Samsel based a great deal of their research on the CYP genes and specifically the Cytochrome P450 gene, I thought you might want to know what this gene family is responsible for in the human body. It will help to understand how glyphosate causes almost every disorder known to woman and man. The shikimate pathway plays a significant part too so we'll discuss that later.

Enzymes produced from the cytochrome P450 genes are involved in the formation (synthesis) and breakdown (metabolism) of various molecules and chemicals within cells. Cytochrome P450 enzymes play a role in the synthesis of many molecules including steroid hormones, certain fats (cholesterol and other fatty acids), and acids used to digest fats (bile acids). Additional cytochrome P450 enzymes metabolize external substances, such as medications that are ingested, and internal substances, such as toxins that are formed within cells. There are approximately 60 CYP genes in humans.

Cytochrome P450 enzymes are primarily found in liver cells but are also located in cells throughout the body. Within cells, cytochrome P450 enzymes are located in a structure involved in protein processing and transport (endoplasmic reticulum) and the energy-producing centers of cells (mitochondria). The enzymes found in mitochondria are generally involved in the synthesis and metabolism of internal substances, while enzymes in the endoplasmic reticulum usually metabolize external substances, primarily medications and environmental pollutants.

Common variations (polymorphisms) in cytochrome P450 genes can affect the function of the enzymes. The effects of polymorphisms are most prominently seen in the breakdown of medications. Depending on the gene and the polymorphism, drugs can be metabolized quickly or slowly. If a cytochrome P450 enzyme metabolizes a drug slowly, the drug stays active longer and less is needed to get the desired effect. A drug that is quickly metabolized is broken down sooner and a higher dose might be needed to be effective. Cytochrome P450 enzymes account for 70 percent to 80 percent of enzymes involved in drug metabolism.

Each cytochrome P450 gene is named with CYP, indicating that it is part of the cytochrome P450 gene family. The gene is also given a number associated with a specific group within the gene family, a letter representing the gene's subfamily, and a number assigned to the specific gene within the subfamily. For example, the cytochrome P450 gene that is in group 27, subfamily A, gene 1 is written as CYP27A1.

Diseases caused by mutations in cytochrome P450 genes typically involve the buildup of substances in the body that are harmful in large amounts or that prevent other necessary molecules from being produced.

Which genes are included in the CYP gene family?

The HUGO Gene Nomenclature Committee (HGNC) provides a list of genes in the CYP family. Genetics Home Reference summarizes the normal function and health implications of these members of the CYP gene family: CYP1B1, CYP4V2, CYP11B1, CYP11B2, CYP19A1, CYP21A2, CYP27A1, CYP27B1, and TBXAS1.

What conditions are related to genes in the CYP gene family?

- 21-hydroxylase deficiency
- aromatase deficiency
- aromatase excess syndrome
- autoimmune Addison disease
- Bietti crystalline dystrophy
- cerebrotendinous xanthomatosis
- congenital adrenal hyperplasia due to 11-beta-hydroxylase deficiency
- corticosterone methyloxidase deficiency
- early-onset glaucoma
- familial hyperaldosteronism
- Ghosal hematodiaphyseal dysplasia
- multiple sclerosis
- Peters anomaly
- vitamin D-dependent rickets

What glossary definitions help with understanding the CYP gene family?

acids ; bile ; breakdown ; cholesterol ; cytochrome P450 ; endoplasmic reticulum ; enzyme ; fatty acids ; gene ; metabolism ; mitochondria ; pharmacogenetics ; polymorphism ; protein ; synthesis

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You Might Be Putting Your Life At Risk

And Paying For The Privilege

by Jeff Prager

There aren't enough pages to convey all of my thoughts, theories, known facts, known unknowns, unknown unknowns, as Don said, to say everything that I want to say about GMOs, GMO seeds and the related pesticides, but I'll try to be brief, less than 2 page spreads, and I'll word my statements carefully.

GMO foodstuffs, their seeds and their related pesticides kill aquatic animals, soil bacteria and even humans over decades of consumption. It seems to kill smaller animals much more slowly. And while they don't kill for decades they do make all of us extremely ill often to the point of total disability. The single most recognized and fully acknowledged neurological disease caused by glyphosate and known and well documented by researchers in this field is the neurological affect of glyphosate contamination in even low doses in Parkinson's Disease. Glyphosate is one of the causes of Parkinson's. Causation is recognized.

The International Union Of Pure And Applied Cheistry (IUPAC) uses the name N-(phosphonomethyl) glycine. The rest of us call it glyphosate. The primary degradation product of glyphosate in plants, soil, water, animals, insects and humans is aminomethylphosphonic acid (AMPA) whose chemical structure is very similar to glyphosate anyway. By the way, AMPA is worse than urine or feces, which do have some commercial uses. APMA has no commercial use. And no long term study of the toxicity or carcinogenicity of AMPA has ever been carried out.

Glyphosate also bonds tightly to soil and affects the soil bacteria such that we may not have soil with a positive growth microbiome since glyphosate kills certain critically important soil bacteria. Glyphosate chelates, which means it removes valuable and necessary natural nutrients from the soil and is designed to prevent those nutrients from getting to the plant, starving the plant to death, so-to-speak/

The major human exposure to glyphosate is our food. Glyphosate is absorbed by the crops it's used on and becomes a part of foodstuffs DNA. Glyphosate can't be washed off of fruits or vegetables because it's not on the outside, it's part of the plant and it's dispersed throughout the inside of that GMO derived plant, fruit, fish or vegetable. Heating glyphosate, as in cooking some good looking vegetables saturated with 3, 6 or 11% glyphosate content can concentrate the glyphosate but extreme heat has no other affect on the pesticide.

From a manuscript accepted for publication in Applied and Environmental Microbiology on December 14th, just a couple of memorably cold months ago titled, "Novel Isolate of Bacillus thuringiensis subsp. thuringiensis That Produces a Quasicuboidal Crystal of Cry1Ab21 Toxic to Larvae of Trichoplisia ni," researchers Swiecicka, Bideshi and Frederici reach the conclusion that our pesticides are altering the soil microbiome significantly by allowing some species to flourish and others to perish. The authors write:

"As a consequence of widespread use" these various elements "could contribute to the evolution of resistance in insect populations to [certain] bacterial insecticides"

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"As a consequence of widespread use, the evolution of resistance to these isolates or strains derived from them and the subsequent proliferation of resistant populations are of concern (20). For example, field populations of the diamondback moth, Plutella xylostella, and the cabbage looper, Trichoplusia ni, have already developed high levels of resistance due to repeated exposure to formulations based on HD1 (11, 26). Furthermore, in laboratory selection studies, resistance to B. thuringiensis has evolved in the pink bollworm, Pectionphora gossypiella, and the tobacco budworm, Heliothis virescens (13, 31). It is also thought that the selection pressure imposed by use of Cry proteins in transgenic plants (9, 31), most of which are based on Cry1Ac or Cry1Ab, could contribute to the evolution of resistance in insect populations to bacterial insecticides based on HD1."

Bending over backwards to cover the cost of their donations from Monsanto, et al., the US EPA proposed to hike the allowed residue limits—yet again, and did—of the herbicide glyphosate in various food and feed crops. Acceptable levels of glyphosate residue found in fruits and vegetables have been increased by The Environmental Protection Agency (EPA) as well. This happened in 2013 when the EPA quietly promoted the rule change regarding glyphosate levels without much attention from the media or the public.

Regulation raises glyphosate levels in oilseed crops, which include sesame, flax, and soybean, from 20 parts per million (ppm), to 40 ppm. It also raises the allowable glyphosate contamination level for sweet potatoes and carrots from 0.2 ppm to 3 ppm for sweet potatoes and 5ppm for carrots, that's 15 and 25 times the previous levels.

The change in tolerance levels affects several other agricultural products, including animal feed, root crops and fruit trees. While the regulation is effective beginning May 1, 2013, there was an open comment session, closing July 1, that received over 10,800 comments against the proposed change in regulation. Public commentary never has an impact or any bearing on the decision making process.

Glyphosate is used on over 150 crops in over 90 countries. First used in the 1970s, by 2007 glyphosate was the most widely used herbicide in US agriculture and second most widely used herbicide in the home and garden sector. In that year, the agricultural sector applied 180 to 185 million pounds, the home and garden sector applied five to eight million pounds, and industry, commerce and government applied 13 to 15 million pounds of glyphosate.

The rise in tolerance levels for glyphosate residue came as a result of a petition prepared by Monsanto in early 2012. While FDA did not perform independent tests on whether higher residue levels of glyphosate were dangerous to humans or the environment, it relied on tests and data provided by Monsanto.

Alarmed, many activists believe that a rise in tolerance levels will allow farmers to spray food with more chemicals, which will increase health and environmental risks. While Monsanto (and by default the EPA) guarantees the safety of glyphosate in general and Round Up in particular, recent independent studies conclude the opposite.

Even the EPA's technical factsheet on glyphosate states that chronic long-term exposure can cause kidney damage and reproductive effects. It also states that and there is "inadequate evidence" as to whether it can cause cancer.

A 2013 MIT study argues that glyphosate residue in food and water induces disease by disrupting normal cellular detoxifying functions. According to the study, "negative impact on the body is insidious and manifests slowly over time as inflammation damages cellular systems throughout the body." The damage is manifested in increased risk of gastrointestinal disorders, obesity, diabetes, heart disease, depression, autism, infertility, cancer and Alzheimer's disease.

In another recent European study, commissioned by Friends of The Earth (FoE) and GM Freeze, volunteers from 18 countries submitted urine samples to be tested for traces of glyphosate. All of the volunteers lived in cities and had never used or handled glyphosate prior to the test. Laboratory tests concluded that 44% of people had traces of glyphosate in their urine. The rate of positive samples varied by country, with Malta, Germany, the UK, and Poland having the highest rates and Switzerland and Macedonia having the lowest rates.

Finally, who other than Monsanto will benefit from this raise in tolerance levels in the long run? While farmers may benefit for a short while because being able to spray more herbicide may give them a larger crop yield, it may be possible that other countries will refuse to import U.S. produce due to the higher tolerance levels.

After all, it was a little over a month ago that Japan refused to buy U.S. wheat after a strain of unapproved Monsanto GMO wheat was unexplainably found in an Oregon field. A week before that China incinerated three shipments of U.S. corn after discovering it contained unsanctioned GMO corn.

It is unclear whether the EPA took the above independent and other studies into account when making its decision to raise glyphosate residue tolerance levels in many of the foods we eat. Monsanto and corporate agriculture will argue, as they usually do, that the new tolerant levels are "insignificant" and could not harm humans. The research science itself, as you'll soon see, disagrees formidably.

Who's making your baby a lab rat?

Monsanto, Abbott, Enfamil, Mead Johnson, Similac and all of the major manufacturers use GMO ingredients. They make these products because we buy them. Stop buying them and they will stop making them. Our children deserve so much more.

Silent Partners

Over 7 Billion Humans Have Been Colonized By Bacteria - Not A Shot Fired

by Jeff Prager

Even the British Empire had nothing on gut bacteria. The successful colonization of the human species by gut bacteria is a largely untold story of stealth, evolution and an unstoppable desire to simply live. Bacteria want to live. Inside our bodies lives a vast number of bacteria without which we could not remain in good health. Factually, from a purely medical perspective, most of us couldn't remain alive without them. There are over 100 trillion in each of us with over 400 different species, (*some estimate as many as 1000 species but we'll stick to the conservative estimate for now*) most of them living in the digestive tract. Certain types of these bacteria help to maintain good health and others have value in regaining it back once it is lost because they actively assist your immune system. They talk to it.

The Role Of Friendly Bacteria

Lactobacillus acidophilus is the predominant friendly bacteria in the upper intestinal tract. It helps reduce the levels of harmful bacteria and yeasts in the small intestine and also produces lactase, an enzyme important in the digestion of milk. Acidophilus is also involved in the production of B vitamins during the digestive process.

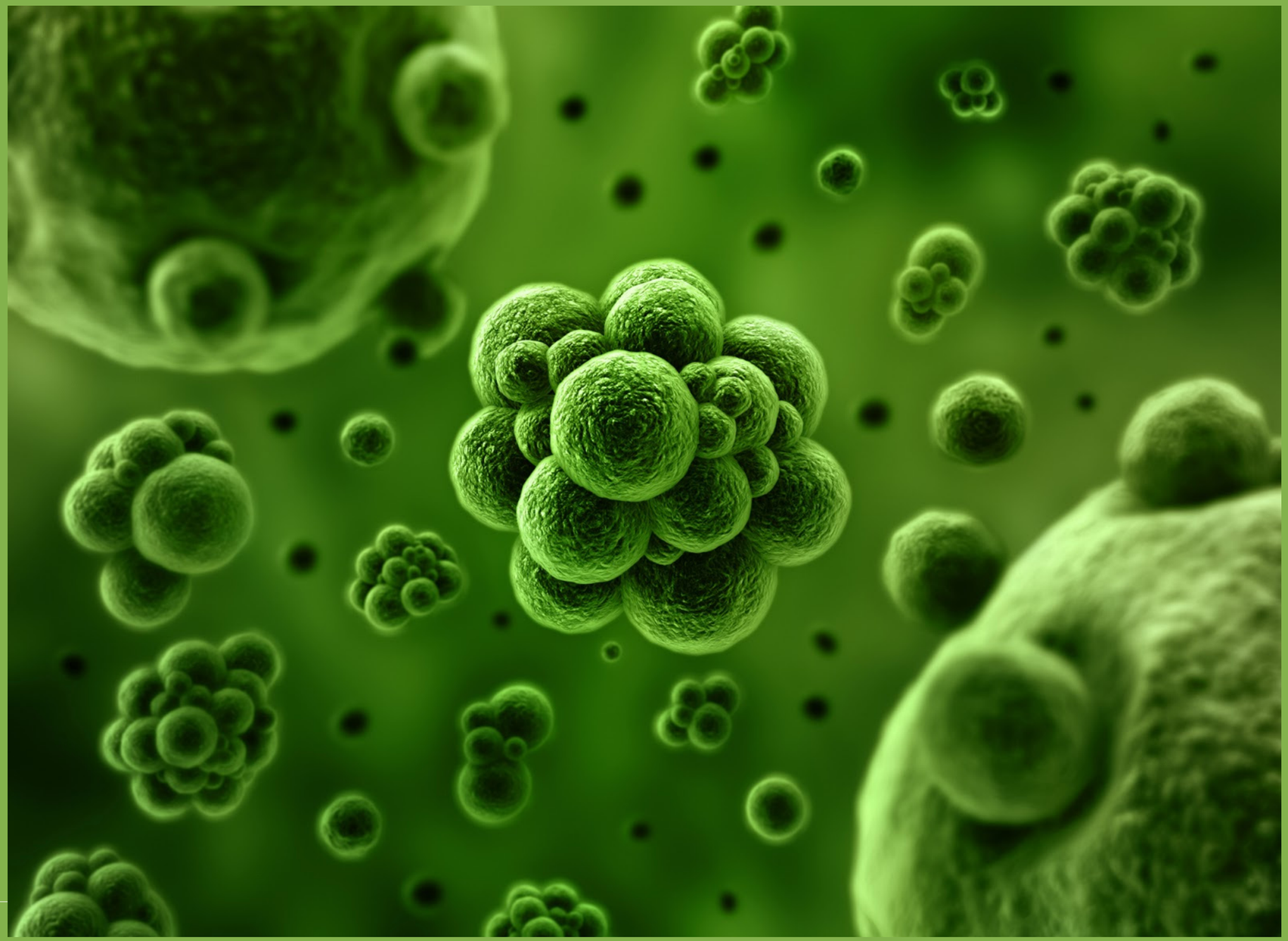
Bifidobacterium bifidum and B. longum are the primary friendly bacteria in the large intestine. Bifidobacteria protect the large intestine from invading bacteria and yeasts, and also manufacture B vitamins and help the body detoxify bile. Bifidobacterium infantis is the prevalent friendly bacteria found in the intestines of infants.

Streptococcus thermophiles and L. bulgaricus are most commonly found in yogurt and exist only transiently in the digestive tract. They produce lactic acid, which encourages the growth of other friendly bacteria, and they also synthesize bacteriocins (*natural antibiotics like substances*) that kill harmful bacteria.

Lactobacilli, Bifidobacteria, and Streptococci are the bacteria mostly commonly found in probiotic supplements. Other beneficial species that may be included are L. casei, L. plantarum, L. sporegenes, L. brevis, and saccharomyces boulardii. Without bacteria like acidophilus, one would not be able to properly digest food and absorb vitamins and other nutrients.

The Benefits Of Probiotics

We don't even know if probiotics work. We don't know if they manufacture our needed B vitamins, including niacin, pyridoxine, folic acid, and biotin. We don't know if they enhance our immune system activity. We don't know if antibacterial substances that kill or deactivate hostile disease causing bacteria actually work at all. Friendly bacteria do this by changing the local levels of acidity, by depriving pathogenic bacteria of their nutrients, or by actually producing their own antibiotic substances, yet we don't know if drinking kefir, eating pickles and sauerkraut or ingesting probiotics even works. We don't know if the ingested bacteria builds a house on your intestinal wall, so to speak, and lives in your gut for a day, a week, a month or forever or whether they take the next gut-wrenching feces train to Sewer City, USA on the Toilet Express. Honestly, we're clueless. But we believe probiotics help.



Gut Bacteria

by Jeff Prager

Gut microorganisms benefit the host by gleaning the energy from the fermentation of undigested carbohydrates and the subsequent absorption of short-chain fatty acids. The most important of these fatty acids are:

• Butyrates, metabolized by the colonic epithelium

• Propionates metabolized by the liver

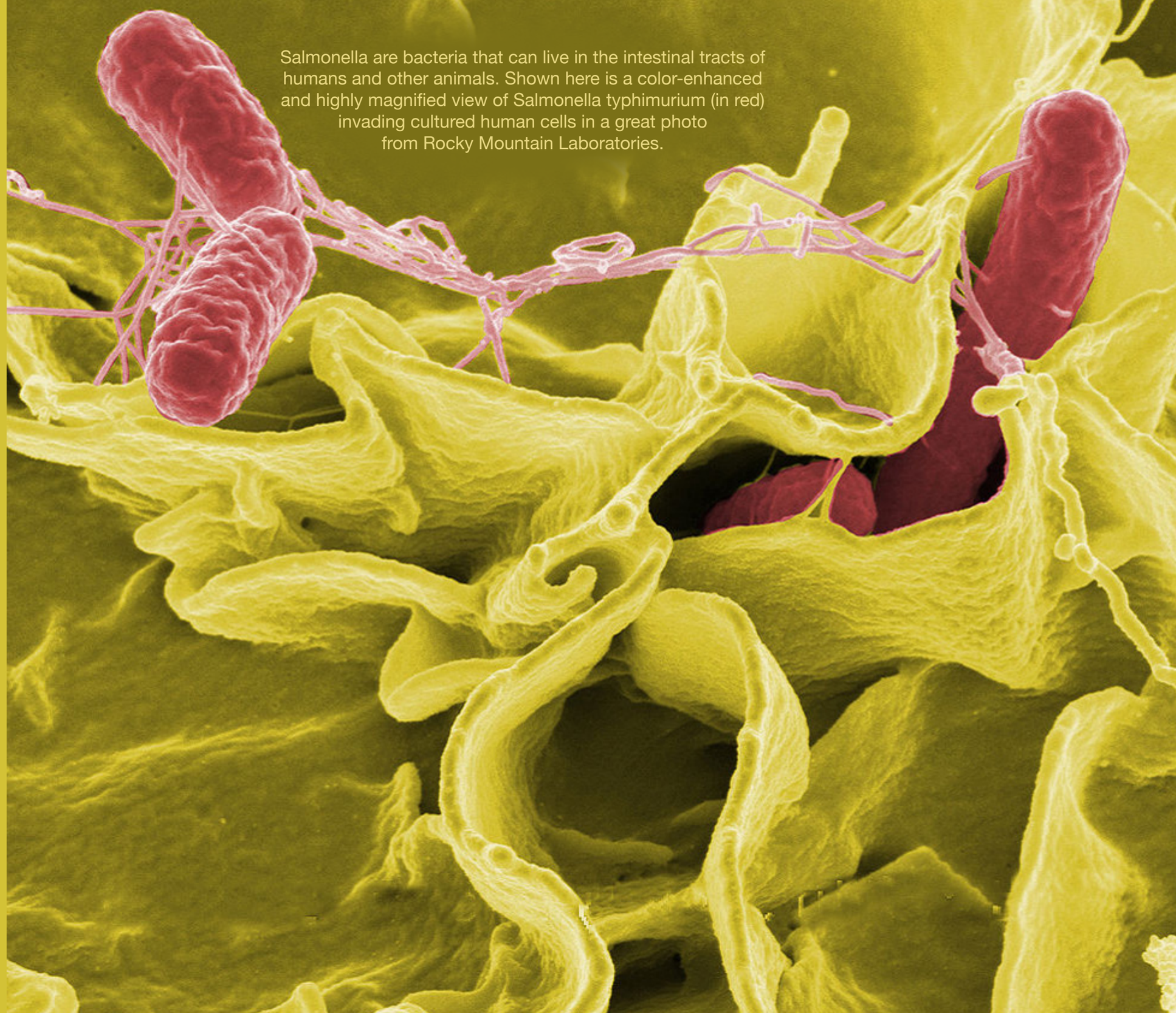
• and acetates metabolized through the action of muscle tissue

Intestinal bacteria also play a role in synthesizing vitamin B and vitamin K as well as metabolizing bile acids, sterols and xenobiotics. Xenobiotics are typically a synthetic chemical that is foreign to the body or in some cases to an entire ecological system. Xenobiotics are intestinal janitors.

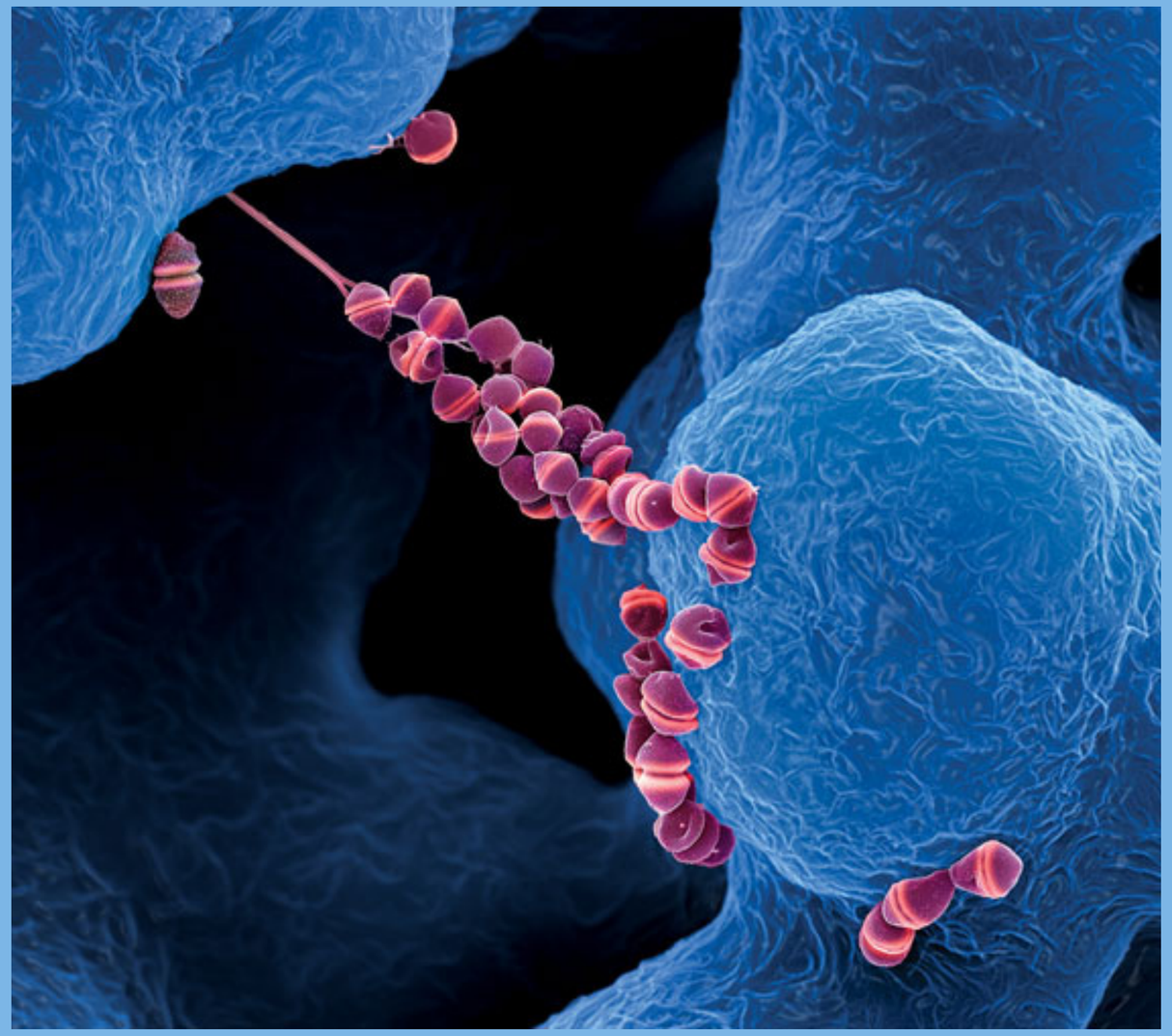
The human body carries about 100 trillion microorganisms in its intestines, a number ten times greater than the total number of human cells in the body. The metabolic activities performed by these bacteria resemble those of an actual organ like a heart or a ling, leading some to liken gut bacteria to a “forgotten” organ. It’s estimated that these gut flora have around a hundred times as many genes in aggregate as there are in the human genome.

Our microbiota so very obviously play a large, significant and unquestionably necessary part in good human health and a part we still know vert, very little about.

As a species we human beings are rapidly developing a new genera of innumerable and often times rare disorders manifesting with such intrusive and unimaginably odd neurological symptoms such that it’s a wonder all approximately 305 million of us aren’t already on the verge of a completely and swiftly disabling disorder.

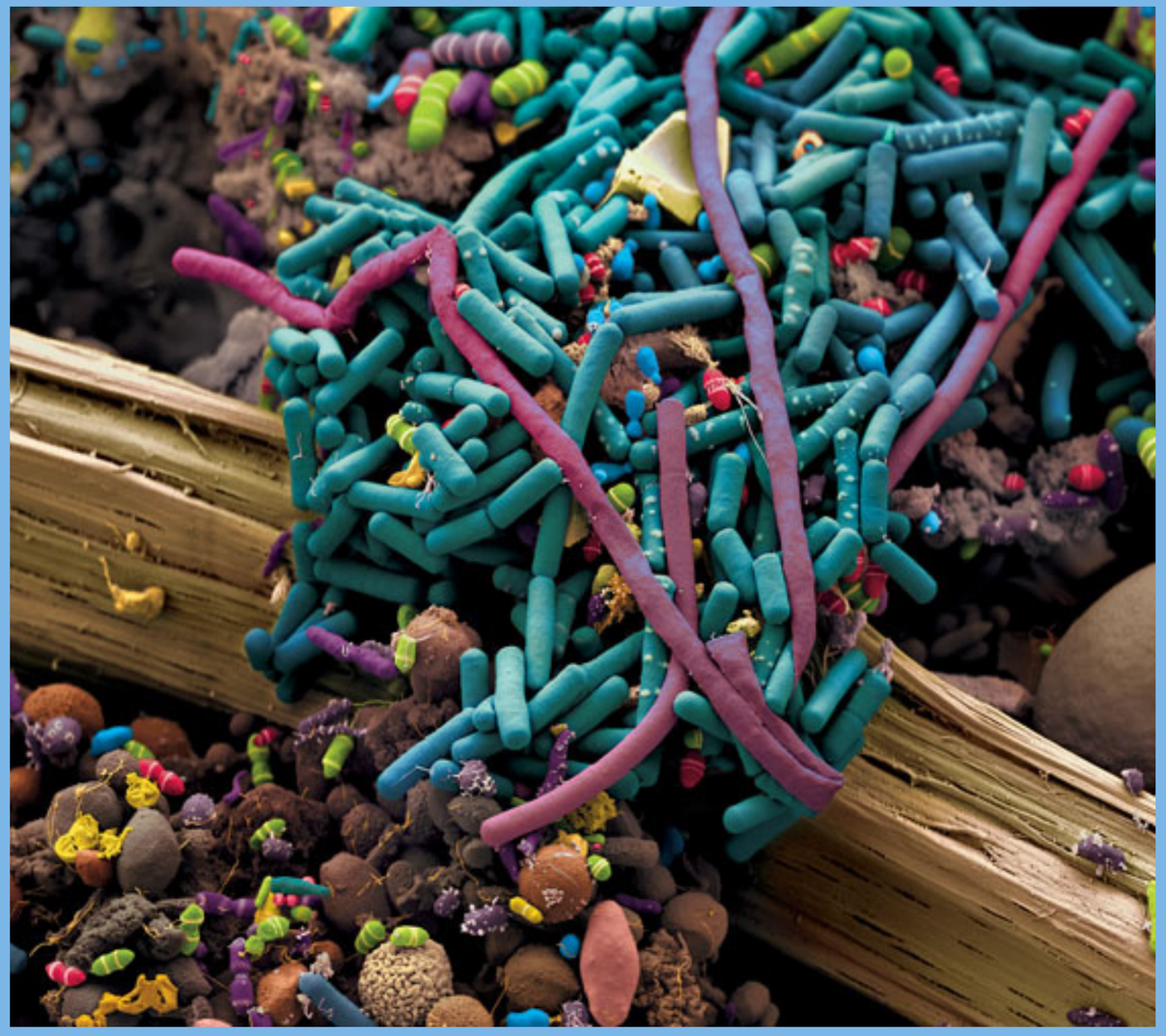


Salmonella are bacteria that can live in the intestinal tracts of humans and other animals. Shown here is a color-enhanced and highly magnified view of Salmonella typhimurium (in red) invading cultured human cells in a great photo from Rocky Mountain Laboratories.



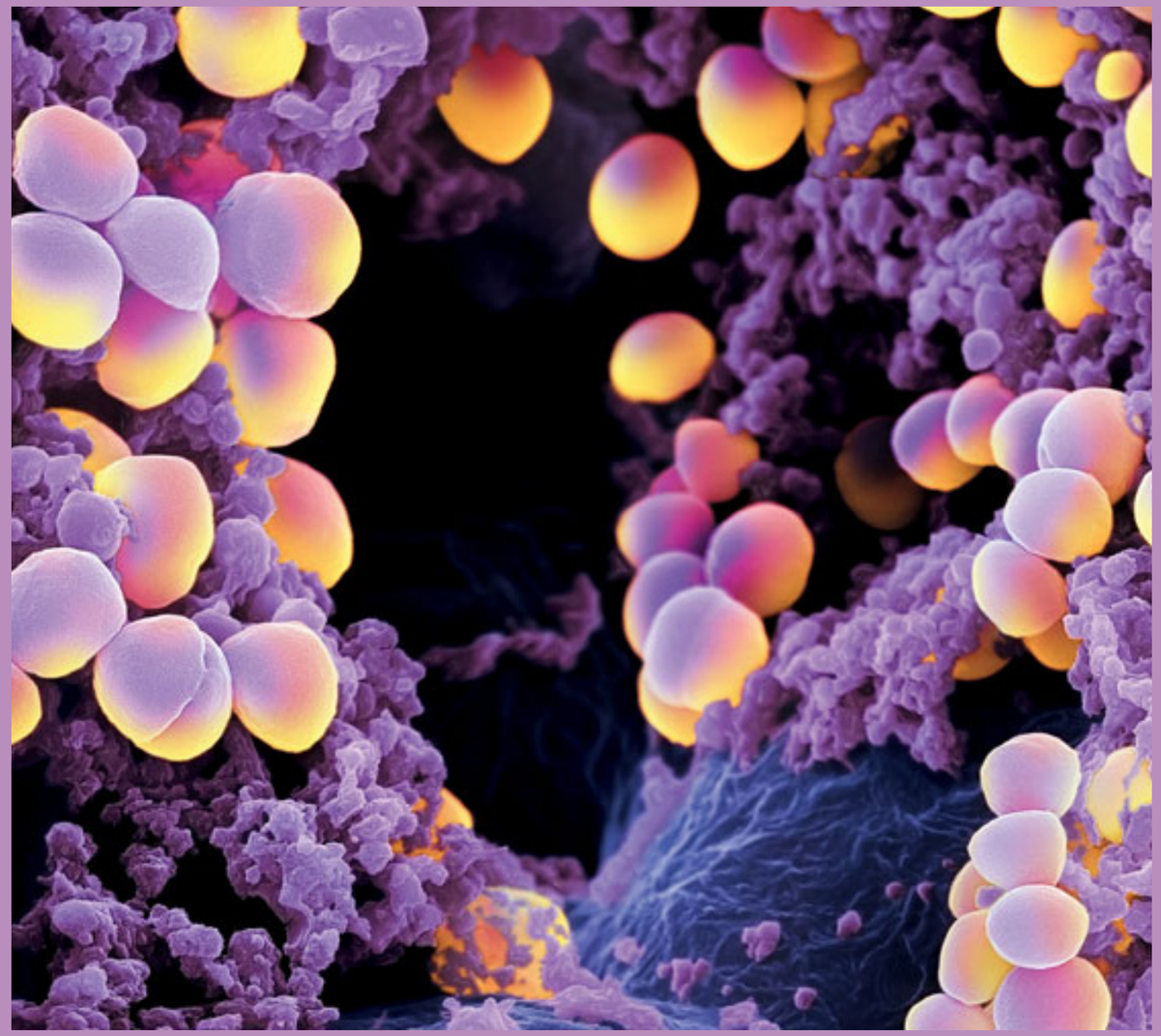
STREPTOCOCCUS

A colorized electron microscope image captures delicate chains of streptococcus in a laboratory sample. Though some strep infections can be deadly, many strains are harmless—among the thousands of benign beings that make their home in our bodies. Most Streptococcus genomes are 1.8 to 2.3 Mb in size and encode 1,700 to 2,300 proteins. There are two types of Strep: group A and group B. Group A strep causes Strep throat - a sore, red throat, sometimes with white spots on the tonsils; Scarlet fever - an illness that follows strep throat. It causes a red rash on the body; Impetigo - a skin infection; Toxic shock syndrome; Cellulitis and necrotizing fasciitis (flesh-eating disease). Group B strep can cause blood infections, pneumonia and meningitis in newborns. A screening test during pregnancy can tell if you have it. If you do, I.V. antibiotics during labor can save your baby's life. Adults can also get group B strep infections, especially if they are elderly or already have health problems. Strep B bacteria can cause urinary tract infections, blood infections, skin infections and pneumonia in adults.



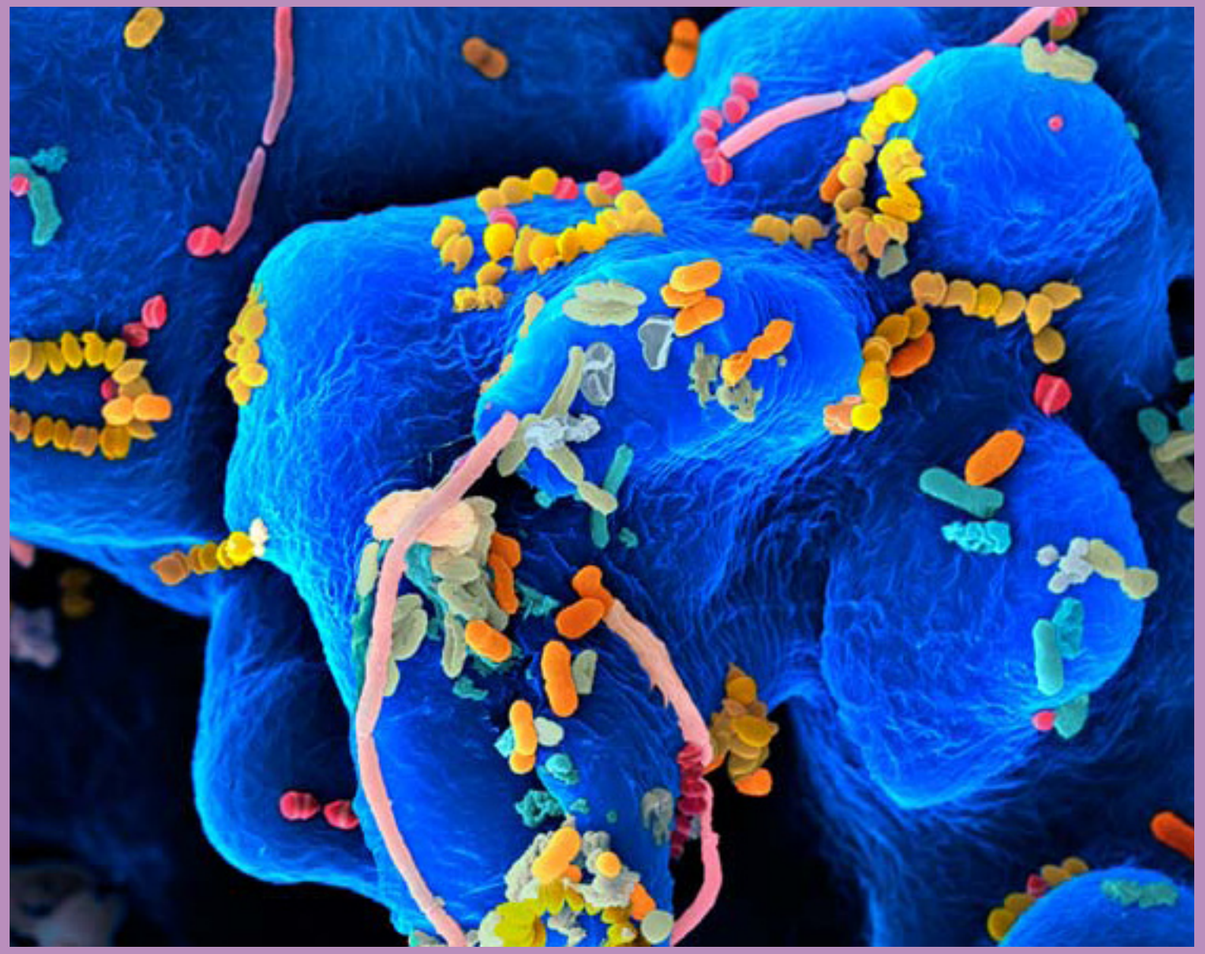
HELICOBACTER

Helicobacter pylori (yellow), a common bacterium that lives in the stomach lining, increases the risk of stomach cancer (brown cells) and peptic ulcers. But over time H. pylori can reduce stomach acid and acid reflux, which may help fend off esophageal cancer. The microbe also appears to help protect us from allergies and asthma. Some scientists suspect that the dramatic increase in those conditions in the industrialized world could be related to the decreasing frequency of H. pylori in our stomachs, which is partly due to high doses of antibiotics in childhood. Helicobacter pylori is a Gram-negative, microaerophilic bacterium found in the stomach, and may be present in other parts of the body, such as the eye. It was identified in 1982 by Australian scientists Barry Marshall and Robin Warren with further research led by British scientist Stewart Goodwin, who found that it was present in patients with chronic gastritis and gastric ulcers, conditions not previously believed to have a microbial cause. It is also linked to the development of duodenal ulcers and stomach cancer. However, over 80% of individuals infected with the bacterium are asymptomatic and it may play an important role in the natural stomach ecology.



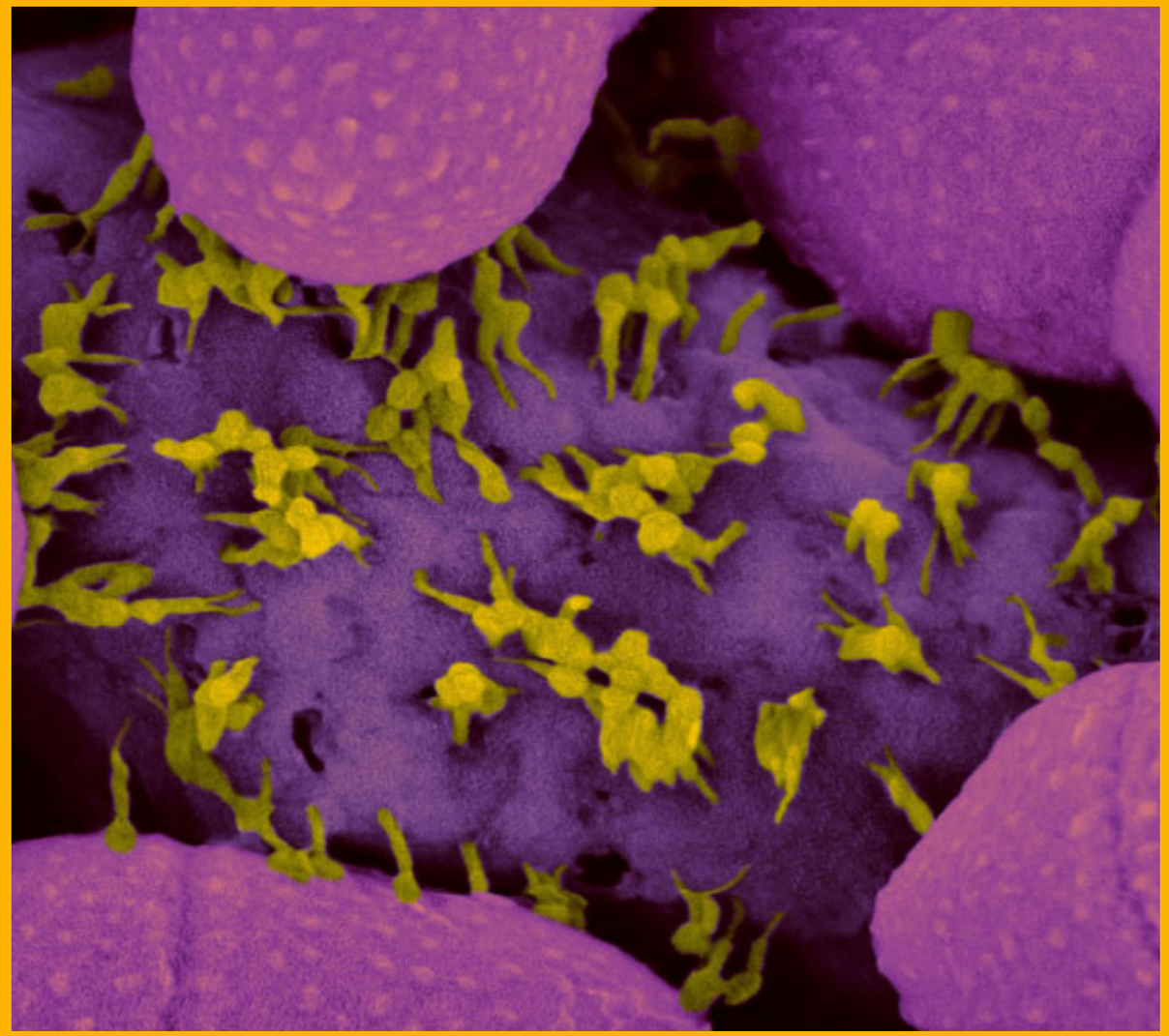
STAPHYLOCOCCUS AUREUS

The bug lives harmlessly in the noses of about a third of us. But it can turn rogue, causing skin infections—or worse. Heavy use of antibiotics since the middle of the last century has prompted the evolution of deadly superbug strains. Staphylococcus aureus is a Gram-positive coccal bacterium that is a member of the Firmicutes, and is frequently found in the human respiratory tract and on the skin. It is positive for catalase and nitrate reduction. Although S. aureus is not always pathogenic, it is a common cause of skin infections (e.g. boils), respiratory disease (e.g. sinusitis), and food poisoning. Disease-associated strains often promote infections by producing potent protein toxins, and expressing cell-surface proteins that bind and inactivate antibodies. The emergence of antibiotic-resistant forms of pathogenic S. aureus (e.g. MRSA) is a worldwide problem in clinical medicine.



MOUTH MICROBES

The human mouth hosts a panoply of microbes, some taking up residence on the mouth lining (blue) within days after birth. Harmful species form biofilms, like the plaque that encourages tooth decay, or colonize the crevices between teeth and gums, causing periodontal disease. Oral probiotics designed to boost the population of species that outcompete pathogenic ones could help prevent or reverse dental disease. Researchers (very patient researchers) have painstakingly harvested all the plaque from every surface of every tooth. It weighs, on average, about 10 mg. But the teeth only comprise 1/20 of all the oral surfaces. You have to multiply the 10 mg from the teeth by 20 to get the total biomass including cheeks, tongue, etc. We also know that 1 mg of oral biomass typically contains about 100 million microbes. By multiplying the number of microbes in 1 mg by 20, we get the total number of microbes in the entire oral cavity. 100 million microbes x 20 mg biomass = 20 billion oral microbes living in your mouth right now. almost all of those billions of microbes that we swallow began their lives in an oral biofilm. Thus, despite only having (at any given time) 20 billion microbes in our mouths, we nevertheless swallow 100 billion! Five times more than we have. So, those 20 billion microbes in our mouths must be producing and shedding 100 billion additional microbes every day. That's five times their original number. Said another way, they are doubling their numbers five times every 24 hours. Dividing 24 hours by 5 = 4.8 hours, the amount of time it takes for the microbes in our mouths to double their number. There are 20 billion bacteria in your mouth and they reproduce every five hours. If you go 24 hours without brushing, those 20 billion become 100 billion!



PHAGES IN ACTION

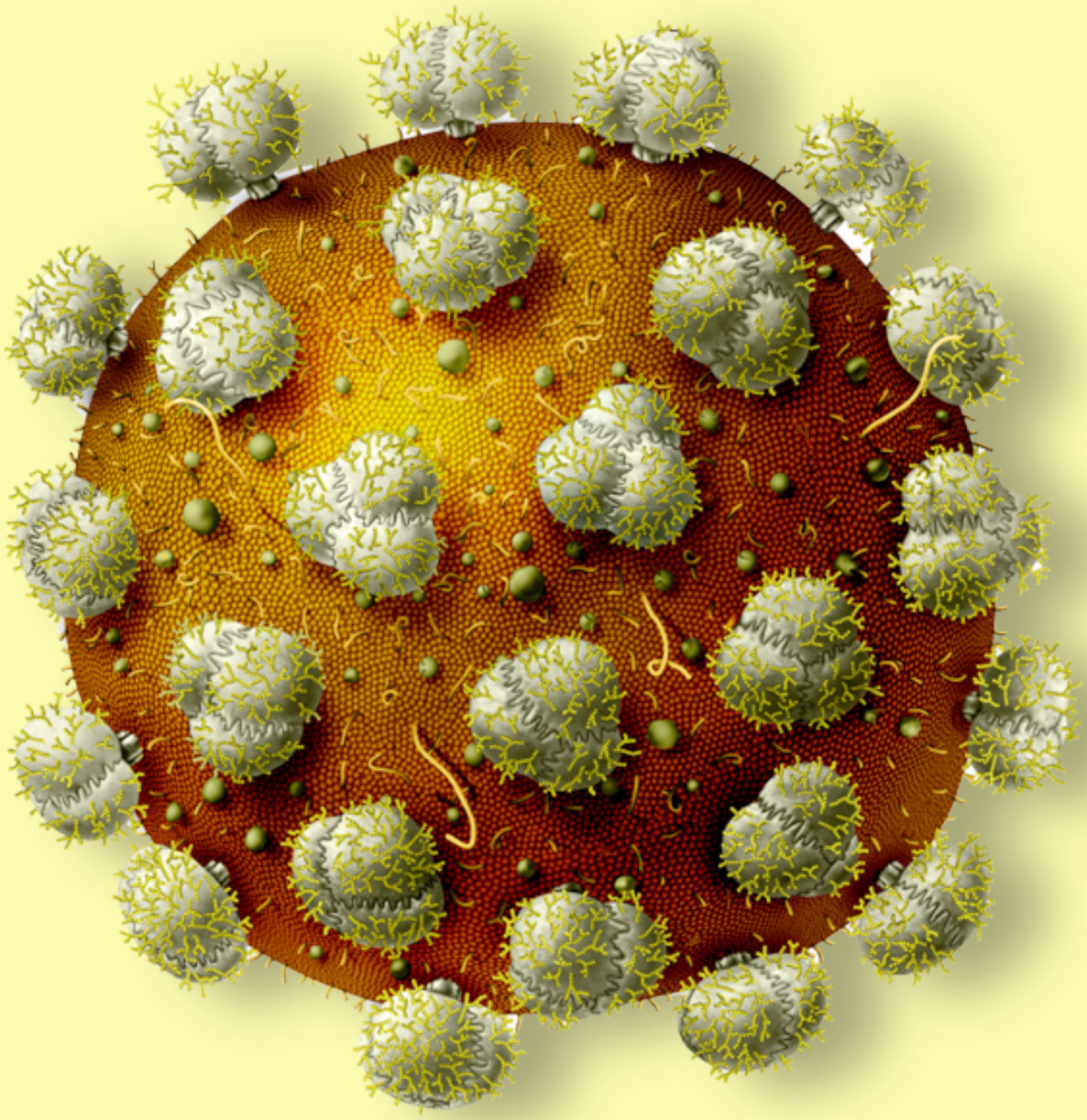
Bacteriophages escape from a dying streptococcus bacterium, ready to find another victim. Their ability to infect and kill specific strains may lead to new treatments for antibiotic-resistant bacteria. Individuals infected with H. pylori have a 10 to 20% lifetime risk of developing peptic ulcers and a 1 to 2% risk of acquiring stomach cancer.[11] Inflammation of the pyloric antrum is more likely to lead to duodenal ulcers, while inflammation of the corpus (body of the stomach) is more likely to lead to gastric ulcers and gastric carcinoma.[12] However, H. pylori possibly plays a role only in the first stage that leads to common chronic inflammation, but not in further stages leading to carcinogenesis.[6] A meta-analysis conducted in 2009 concluded the eradication of H. pylori reduces gastric cancer risk in previously infected individuals, suggesting the continued presence of H. pylori constitutes a relative risk factor of 65% for gastric cancers

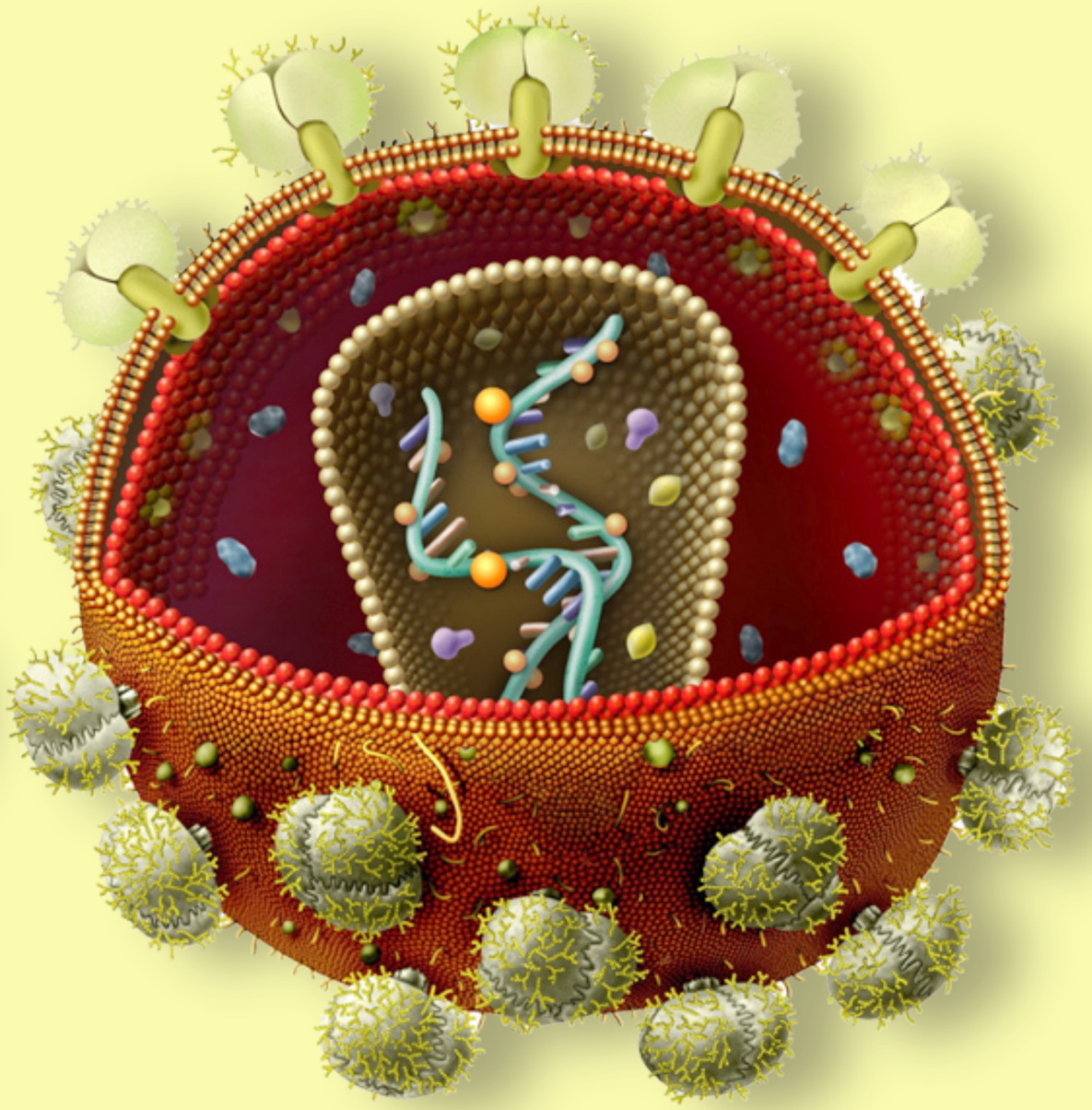
HELICOBACTER

Helicobacter pylori (yellow), a common bacterium that lives in the stomach lining, increases the risk of stomach cancer (brown cells) and peptic ulcers. But over time H. pylori can reduce stomach acid and acid reflux, which may help fend off esophageal cancer. The microbe also appears to help protect us from allergies and asthma. Some scientists suspect that the dramatic increase in those conditions in the industrialized world could be related to the decreasing frequency of H. pylori in our stomachs, which is partly due to high doses of antibiotics in childhood.

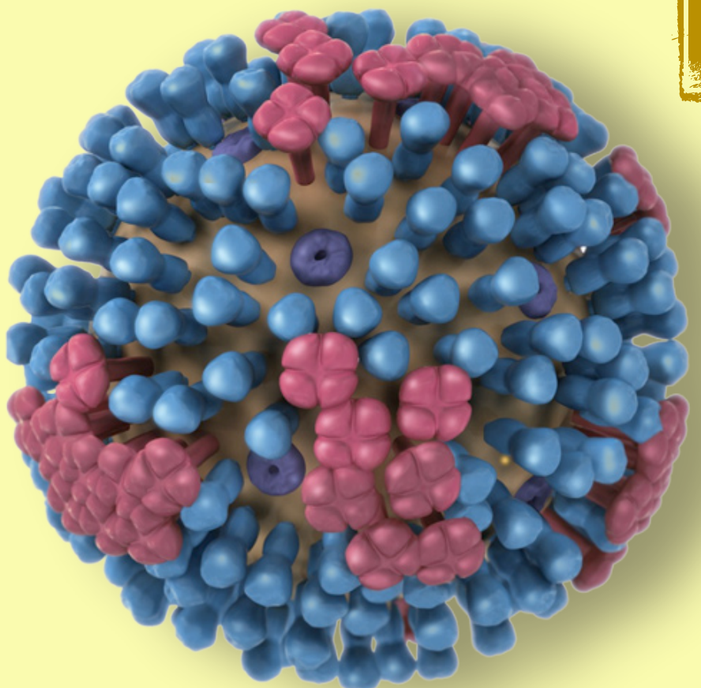
INSIDE VIRUSES

This image at left shows the human immunodeficiency virus (HIV) that causes AIDS and the illustration at right shows the interior of the human immunodeficiency virus (HIV).





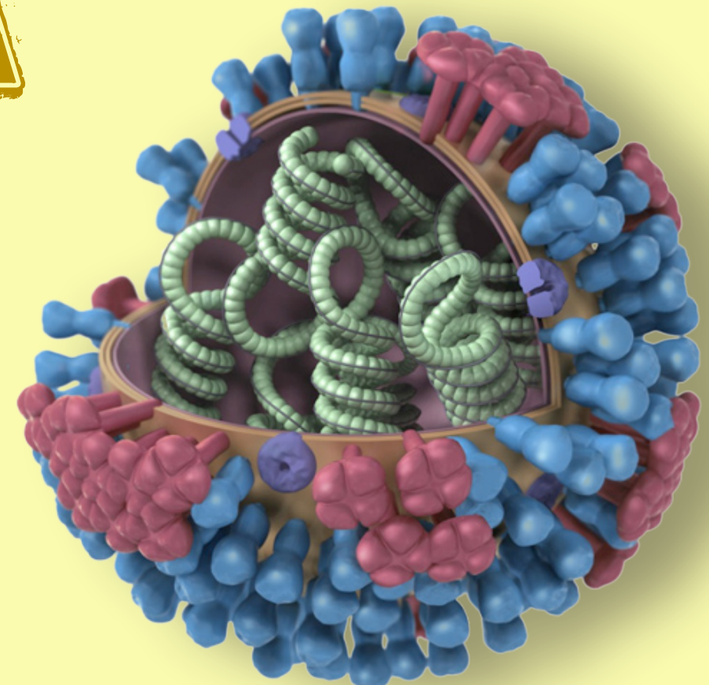
INFLUENZA AND HPV VIRUSES



At top, left and right, we have 3-D graphical representations of a generic influenza virus. A view of the influenza virus in which a portion of the protein coat, or capsid, has been cut away, showing the RNA inside is on the right. The images at bottom, left and right, show the structure of human papillomavirus (HPV), a virus that can cause warts and cervical cancer. On the right we see the human papillomavirus (HPV), in which a portion of the protein coat, or capsid, has been cut away to reveal the DNA inside.

Glyphosate chelates minerals, one of the many components of glyphosates murder arsenal. With a standard diet one might consume enough glyphosate each day to experience constant and continuous mineral depletion and the regular stress of the immune system weakens your defenses and lays the groundwork for opportunistic diseases to easily, rapidly and firmly take hold.

Glyphosate causes disease in everyone that consumes foods containing this antibiotic poison.



Microbes

A Vital Relationship For Health

by Jeff Prager

Microorganisms live all over and inside the human body—on our skin, mouth, nose, teeth, throat, heart, lungs, brain, arteries, veins—as well as in the gut.

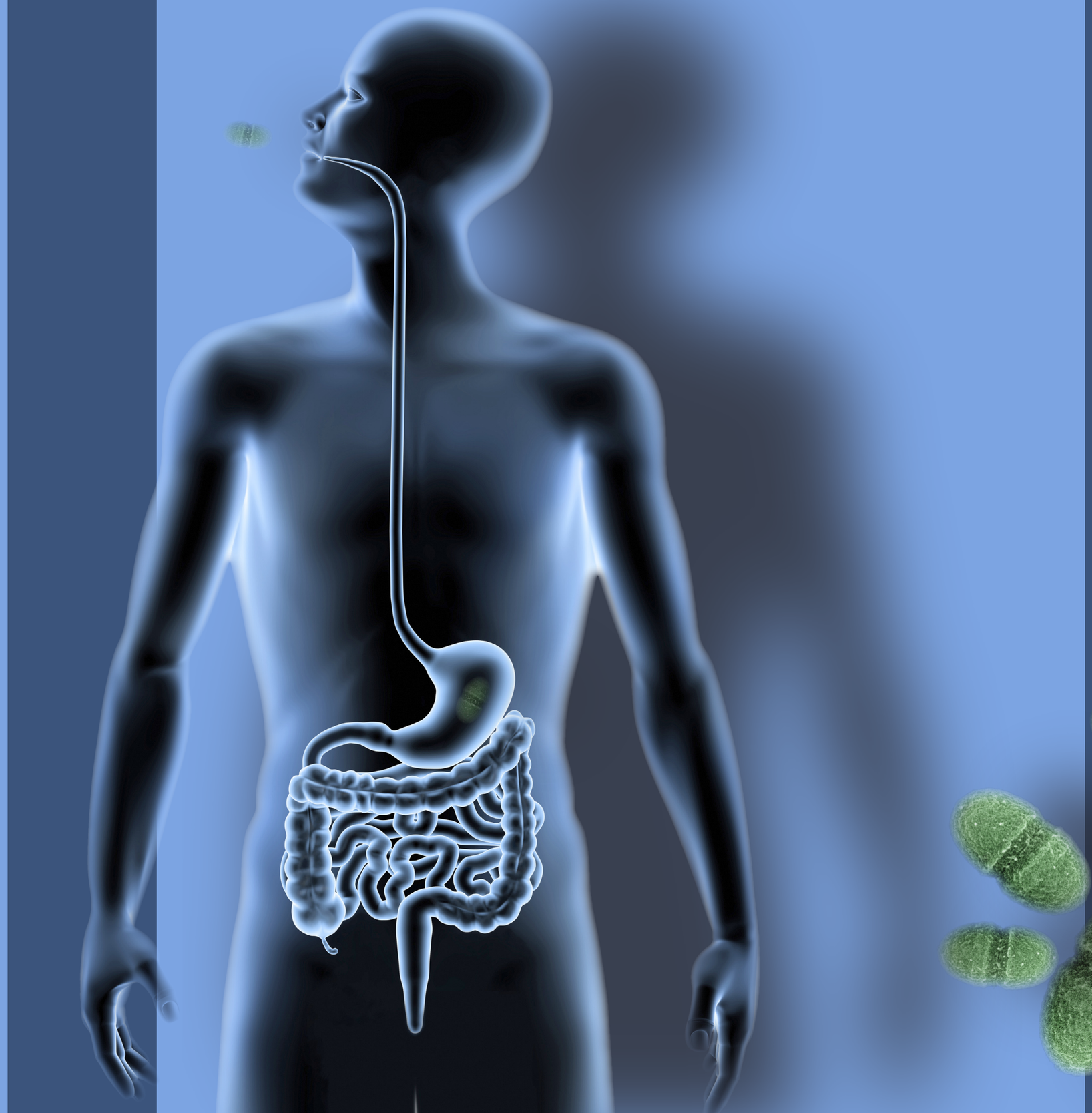
Microbes play a key role in digestion in general and gut health in particular. The intestines contain millions of bacteria that help break down food that our own bodies can't. Without gut bacteria overall gut health declines causing issues ranging from diarrhea, constipation, and gas to autoimmune diseases, cancer, and autism. New research is linking a number of other medical issues to microbes at a rapidly growing pace. The field of Adversomics is directing the strategy by investigating "adverse medical events" as a medical category in and of itself—Adversomics. Look into it.

Imbalance

In adults, there are a number of causes of poor microbial health. One of the most common issues is having an incident of food poisoning or infection, which causes diarrhea and basically "wipes out" the microbes that normally live in the gut. This issue also occurs when you take antibiotics. A healthy gut can recolonize after such an incident, but in the meantime, you are more prone to infection and the other effects of a poor microbial balance in the gut. People with chronic inflammatory bowel diseases like Crohn's disease may be especially prone to these effects.

Cutting-Edge Findings

The fact that microbes affect gut health is well-established and important, but a number of research studies have suggested that the effects of microbes on overall health may go much further. Research is still preliminary in these areas; some studies were performed only in animals, and many more studies will be needed to draw more conclusive connections. However, the current findings suggest that gut health may be connected to many other aspects of health. Neurological problems like autism, depression, and ADHD; obesity; heart disease, various autoimmune diseases, Crohn's, arthritis, diabetes, coronary blockages; and more. In fact, they may play a significant part in every single disease, illness or disorder known to women and men.



Harvard Study Finds Diet Changes Gut Bacteria Within A Single Day

A change in diet quickly alters the types of bacteria living in the human gut, a finding that suggests this rapid adaptability to different foods can be used to control illnesses tied to stomach microbes, researchers said.

Switching to an animal-based diet increased the number of micro-organisms that process protein, while a plant-based diet increased the number of bacteria that help process starch and cellulose, according to a study led by Harvard University researchers. The change in the bacteria populations occurred within a day.

Trillions of microorganisms live in the human gut, helping to digest food, fight disease-causing germs and process nutrients. They also react with vaccines, gglyphosate and other pesticides, any and all environmental poisons. Research has suggested that diets high in fat and sugar may change the human gut's bugs, perhaps contributing to chronic illness, the study authors wrote. Previous work in mice suggested that the microbiome could change within a day, though until now, the effect hadn't been replicated in humans.

"It's exciting and gratifying to find out this holds up in people," said Lawrence David, who was one of the Harvard researchers and is now an assistant professor at Duke University's Molecular Genetics & Microbiology and Institute for Genome Sciences & Policy. "*We're getting an increasing appreciation of how flexible and responsive the microbiome is, even on a very short time scale."*

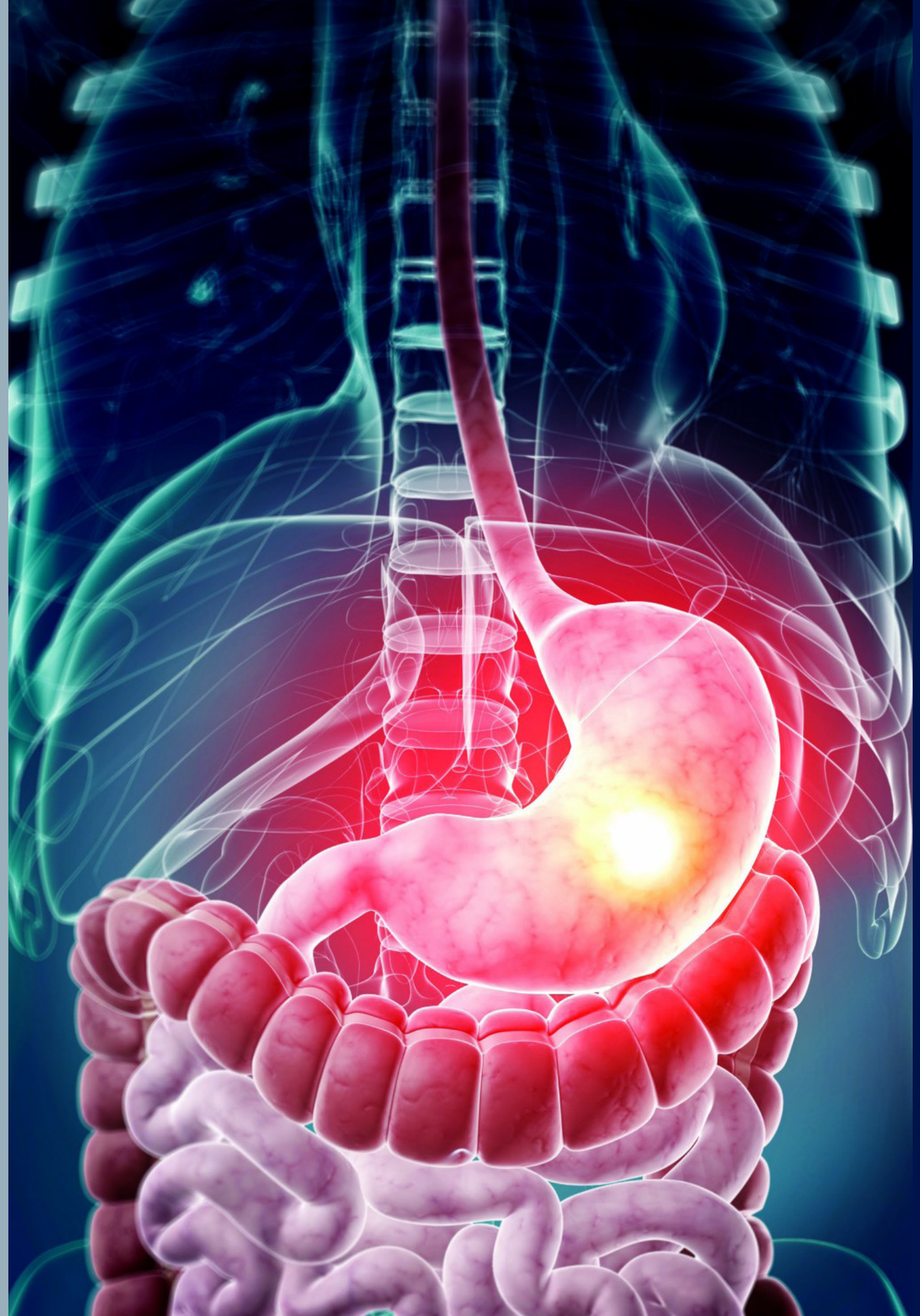
Humans are home to more than 10,000 species of microbes, mostly bacteria that live in healthy symbiosis, according to the Human Microbiome Project. The trillions of micro-organisms that live in and on the body outnumber human cells by 10 to 1, according to research published in 2012.

Scientists are just beginning to explore the composition of these ecosystems. Knowing how these organisms interact with their host and the hundreds of chemicals and foods that also enter the host can reveal more about illnesses such as inflammatory bowel disease and obesity and many other disorders while at the same time identifying the offending chemicals so we can once and for all eliminate chronic disease.

The 11 people studied were allowed to eat as they normally did for four days, writing down what they ate and submitting samples of body waste to the researchers. Then they consumed what was provided to them by researchers for four days, and were watched for six days afterward. That meant that each person essentially served as their own control group, David said.

The plant-based diet, which boosted fiber intake significantly and dropped fat and protein intakes, led to very few changes in the existing microbes. The animal-based diet with almost no fiber intake had a "really big shift."

The animal-based diet caused changes in the population, including an increase in the anaerobic bacteria Bilophila wadsworthia, which is known to cause colitis in mice. The bacteria seem to thrive with the increased intake of fat. Some bacteria also changed their gene expression with the diet, the study found. For me, you are what you eat hits home right here.



Facts Survive Persecution

FDA Policy on GMOs is “irresponsible and illegal” and we Finally have the facts.

It is often stated that the American policy on GMOs is underpinned by this strange thing called “substantial equivalence.” As Steven Druker of the Alliance for Bio-Integrity points out, it is not. American policy is based -- very loosely -- on the principle called GRAS. On the other hand, Europe has placed much greater stress on the woolly and unscientific term “Substantial Equivalence” -- and some bodies have even tried to elevate the term to the status of a “Principle.” we will look at that problem -- and it is a problem in Europe -- in a future post. In the meantime, Steven Druker’s account below is a chilling reminder that politicians and even judges will go where they want to go, in order to foster the interests of industry, regardless of what the law actually says.

Unfortunately, the confusion about whether “substantial equivalence” is an operative legal concept in US food safety law continues. It is not. And that’s very clear. The operative legal concept is “Generally Recognized as Safe” (GRAS). In contrast to SE, GRAS is well-defined. The document below provides clear definitions of the two GRAS criteria, each of which should have been satisfied by every GE food.

GRAS status cannot rest on hypotheses or theoretical reasoning but must be grounded in solid technical evidence of safety; and that evidence must positively demonstrate that there’s a reasonable certainty the specific product will not be harmful. Further, the evidence has to be so well-known and compelling that almost all experts have become convinced of the product’s safety. Therefore, such compelling evidence should have been generated for each GE food (*and for each insertion event*), and it should have been widely available to the scientific community. Moreover, there should not be a significant dispute among experts as to whether safety has been established; and the fact that there always has been, and that it has progressively grown larger, demonstrates that no GE food has ever been legally GRAS.

In our lawsuit challenging FDA policy on GE foods, the issue of “substantial equivalence” was never debated, and the term was not even mentioned in the the judge’s opinion. The argument centered on whether the two GRAS criteria had both been met. And because neither had, the judge was forced to play strange games in order to uphold the FDA and avoid upsetting the applecart. The 2nd document posted just after this one explains how the judge evaded confronting the unpleasant truth that neither of the criteria had been met.

THE JUDGE EVADED CONFRONTING THE UNPLEASANT TRUTH

Social Evolution In Action

Roundup and Birth Defects: Is The Public Being Kept In The Dark?

by Michael Antoniou, Mohamed Ezz El-Din, Mostafa Habib, C. Vyvyan Howard, Richard C. Jennings, Carlo Leifert, Rubens Onofre Nodari, Claire Robinson and John Fagan

Executive Summary

Concerns about the best-selling herbicide Roundup® are running at an all-time high. Scientific research published in 2010 showed that Roundup and the chemical on which it is based, glyphosate, cause birth defects in frog and chicken embryos at dilutions much lower than those used in agricultural and garden spraying. The EU Commission dismissed these findings, based on a rebuttal provided by the German Federal Office for Consumer Protection and Food Safety, BVL. BVL cited unpublished industry studies to back its claim that glyphosate was safe.

The Commission has previously ignored or dismissed many other findings from the independent scientific literature showing that Roundup and glyphosate cause endocrine disruption, damage to DNA, reproductive and developmental toxicity, neurotoxicity, and cancer, as well as birth defects. Many of these effects are found at very low doses, comparable to levels of pesticide residues found in food and the environment.

This issue is of particular concern now that Monsanto and other producers of genetically modified seed are trying to get their glyphosate-tolerant crops approved for cultivation in Europe. If the EU Commission gives its approval, this will lead to a massive increase in the amount of glyphosate sprayed in the fields of EU member states, as has already happened in North and South America. Consequently, people's exposure to glyphosate will increase.

All these concerns could be addressed by an objective review of Roundup and glyphosate in line with the more stringent new EU pesticide regulation due to come into force in June 2011. Just such a review was due to take place in 2012. However, shortly after the Commission was notified of the latest research showing that glyphosate and Roundup cause birth defects, it quietly passed a directive delaying the review of glyphosate and 38 other dangerous pesticides until 2015. This delay is being challenged in a lawsuit brought against the Commission by Pesticides Action Network Europe and Greenpeace.

Delaying the review of glyphosate until 2015 is serious enough. But in reality, the Commission's slowness in preparing the new data requirements for the incoming regulation mean that glyphosate may well not be re-assessed in the light of up-to-date science until 2030. The beneficiary will be the pesticide industry; the victim will be public health.

The need for a review of glyphosate is particularly urgent in the light of the shortcomings of the existing review of the pesticide, on which its current approval rests. In this report, we examine the industry studies and regulatory documents that led to this approval. We show that industry and regulators knew as long ago as the 1980s and 1990s that glyphosate causes malformations – but that this information was not made public. We demonstrate how EU regulators reasoned their way from clear evidence of glyphosate's teratogenicity in industry's own studies (the same studies that BVL claimed show the safety of glyphosate) to a conclusion that minimized these findings in the EU Commission's final review report. The German government and its agencies played a central role in this process. As the "rapporteur" member state for glyphosate, Germany was responsible for liaising between industry and the EU Commission and reporting the findings of industry studies. We show how Germany played down findings of serious harm in industry studies on glyphosate. It irresponsibly proposed a high "safe" exposure level for the public that ignored important data on glyphosate's teratogenic effects. This level was accepted by the Commission and is now in force.

Taken together, the industry studies and regulatory documents on which the current approval of glyphosate rests reveal that:

- Industry (including Monsanto) has known since the 1980s that glyphosate causes malformations in experimental animals at high doses.
- Industry has known since 1993 that these effects could also occur at lower and mid doses.
- The German government has known since at least 1998 that glyphosate causes malformations.
- The EU Commission's expert scientific review panel knew in 1999 that glyphosate causes malformations.
- The EU Commission has known since 2002 that glyphosate causes malformations. This was the year its DG SANCO division published its final review report, laying out the basis for the current approval of glyphosate.

The public, in contrast, has been kept in the dark by industry and regulators about the ability of glyphosate and Roundup to cause malformations. In addition, the work of independent scientists who have drawn attention to the herbicide's teratogenic effects has been ignored, denigrated, or dismissed. These actions on the part of industry and regulators have endangered public health. They have also contributed to the growing division between independent and industry science, which in turn erodes public trust in the regulatory process.

This report provides a comprehensive review of the peer-reviewed scientific literature, documenting the serious health hazards posed by glyphosate and Roundup herbicide formulations. On the basis of this evidence, we call on the Commission to cancel its delay in reviewing glyphosate and to arrange an objective review of the pesticide. The review must take into account the full range of independent scientific literature, as demanded by the new pesticides regulation, and should be started as soon as the new data requirements are in place this year. In the meantime, the Commission should use its powers to withdraw glyphosate and Roundup from the market.

Taken together, the industry studies and regulatory documents on which the current approval of glyphosate rests reveal that:

- Industry (including Monsanto) has known since the 1980s that glyphosate causes malformations in experimental animals at high doses.
- Industry has known since 1993 that these effects could also occur at lower and mid doses.
- The German government has known since at least 1998 that glyphosate causes malformations and birth defects in both animals and humans.

Now, in 2015, based on the evidence from numerous new studies and reports we know that glyphosate causes neurological disorders in amounts 100 times lower than those allowed by the FDA

We Just Really Dont Know!

A Review

GM crops and the rat digestive tract: A critical review

by I.M. Zdziarski (a), J.W. Edwards (b), J.A. Carmanb, (c) and J.I. Haynes

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c. Institute of Health and Environmental Research (IHER), P.O. Box 155, Kensington Park, SA 5068, Australia

Conclusions

The evidence reviewed here demonstrates an incomplete picture regarding the toxicity (*and safety*) of GM crops consumed by humans and animals. The majority of studies reviewed lacked a unified approach and transparency in their methodology and results, making it impossible to properly review or repeat these studies. Furthermore, such lack of detail makes it difficult to generate evidence-based guidelines to aid in the delivery of an optimum safety assessment process for GM crops for animal and human consumption.

When considering how a better risk assessment could be done, it is important to consider systems established for other novel substances that may generate unintended effects. For example, the registration of pharmaceutical products requires an examination of both benefits and risks associated with their use and a complete assessment of those benefits and risks to establish whether the products are appropriate for general use at a range of doses.

We argue that each GM crop should be assessed using similar methods, where a GM crop is tested in the form and at the rates it will be consumed by animals and people. Whilst this provides for an effective general approach, there are additional issues for assessing GM crops that need to be taken into account.

For example, the process of developing GM crops may generate unintended effects. Furthermore, the plant developed is a novel entity with genes, regulatory sequences and proteins that interact in complex ways. Therefore, the resultant plant should be assessed as a whole so that any pleiotropic effects (*the production by a single gene of two or more apparently unrelated effects*) can also be assessed. As a result, long-term animal feeding studies should be included in risk assessments of GM crops, together with thorough histopathological investigations (*the study of changes in tissues caused by disease*) using a variety of methods to better detect subtle changes or the beginning or presence of pathologies. Such robust and detailed studies will then make it possible to put evidence-based guidelines in place, which will substantially help to determine the safety of GM crops for human and animal consumption.

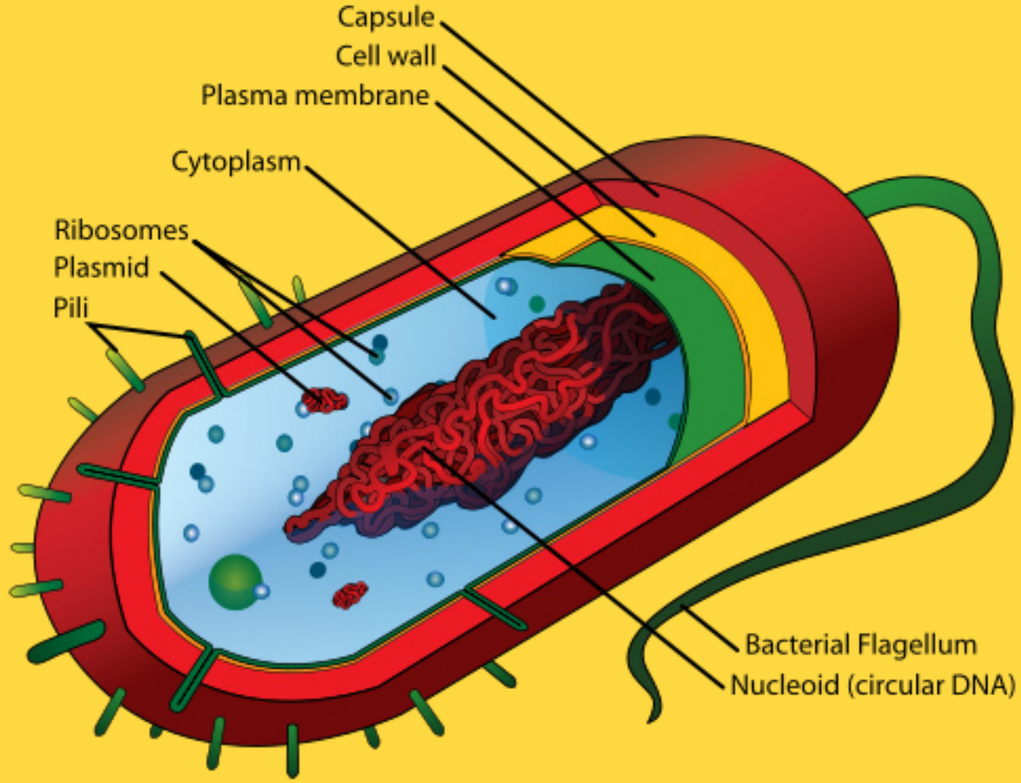
The Confusing Bacteria

by Jeff Prager

The Prokaryote illustrated below is a microscopic single-celled organism, included in the group bacteria and cyanobacteria, that has neither a distinct nucleus with a membrane nor other specialized organelles. A Eukaryote, not pictured, is an organism consisting of a cell or cells in which the genetic material is DNA in the form of chromosomes contained within a distinct nucleus.

Eukaryotes include all living organisms other than the eubacteria and archaebacteria. Eubacteria is a bacterium found mainly in the intestines of vertebrates and in the soil. It's a bacterium of a large group typically having simple cells with rigid cell walls and often flagella for movement. The group comprises the "true" bacteria and cyanobacteria, as distinct from archaebacteria.

Archaebacteria are microorganisms that are similar to bacteria in size and simplicity of structure but radically different in molecular organization. They are now believed to constitute an ancient intermediate group that came between the bacteria and eukaryotes.



Teratogenic Effects of Glyphosate-Based Herbicides: Divergence of Regulatory Decisions From Scientific Evidence.

by Antoniou et al., published on the journal Environmental Analytical Toxicology 2012 and the Journal Environmental Analytical Toxicology of Pesticides, also 2012,

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Introduction

An investigation (Paganelli et al.) of the toxicity of a commercial Roundup® herbicide formulation and its active ingredient glyphosate found that these substances caused severe malformations in embryos of the South African clawed frog Xenopus laevis and chickens.

In frogs, dilutions of 1/5000 of the formulation (equivalent to 430 μM of glyphosate) were sufficient to induce malformations, including shortening of the anterior posterior axis, microcephaly, microphthalmia, cyclopia, and craniofacial malformations at tadpole stages. Embryos injected with pure glyphosate showed similar phenotypes, suggesting that glyphosate itself, rather than a surfactant or other adjuvant present in the formulation, was responsible for these developmental abnormalities.

Roundup® produced similar effects in chicken embryos, which showed a loss of rhombomere domains, reduction of the optic vesicles, and microcephaly.

Through the use of reporter gene assays and phenotypic rescue via administration of an antagonist, the authors confirmed that the mechanism by which glyphosate and Roundup caused the observed teratogenic effects in Xenopus embryos was via disruption of the retinoic acid signalling pathway. This resulted in dysregulation of the shh, slug and otx2 regulatory genes, which are crucial to the development of the central nervous system [1].

The study, while not a classical toxicological study, is relevant to human risk assessment because the retinoic acid signalling pathway is a central signalling pathway in embryonic development that operates in virtually all vertebrates, whether amphibians, birds, or mammals.

Other Studies Showing Malformations from Glyphosate and Roundup® Exposure

Paganelli et al.'s study was one among several to find malformations from glyphosate and Roundup exposure. Jayawardena et al. (2010) found nearly 60% malformations in tadpoles of the tree frog Polypedates cruciger treated with an environmentally relevant concentration of 1 ppm Roundup. Effects included kyphosis, scoliosis, and edema [2].

Relyea (2012) found that environmentally relevant concentrations of Roundup induced relatively deeper tails

similar to the adaptive changes caused by the presence of a predator in the tadpoles of the wood frog (Rana sylvatica or Lithobates sylvaticus) and leopard frog (R. pipiens or L. pipiens) [3]. A study on tadpoles of Scinax nasicus.

(Lajmanovich et al., 2005) found that exposure to glyphosate herbicide caused craniofacial and mouth deformities, eye abnormalities and bent, curved tails, as well as mortality. Malformations and mortality increased with dose and time of exposure. A 2-day exposure to 3.07 mg/l glyphosate.

Abstract

The publication of a study in 2010, showing that a glyphosate herbicide formulation and glyphosate alone caused malformations in the embryos of Xenopus laevis and chickens through disruption of the retinoic acid signalling pathway, caused scientific and regulatory controversy. Debate centred on the effects of the production and con= sumption of genetically modified Roundup Ready® soy, which is engineered to tolerate applications of glyphosate herbicide. The study, along with others indicating teratogenic and reproductive effects from glyphosate herbicide exposure, was rebutted by the German Federal Office for Consumer Protection and Food Safety, BVL, as well as in industry-sponsored papers.

These rebuttals relied partly on unpublished industry-sponsored studies commissioned for regulatory purposes, which, it was claimed, showed that glyphosate is not a teratogen or reproductive toxin. However, examination of the German authorities' draft assessment report on the industry studies, which underlies glyphosate's EU authorisation, revealed further evidence of glyphosate's teratogenicity. Many of the malformations found were of the type defined in the scientific literature as associated with retinoic acid teratogenesis. Nevertheless, the German and EU authorities minimized these findings in their assessment and set a potentially unsafe acceptable daily intake (ADI) level for glyphosate. This paper reviews the evidence on the teratogenicity and reproductive toxicity of glyphosate herbicides and concludes that a new and transparent risk assessment needs to be conducted. The new risk assessment must take into account all the data on the toxicity of glyphosate and its commercial formulations, including data generated by independent scientists and published in the peer-reviewed scientific literature, as well as the industry-sponsored studies.

"The new risk assessment must take into account all the data on the toxicity of glyphosate and its commercial formulations, including data generated by independent scientists and published in the peer-reviewed scientific literature, as well as the industry-sponsored studies."

Potential Health Effects of Foods Derived from Genetically Modified Plants: What Are the Issues?

by Arpad Pusztai and Susan Bardocz

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11600 Penang, Malaysia

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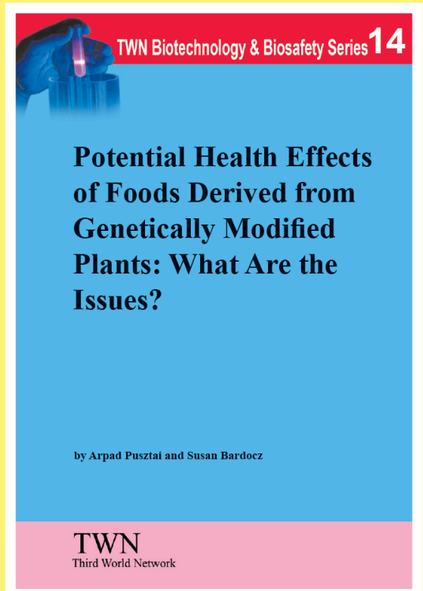
Alimentary Tract as the First Target of GM Food Risk Assessment

Excerpts

To show by chemical methods the presence of new toxins/allergens in GM food products is, at best, difficult. In contrast, the presence of even minute amounts of unexpected but harmful potent bioagents in GM foods could be more easily established from their possibly disproportionally large effect on health. Thus, exposure of individuals to biologically active transgenic proteins can have major effects on their gastrointestinal tract. As most proteins are immunogenic their consumption may trigger immune/allergic effects both in the mucosal immune system of the gut and the body. It is also likely that, in addition to the effects on the gastrointestinal tract, the size, structure, and function of other internal organs will be affected, particularly in young and rapidly growing humans or animals. According to some recent unconfirmed reports, the dietary exposure to GM foods may also have harmful effects on reproduction (see Annex). In addition, the risks will also have to be investigated as to whether measurable amounts of the transgenic DNA constructs in GM crops/foods survive in a functionally active state/size in the gastrointestinal tract of the human/animal ingesting them, and whether they can incorporate into the genome of the cells of their gut and body organs and what will be the consequences, if any, for the individual.

GM potatoes of different origins may have common trophic effects on the gut. Changes in the ultrastructure of other organs, such as the liver, pancreas, etc., on feeding with GM crop containing diets, as shown by the work of the Malatesta group (for references see Pusztai & Bardocz 2006), may also be taken as a first indication of possible harmful effects that should make follow-up studies mandatory.

Changes in blood cells and blood protein levels in GM-fed animals may also suggest serious health problems, including disturbances in erithropoiesis, blood protein synthesis and the immune system. Thus, measurement of immune responsiveness could be a useful follow-up study when blood cell counts show significant differences in lymphocyte numbers that may point to one of the potentially serious hazards of the ingestion of GM foodstuffs (e.g. see our GM potato studies, Table 2). This is a particularly useful method because it is in general clinical use and could therefore be easily carried out with humans. Although no hormone assays were performed on rats fed GM or non-GM diets in our GM potato study, the consistently strong pancreatic growth stimulated by GM potato



diets in the feeding studies suggests that this possibly was the result of the release of CCK (cholecystokinin) or some other humoral growth factor from the duodenum by an unknown growth/proliferative signal only found in the GM potatoes. Again, GNA (Galanthus nivalis lectin) could not be responsible for this because it does not stimulate the enlargement of the pancreas when fed to rats in its original source (Pusztai et al. 1990).

In addition to the changes in protein/metabolite profiles and the possible formation of new toxins and allergens in the plant resulting from the unanticipated effects of transgene insertion and the destabilisation of the recipient genome and the interference with the expression of the plant's own genes, the effects of transgenic plant DNA should also be considered. Thus, it is essential in any risk assessment protocol to determine in humans/animals ingesting GM foods whether appreciable amounts of the DNA vector construct used for developing the GM plant survive in the gut in functional form, whether they are taken up and integrated into the genome of the individual, and what, if any, effects the foreign transgenic DNA will have on them.

GM soy — A senior Russian scientist, Irina Ermakova, published a rat reproductive study in which she examined the effect of glyphosate-resistant (RR) GM soybean seeds fed to pregnant female rats on the number and weight of pups delivered (Ermakova 2006). The study was originally published in Russian, and was heavily criticised for using coated seeds ready for planting instead of beans suitable for feed. The control non-GM soybean was not the isogenic parent line, either. However, because of the possible serious implications of the results of this study for humans and animals it should have been repeated and possibly verified by other scientists with the correct GM soybean diets. Indeed, she has repeatedly pleaded for this but no one dared to try to reproduce her experiments.

Recent Studies on Human Health Impacts of GM Crops

In her study rats were fed with laboratory rat chow and this diet was complemented with GM or conventional soybean for two weeks before mating, during the pregnancy and during suckling and the body mass and the number of pups were observed (Table A1). The data indicated that on the GM soybean-supplemented rat chow significantly fewer pups were born, and with smaller body mass, than on the control non-GM soybeans.

Brasil et al. (2009) found that rats fed on GM soy showed altered morphology of the uterus and the ovaries: had greater volume density of endometrial glanular epithelium, reduced follicle number and increased corpus luteum numbers (a tendency to abort or less of a chance to get pregnant). Although the GM diet was not supplemented with cysteine as the other diets, and it is difficult to assess if the results were due to consumption of the transgenic soy itself or were due to the presence of glyphosate (and/or AMPA), always present in GM seeds, the findings are disturbing and warrant further studies. A recent study found that GM soy-fed animals have developed hair inside the oral cavity more often than control (Baranov et al. 2010).

The results of histological investigations by electron microscopy of cell nuclei revealed differences in fibrillar centres, dense fibrillar components and in the pore density of hepatocytes, and cells from the spleen and pancreas. This indicates metabolic differences caused by the GM diet in the cell nucleus of some internal organs. Micro array investigations of the small bowel tissue also showed significant differences between the GM- and non-GM-fed groups. Analyses of the metabolic pathways indicated differences in the activity of the interleukin-signalling pathway, cholesterol biosynthesis and in protein synthesis, metabolism and post-synthetic processing of proteins.

All the females fed the ISO line maize got pregnant all the time, while infertility of more females was observed in the GM maize-fed group, and this became significant by the fourth generation

(Table A3). The number of pups was always fewer on GM, and the litter size was also smaller, but not statistically significantly for the first two deliveries, but it become significant for the 3rd and 4th litters (Table A3).

To summarise, in these experiments the GM maize had no influence on the life span of mice, but influenced their reproductive performance. Fewer pups with smaller body mass were produced by mothers fed the GM-containing diet, and more animals died before weaning. In the RACB study the differences become statistically significant with the 3rd and 4th litters. Although it is impossible to extrapolate from animal experiments to the human condition the results of these experiments demand that similar reproduction experiments must be incorporated in safety analysis protocols with all GM crops before they are commercialised. These results are all the more important because they have been obtained with GM crops already approved in the EU and several other countries.

This preliminary study has been criticised with regard to its statistical analysis. However, its findings remain a serious cause of concern that needs to be investigated further.

Glyphosate is not a genetically modified product but because its use in agriculture is inseparable from the cultivation of herbicide-tolerant GM crops in a particular technology package, its effects on health need to be examined also with that of the glyphosate-resistant GM crops.

Although the declared aim of the introduction of glyphosate-resistant GM crops was that with these crops the amount of herbicide sprayed on the land should decrease, due to the ever-increasing area of cultivation of glyphosate-resistant Roundup Ready (RR) GM crops, the use of glyphosate has in fact increased (Benbrook 2004, 2009). The glyphosate-containing sprays destroy all weeds but the growth of the glyphosate-resistant GM crop is protected regardless of how much glyphosate is sprayed on to the land. To make sure that all weeds are destroyed the use of glyphosate and consequently the glyphosate load of the land has been substantially increasing after the first few years of a slight reduction (Benbrook 2004, 2009).

This has happened despite the ever-increasing number of publications showing that glyphosate has many serious and detrimental effects on the environment and biodiversity (Relyea 2005) with the development of herbicide-resistant weeds (Duke 2005; Owen and Zelaya 2005; Warwick et al. 2007; Loux et al. 2007; Zelaya et al. 2007). There is also an urgent need to consider the potentially seriously damaging effects of this total herbicide on human/animal health, particularly as it is used in large amounts. Indeed, there are a number of recently published papers that all indicate possible damaging effects of glyphosate on health and reproduction which need to be taken seriously.

By building on previous work the findings of French scientists (Marc et al. 2005) have confirmed and extended their previous results by showing that the main ingredient of commercial Roundup formulations, glyphosate, in a milimolar concentration range, particularly when used together with the obligatory polyoxyethylene amine surfactant, inhibited the transcription of one of the enzymes involved in hatching of sea urchin embryos and therefore significantly delayed their hatching.

When it is considered that farm workers inhale commercial herbicide sprays in which the active ingredient concentration exceeds by about 25 times of that used in the transcription inhibition studies by the French scientists, health concerns due to the use of glyphosate must be acute.

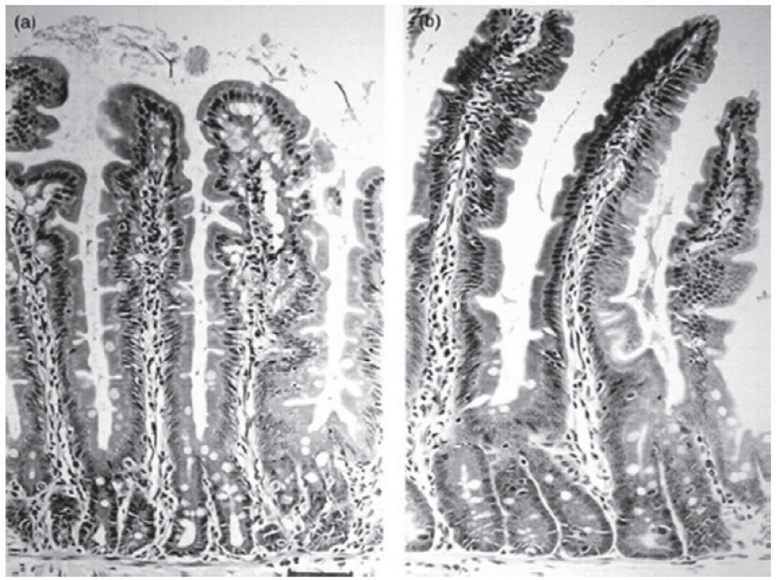


Figure 1. Histology of jejunal sections of rats fed GM potatoes (Pusztai 2002). Jejunal crypt length and cells exhibit marked enlargement after feeding rats a diet of raw GM potato for 10 days, (b) in comparison with that of rats given a parental line potato diet (a). The Villus length is similar in both but intraepithelial lymphocyte cell counts appear to be increased on a GM potato diet.

In another study it was shown that in the oral treatment of Wistar rats with increasing concentrations of the herbicide Glyphosate-Biocarb, a formulation used in many countries such as Brazil, the number of Kupffer cells in hepatic sinusoids increased, followed by large deposition of reticulin fibres and the leakage of hepatic aspartate-aminotransferase and alanine-aminotransferase into the circulation, indicating hepatic damage in these animals (Benedetti et al. 2004).

The work of another group of French researchers showed that glyphosate, particularly as used together with polyoxyethylene amine surfactant in Roundup Ready formulations, was toxic to human placental JEG3 cells at concentrations lower than that used in agricultural practices. Even at subtoxic concentrations RR was an endocrine disruptor on aromatase activity and its mRNA level as glyphosate interacted with the active site of the purified enzyme (Richard et al. 2005; Benachour et al. 2007). It is possible that the pregnancy problems in agricultural workers using Roundup may be traced back to the exposure to this herbicide (Savitz et al. 2000).

All these findings indicate that there is an urgent need to carry out systematic and direct studies, independent of the biotech industry, on the short- and long-term effects on animal (and human) health of exposure to glyphosate and its more effective commercial formulations alone and/or preferably in combination with the appropriate GM crop. With the presently cultivated huge areas of Roundup Ready crops and the anticipated even-larger future extensions of this glyphosate-dependent GM crop technology the potential danger for animal/human health needs to be dealt with in advance and not if or when it occurs. If we consider that RR soybeans may in themselves damage reproduction, a combination of the similar, possibly synergistic effects of the GM crop and glyphosate could be a potential disaster waiting to happen.

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Dr. Arpad Pusztai
The Whistleblower

by Jeff Prager

Dr. Pusztai is the author of the previous report. In August 1998, Dr. Arpad Pusztai was the leading scientist for Food Research, and gave a short interview on British television. He explained that while he believes in the beneficial benefits of genetic engineering in food, but before any authorization for the use of those foods in the human diet and food cahin he would like long-term tests carried out.

Dr. Pusztai made it perfectly clear that he would not eat genetically modified foods. His reasons are simple - he personally conducted a series of studies in which rats were fed a genetically modified potato. They suffered serious organ changes, inflammation, immune organ damage and retarded growth.

Pusztai's explanation burst like an atomic bomb during the still-continuing gold rush of the genetic food, seed and pesticide industry. Ans at the very time, Dr. Pusztai recognizes that more than 65% of the American and British people already eat foods that contain genetically modified ingredients - without suspecting anything of it almost every single day. Dr. Pusztai has an intimate understanding of the severe disorders caused by GMO foods, their seeds and their related pesticides.

Dr. Pusztai's BBC interview went over like a metric tonne of handmade, UK-engineered, genetically modified bricks.

Within hours of the television interview Pusztai's experienced brutally violent political crossfire. He's now forbidden to further comment on his research. His papers have been confiscated and he's denied access to his laboratory. The National Science Board of the Royal Society rejected his membership and excluded him from participation or association with the group. Within just a few short days decades of an active, honest career established with blood, sweat and tears, was personally and professionally ruined by authorities in positions of the highest political office.

Dr. Arpad Pusztai, leading GMO Researcher, made it perfectly clear that he would never eat genetically modified foods based on his research results alone. His career, his income, his associations, his research, his ambitions, his asprations, his hopes, his desires and his dreams were terminated immediately for speaking out about the disease and disorders GMO's cause.

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Authors Biography

Dr Arpad Pusztai (*pictured at left*) is a Fellow of the Royal Society of Edinburgh (FRSE) and holds a BSc in Chemistry and a PhD in Physiology and Biochemistry. Pusztai was formerly Head of Protein Chemistry at the Rowett Research Institute, Aberdeen, Scotland. His main research interest is biologically active food components – lectins, plant anti-nutrients, and the effect of GMOs on animal and human health. His research also focuses on cancer prevention by dietary means. He has published over 300 primary scientific papers and nine scientific books. He is holder of the Stilmark Medal; Honorary Professor of the University of Tartu, Estonia; Leverhulm Fellow; Auber Bequest Fellow; and Recipient of the Federation of German Scientists' Whistleblower Award 2005.

Prof. Susan Bardocz has a BSc in Chemistry and a PhD in Biochemistry and Pharmacology. She was a lecturer and then senior lecturer in Biochemistry at the University of Debrecen, Hungary, up to 1987. Between 1987 and 2000 she was at Rowett Research Institute, where she was the Head of the Food - Gut - Microbial Interaction Group between 1992 and 1998. She is currently Professor of Human Nutrition at the University of Debrecen, Hungary. She has published over 200 papers and book chapters, as well as written and edited several books.

Both received the Pro Biocultura Prize in 2008 in Hungary, and the Stuttgart Peace Prize in 2009.

Does Eating GM Crops Harm The Digestive Tracts Of Rats?

A Review Of The Scientific Evidence

By Dr Judy Carman

September 29, 2014

This is a briefing about a new, peer-reviewed scientific paper titled: GM crops and the rat digestive tract: A critical review, by Irena Zdziarski, Dr John Edwards, Dr Judy Carman and Dr Julie Haynes*. The paper is a review done by researchers at the University of Adelaide, Flinders University and the Institute of Health and Environmental Research, all based in South Australia. The paper reviewed published studies where the health of rats was assessed after the rats were fed certain GM crops.

The most common types of GM crops are designed to do one of two things. The first type has a gene inserted into it *(often the EPSPS gene)* which causes the plant to make a new protein that allows the plant to survive being sprayed with a herbicide such as glyphosate. The most common of these are called Roundup Ready crops. The second type of crop has a gene inserted into it *(often the cry1Ab or cry3Bb1 genes)* so that the plant makes a new protein that is an insecticide, so that when an insect eats the plant, the insect also eats the new insecticidal protein, which results in the insect dying. GM crops are often now grown with two or more of these genes in them at the same time.

We wanted to see how much evidence there was for the safety of crops containing these three genes for animals that eat them. We looked at the evidence for the digestive tract because this is the first place these new proteins go when they are eaten, and where they stay the longest. Therefore, if these new proteins are toxic to animals *(and people)* that eat them, it is most likely that the effects would be seen in the digestive tract. The digestive tract includes the stomach and intestines.

Because it is sometimes very difficult to see if there is damage to tissues without the aid of a microscope, we only considered evidence that involved looking through a microscope. These are called histopathology studies. We also only looked at studies done on rats as these animals are the standard animals used for these sorts of studies.

We found that there were 47 crop varieties approved by government regulators for animal or human consumption that contained these three GM genes. But we could only find published studies for 9 of these crop varieties. We could find no studies whatsoever for the other 38 approved varieties. This means that we could not find any published histopathology studies for 81% of the approved crop varieties.

Most of the studies were general health assessments of the GM crop on rat health but most of these (76%) were done after the crop had been approved for human or animal consumption, with half of these being published at least nine years after approval.

But what is worse is that we could not find a single study that was properly conducted or reported. Faults included: investigators were inconsistent or not transparent in their methods, investigators didn't define what they considered to be a toxic or pathological finding, or they were not transparent in what they found. Many of the studies contained several such faults.

We therefore concluded that there is a lack of evidence to prove that these crop varieties are safe to eat. We also call for detailed guidelines to be developed for how histopathology studies should be done so that these studies can be done properly, studies between investigators can be compared, and the work of one investigator can be repeated by another. We also describe how these histopathology studies should include several specialised methods to better find the beginning of any pathological change. In this way, we can better determine if GM crops are safe

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Detection of Glyphosate Residues in Animals and Humans

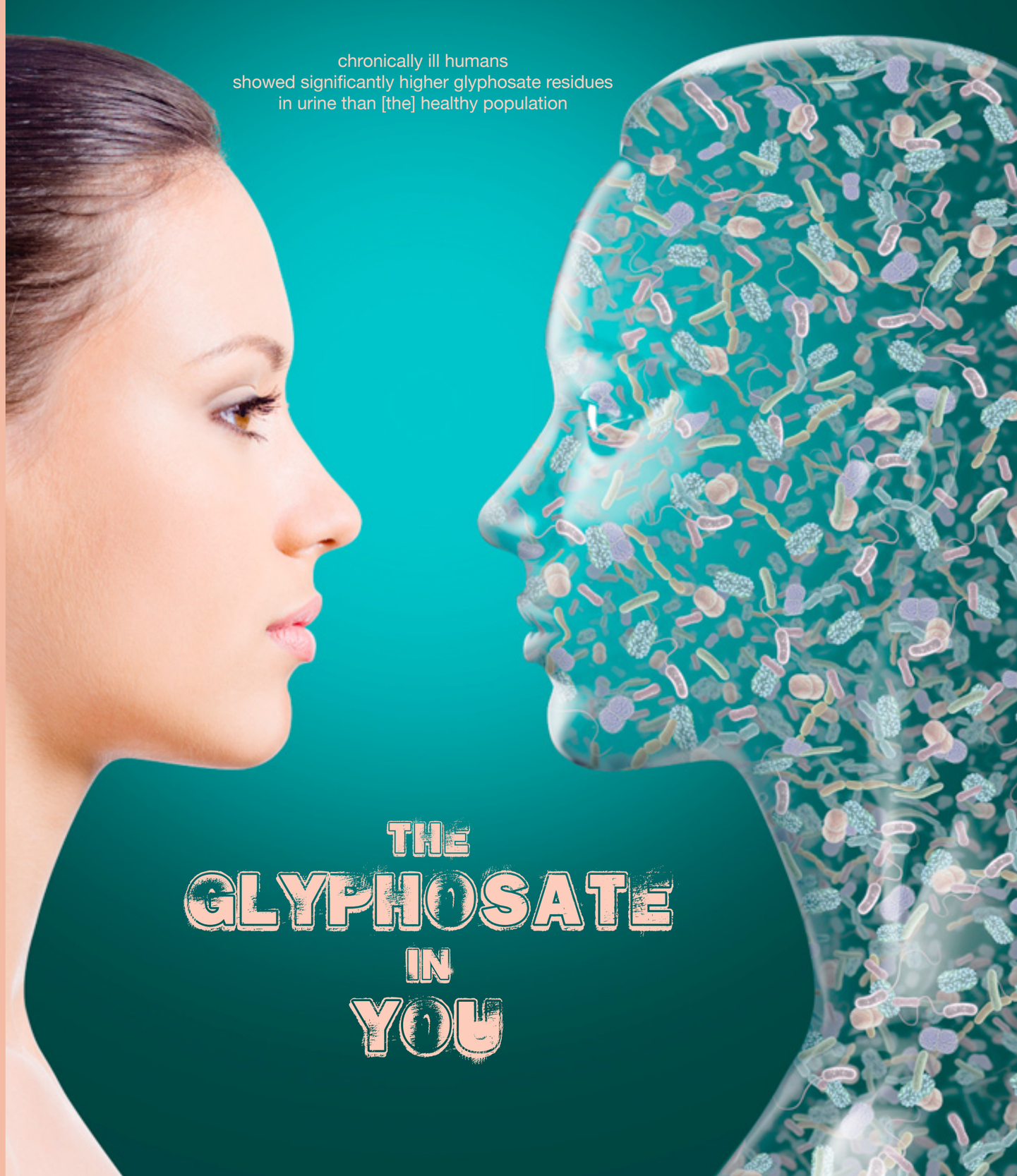
Abstract

In the present study glyphosate residues were tested in urine and different organs of dairy cows as well as in urine of hares, rabbits and humans using ELISA and Gas Chromatography-Mass Spectroscopy (GC-MS). The correlation coefficients between ELISA and GC-MS were 0.96, 0.87, 0.97and 0.96 for cattle, human, and rabbit urine and organs, respectively. The recovery rate of glyphosate in spiked meat using ELISA was 91%. Glyphosate excretion in German dairy cows was significantly lower than Danish cows. Cows kept in genetically modified free area had significantly lower glyphosate concentrations in urine than conventional husbandry cows. Also glyphosate was detected in different organs of slaughtered cows as intestine, liver, muscles, spleen and kidney. Fattening rabbits showed significantly higher glyphosate residues in urine than hares. Moreover, glyphosate was significantly higher in urine of humans with conventional feeding. Furthermore, chronically ill humans showed significantly higher glyphosate residues in urine than healthy population. The presence of glyphosate residues in both humans and animals could haul the entire population towards numerous health hazards, studying the impact of glyphosate residues on health is warranted and the global regulations for the use of glyphosate may have to be re-evaluated.

Exposure of mammals to glyphosate may cause loss of mitochondrial transmembrane potential and result in oxidative stress to liver and brain [27, 28]. Both apoptosis and autophagy are involved in glyphosate toxicity mechanisms [29] Case reports indicated that exposure to glyphosate was related to Parkinsonism [19, 30].

Conclusions

Glyphosate residue could reach humans and animals through feed and excreted in urine. Presence of glyphosate in urine and its accumulation in animal tissues is alarming even at low concentrations. Unknown impacts of glyphosate on human and animal health warrants further investigations of glyphosate residues in vertebrates and other non-target organisms.



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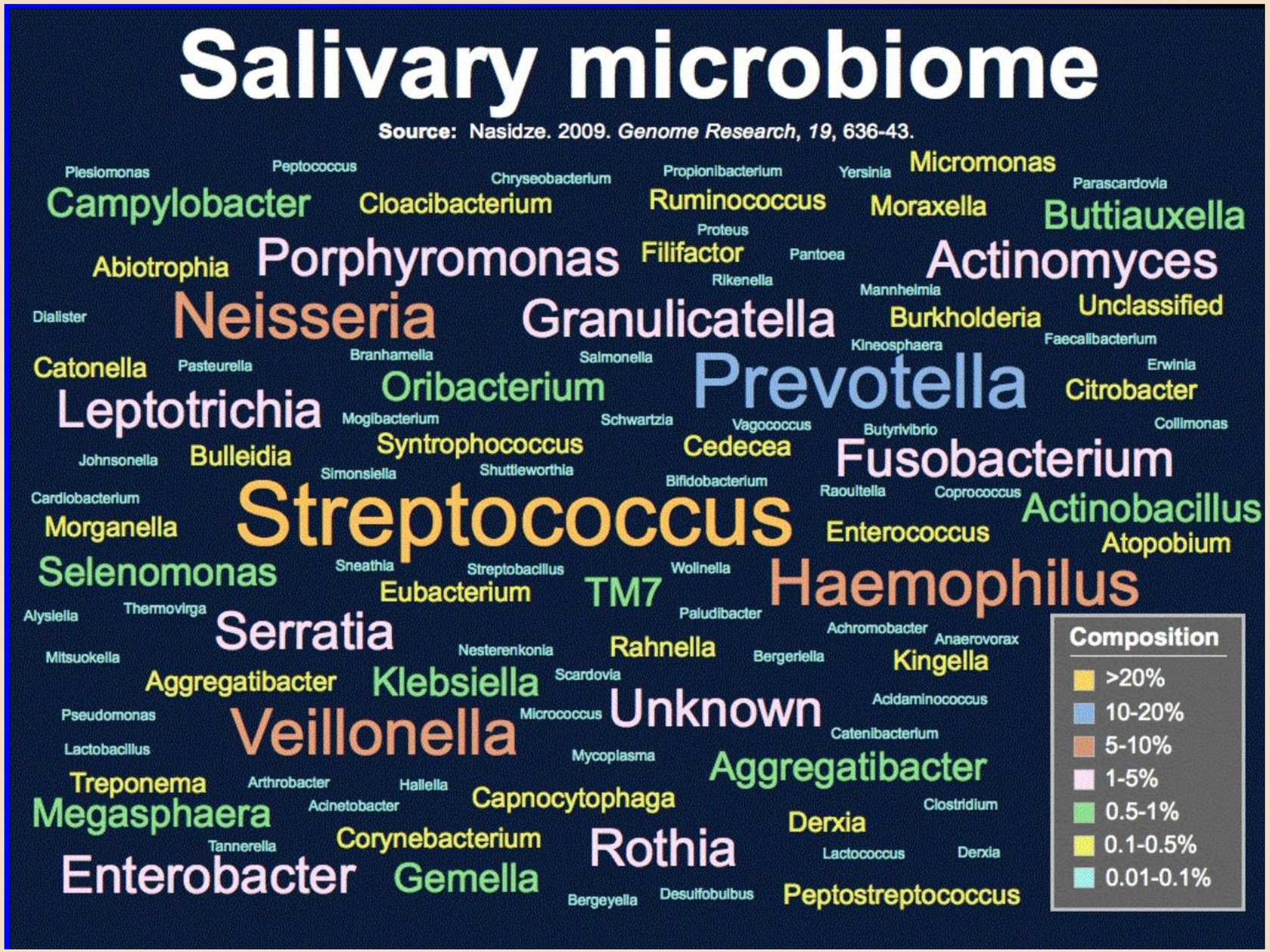

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Reproductive Toxicology

Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada

by Aziz Arisa,b,c, and Samuel Leblancc

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Abstract

Pesticides associated to genetically modified foods (PAGMF),are engineered to tolerate herbicides such as glyphosate (GLYP) and gluphosinate (GLUF) or insecticides such as the bacterial toxin bacillusthuringiensis (Bt). The aim of this study was to evaluate the correlation between maternal and fetal exposure,and to determine exposure levels of GLYP and its metabolite aminomethylphosphoricacid (AMPA),GLUF and its metabolite3-methylphosphinicopropionicacid (3-MPPA) and Cry1Abprotein (aBttoxin) in Eastern TownshipsofQuebec,Canada. Blood of thirty pregnant women (PW) and thirty-nine nonpregnant women (NPW) were studied. Serum GLYP and GLUF-were detected in NPW and not detected in PW. Serum 3-MPPA and CryAb1 toxin were detected in PW, their fetuses and NPW. This is the first study to reveal the presence of circulating PAGMF in women with and without pregnancy, paving the way for fora. a new field in reproductive toxicology including nutrition and utero-placental toxicities.

Journal Homepage: www.elsevier.com/locate/reprotox

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Critical Reviews in Food Science and Nutrition

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Toxicity Studies of Genetically Modified Plants: A Review of the Published Literature

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According to the information reported by the WHO, the genetically modified (GM) products that are currently on the international market have all passed risk assessments conducted by national authorities. These assessments have not indicated any risk to human health. In spite of this clear statement, it is quite amazing to note that the review articles published in international scientific journals during the current decade did not find, or the number was particularly small, references concerning human and animal toxicological/health risks studies on GM foods. In this paper, the scientific information concerning the potential toxicity of GM/transgenic plants using the Medline database is reviewed. Studies about the safety of the potential use of potatoes, corn, soybeans, rice, cucumber, tomatoes, sweet pepper, peas, and canola plants for food and feed were included. The number of references was surprisingly limited. Moreover, most published studies were not performed by the biotechnology companies that produce these products. This review can be concluded raising the following question: where is the scientific evidence showing that GM plants/food are toxicologically safe?

Although the WHO declares that the GM products that are currently on the international market have all passed risk assessment conducted by national authorities, in a review on the scientific literature performed in 2000, we were not able to find sufficient published information concerning that assessment (Domingo andG´omez, 2000).

In particular, the lack of published toxicological studies on adverse health effects was evident. Although a considerable number of commentaries, general news, and letters to the Editor were published in reputable international journals, papers about experimental investigations on the safety of GM foods were surprisingly very scant. We concluded that if data on toxicological assessment of GM foods were obtained, these were not reported in scientific journals and subjected to the scientific judgment (Domingo, 2000; Domingo and G´omez, 2000).

The World Health Organization indicates that gene transfer from GM foods to cells of the body or to bacteria in the gastrointestinal tract would cause concern if the transferred genetic material adversely affects human health, which would be particularly relevant if antibioti resistance genes, used in creating GMOs, were to be transferred (WHO, 2002).

Although intact foreign DNA is not thought to be available for transfer into human cells, there is a remote possibility that DNA fragments may be taken up by bacteria in the gut (Donaldson and May, 1999) DNA fragments, after passing through the intestinal wall, might be actively removed by cells of the gut immune system OR they might enter the circulation system (Jonas et al., 2001). In relation to this, Schubbert et al. (1997) demonstrated that food-ingested foreign DNA was not completely degraded in the gastrointestinal tract.

This review can be concluded by raising the following question: "Where is the scientific evidence showing that GM plants and foods are toxicologically safe?"

Complete Genes May Pass from Food to Human Blood

Sa´ndor Spisa´k1,2*, Norbert Solymosi3,4, Pe´ ter Ittze´ s3, Andra´ s Bodor3, Da´ niel Kondor3, Ga´bor Vattay3, Barbara K. Barta´k5, Ferenc Sipos5, Orsolya Galamb5, Zsolt Tulassay1,5, Zolta´n Sza´ lla´ si2, Simon Rasmussen6, Thomas Sicheritz-Ponten6, Søren Brunak6, Be´ la Molna´ r1,5, Istva´n Csabai3,7

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5 2nd Department of Internal Medicine, Semmelweis University, Budapest, Hungary,
6 Center for BiologicalSequence Analysis, Technical University of Denmark, Lyngby, Denmark,
7 Department of Physics and Astronomy, The Johns Hopkins University, Baltimore, Maryland, USA

Abstract

Our bloodstream is considered to be an environment well separated from the outside world and the digestive tract. According to the standard paradigm large macromolecules consumed with food cannot pass directly to the circulatory system. During digestion proteins and DNA are thought to be degraded into small constituents, amino acids and nucleic acids, respectively, and then absorbed by a complex active process and distributed to various parts of the body through the circulation system. Here, based on the analysis of over 1000 human samples from four independent studies, we report evidence that meal-derived DNA fragments which are large enough to carry complete genes can avoid degradation and through an unknown mechanism enter the human circulation system.

In one of the blood samples the relative concentration of plant DNA is higher than the human DNA. The plant DNA concentration shows a surprisingly precise lognormal distribution in the plasma samples while non-plasma (cord blood) control sample was found to be free of plant DNA.

Citation: Spisa´k S, Solymosi N, Ittze´s P, Bodor A, Kondor D, et al. (2013) Complete Genes May Pass from Food to Human Blood. PLoS ONE 8(7): e69805. doi:10.1371/journal.pone.0069805
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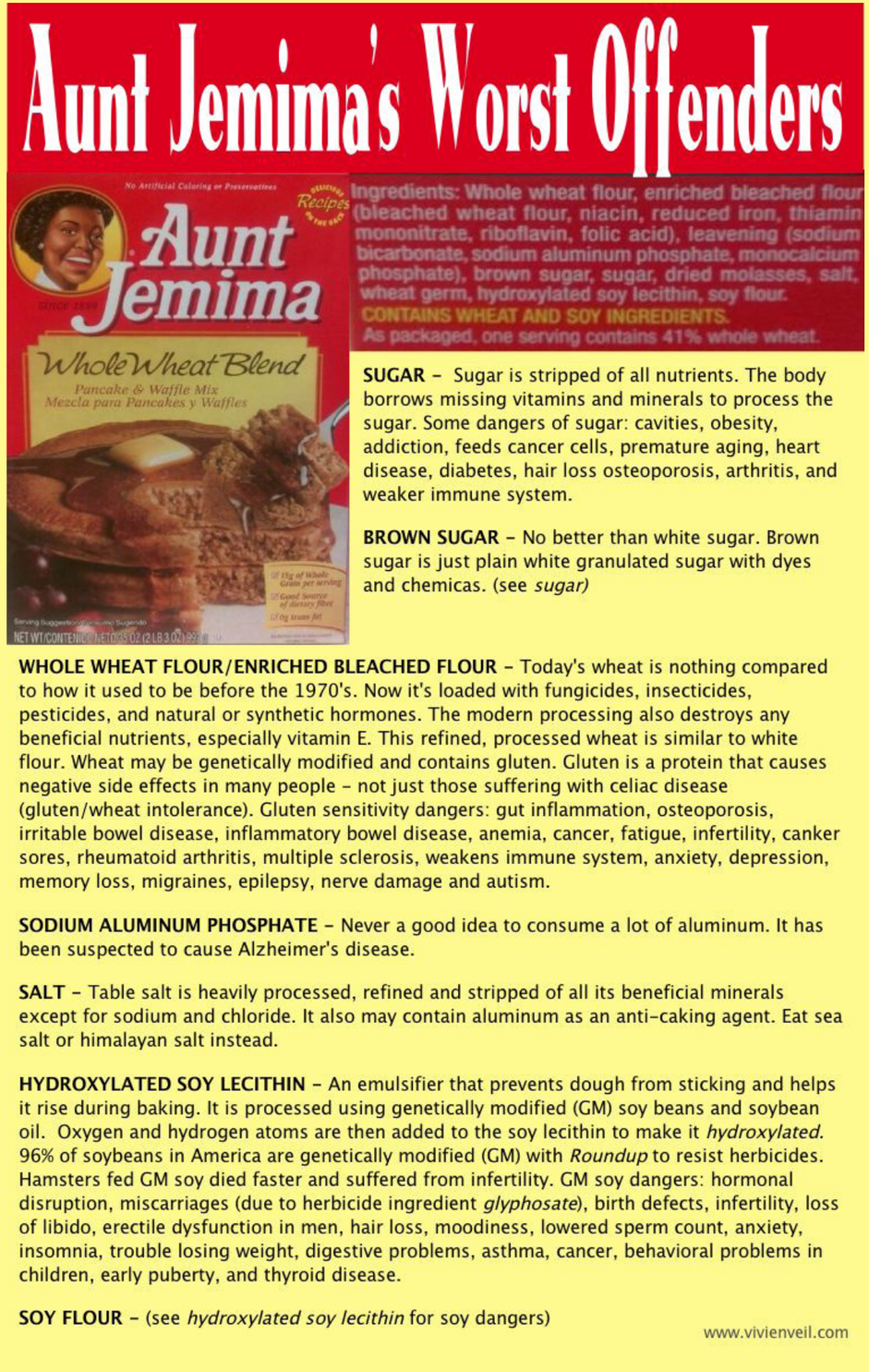
Here, based on the analysis of over 1000 human samples from four independent studies, we report evidence that meal-derived DNA fragments which are large enough to carry complete genes can avoid degradation and through an unknown mechanism enter the human circulation system.



During digestion proteins and DNA are thought to be degraded into smaller constituents, amino acids and nucleic acids, respectively, and then absorbed by a complex active process and distributed to various parts of the body through the circulation system.

Genetically Modified Foods
Proposed as Trigger for Gluten Sensitivity

The Institute for Responsible Technology (IRT) released a report today proposing a link between genetically modified (GM) foods and gluten-related disorders. In today's report, a team of experts suggests that GM foods may be an important environmental trigger for gluten sensitivity, which is estimated to affect as many as 18 million Americans.

Citing U.S. Deptartment of Agriculture data, Environmental Protection Act records, medical journal reviews, and international research, the authors relate genetically modified foods to five conditions that may either trigger or exacerbate gluten-related disorders, including the serious autoimmune disorder, Celiac Disease:

1. Impaired digestion
2. Intestinal permeability
3. Imbalanced gut bacteria
4. Damage to the intestinal wall
5. Immune activation and allergic response

Although wheat has been hybridized over the years, it is not a genetically modified organism (GMO), which can only be created by a laboratory process that inserts genetic material into plant DNA. There are nine GMO food crops currently being grown for commercial use: soy, corn, cotton (oil), canola (oil), sugar from sugar beets, zucchini, yellow squash, Hawaiian papaya, and alfalfa.

Most GMOs are engineered to tolerate a weed killer called glyphosate, trade name Roundup®. They contain high levels of this toxin at harvest. Corn and cotton varieties are also engineered to produce an insecticide called Bt-toxin. The report focuses primarily on the effects of these two toxins.

Executive Director of the Institute for Responsible Technology, Jeffrey Smith, explains, "*The Bt-toxin in corn is designed to puncture holes in insect cells, but studies show it does the same in human cells. Bt-toxin may be linked to leaky gut, which physicians consistently see in gluten-sensitive patients.*"

Stephanie Seneff, Senior Research Scientist at MIT, expresses concern about Roundup®: "Glyphosate is a patented antibiotic that destroys beneficial gut bacteria. An imbalance of gut flora commonly accompanies Celiac Disease and other gluten-related disorders."

Mary Waldner, founder of Mary's Gone Crackers®, a Non-GMO Project verified and gluten-free certified food manufacturer, says, "I'm excited by the research that offers an explanation for the dramatic increase in gluten-related disorders. I encourage everyone to avoid GMOs in their diets. I have always been concerned about the effects of GMOs and Mary's Gone Crackers has never used GMO ingredients in our products."

Dr. Tom O'Bryan, internationally recognized expert on gluten sensitivity and Celiac Disease, says, "The introduction of GMOs is highly suspect as a candidate to explain the rapid rise in gluten-related disorders over the last 17 years." Internist, Emily Linder MD, says, "Based on my clinical experience, when I remove genetically modified foods as part of the treatment for gluten sensitivity, recovery is faster and more complete. I believe that GMOs in our diet contribute to the rise in gluten sensitivity in the U.S. population."

The best way to avoid GMOs is to purchase certified organic or Non-GMO Project verified products. Download a shopping guide at NonGMOShoppingGuide.com or a free iPhone app, ShopNoGMO.

The markets for both gluten-free products and non-GMO products are expanding. Gluten-free sales are expected to exceed $5 billion by 2015 and Non-GMO Project Verified sales went from $0 to over $3.5 billion in the last three years. Just as Mary's Gone Crackers® did in 2011, the conclusions in this report may inspire more gluten-free food manufacturers to pursue Non-GMO Project Verified status.

For a full report see www.glutenandgmos.com.

About the Institute for Responsible Technology

The Institute for Responsible Technology is a world leader in educating policy makers and the public about genetically modified foods and crops. The Institute investigates and reports on the impact GM foods have on health, environment, economy, and agriculture, as well as the problems associated with current research, regulation, corporate practices, and reporting.

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"Glyphosate is a patented antibiotic that destroys beneficial gut bacteria. An imbalance of gut flora commonly accompanies [numerous medical] disorders."

~ Stephanie Seneff, Senior Research Scientist at MIT

The Journal of Hematology
And Thromboembolic Diseases

Hematotoxicity of Bacillus thuringiensis as Spore-crystal Strains Cry1Aa, Cry1Ab, Cry1Ac or Cry2Aa in Swiss Albino Mice

by Bélin Poletto Mezzomo, Ana Luisa Miranda-Vilela*, Ingrid de Souza Freire, Lilian Carla Pereira Barbosa, Flávia Arruda Portilho, Zulmira. Guerrero Marques Lacava and Cesar Koppe Grisolia. The Department of Genetics and Morphology, Institute of Biological Sciences, University of Brasilia, Brasilia/DF, Brazil

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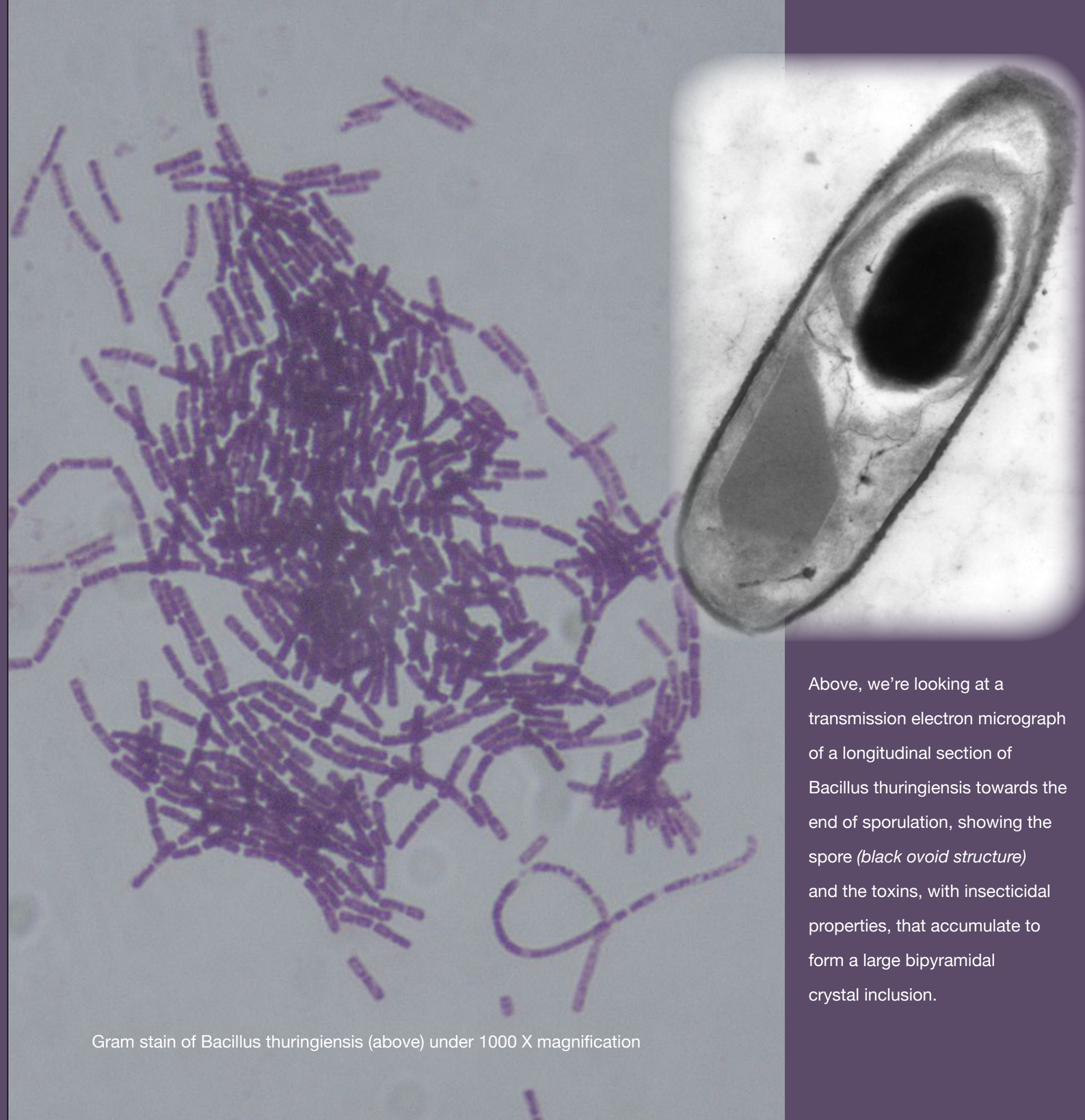
"Similar results were observed for binary combinations at 24 hours, suggesting that further studies are required to clarify the mechanism involved in the hematotoxicity found in mice, and to establish the toxicological risks to non-target organisms, especially mammals, before concluding that these microbiological control agents are safe for mammals."



Gram stain of Bacillus thuringiensis (above) under 1000 X magnification

Above, we're looking at a transmission electron micrograph of a longitudinal section of Bacillus thuringiensis towards the end of sporulation, showing the spore *(black ovoid structure)* and the toxins, with insecticidal properties, that accumulate to form a large bipyramidal crystal inclusion.

Testimony of Dr. Joseph Cummins

EDUCATION

Stadium High School, Tacoma, Wash. 1951
B.S., (Horticulture) Washington State University, 1955
Ph.D., (Cell Biology) University of Wisconsin, 1962
Postdoctoral Fellow, Univ. of Edinburgh. (Prof. J.M. Mitchinson, Dept. of Zoology) 1962-64
Postdoctoral Fellow, McArdle Lab. for Cancer Research (Univ. of Wisconsin, Prof. H.P. Rusch) 1964-66
Postdoctoral Fellow, The Karolinska Inst., Stockholm (Prof. J.E. Edstrom) 1969

PREVIOUS ACADEMIC AND PROFESSIONAL EMPLOYMENT

Visiting Assistant, Prof. Radiology, Dept. of Radiology, Case-Western Reserve University, Cleveland, Ohio, 1967

Assistant Professor, Biol. Sci., Dept. of Biol. Sci., Rutgers University, New Brunswick, N.J., 1966-67

Assistant Professor, Dept. of Zoology, Univ. of Washington, Seattle, Washington, 1967-71

Assistant Professor to Professor Emeritus 1972 to 1996

TEACHING CREDENTIALS

Advanced Genetics (molecular genetics), microbial genetics, microbiology, human genetics, environmental pathology and toxicology (medical faculty) and graduate topics in environmental issues.

PROFESSIONAL ASSOCIATIONS

American genetics society, American society for cell biology, and Society for Environmental Mutagens along with that sit or sat on boards of environmental organizations. Received a number of recognitions for participating in and advising environmental issues.

PUBLICATIONS

Career total : over 210 publications
Over 70 peer reviewed journal articles
Over 5 chapters in books
Numerous reviews, reports to government agencies, reports in meetings proceedings and popular magazines

CURRENT ACTIVITIES

Actively engaged in preparing reviews and reports in areas related to genetic engineering, global pollution with persistent organic pollutants and pesticides.

Presently GM crops on the market have been modified to fight pests , later releases may deal with nutrition and shelf life of the GM foods. Several years ago a GM tomato with very long shelf life was introduced but then removed when consumers found the tomatoes did not taste good. However, the safety of GM crops is still in question because crop approval has been based on a concept called “substantial equivalence”. Substantial equivalence is the doctrine that maintains that if GM crops are grossly similar to crops that have not been genetically modified they are equivalent to those crops and need not be labeled in the market and they need not be tested similarly to the test required for pesticides or pharmaceutical drugs. Governments in Canada and the United States employ that doctrine to evade labeling and testing the GM crops before they are marketed.

These results on an allergic (IgE) response was associated with Cry9 in corn powder. Considering that the Cry 9 containing corn was fed millions of farm animals and probably as many humans eating corn products contaminated with corn designated only for animal use any evidence of IgE response to Cry 9 corn should not be allowed to be buried.

Here, Dr. Cummins references and criticizes a Monsanto study:

Glyphosate tolerant (Roundup Ready) corn in a demonstration of substantial equivalence: Glyphosate-Tolerant Corn: “The Composition and Feeding Value of Grain from Glyphosate-Tolerant Corn Is Equivalent to That of Conventional Corn (Zea mays L.)” Ravinder S. Sidhu,* Bruce G. Hammond, Roy L. Fuchs, Jean-Noel Mutz, Larry R. Holden,Beverly George, † and Tammy Olson ‡

Monsanto Company
700 Chesterfield Parkway North
St. Louis, Missouri 63198
J. Agric. Food Chem. 2000, 48, 230 -2312

Monsanto Abstract

Glyphosate-tolerant (Roundup Ready) corn line GA21 has been developed by genetic modification to tolerate glyphosate, the active ingredient in Roundup herbicide. The purpose of this study was to evaluate the compositional and nutritional safety of corn line GA21 compared to that of conventional corn. Compositional analyses were conducted to measure proximate, fiber, amino acid, fatty acid, and mineral contents of grain and proximate, fiber, and mineral contents of forage collected from 16 field sites over two growing seasons.

The nutritional safety of corn line GA21 was evaluated in a poultry feeding study conducted with 2-day old, rapidly growing broiler chickens, at a dietary concentration of 50-60% w/w. Compositional analysis results showed that, except for a few minor differences that are unlikely to be of biological significance, the grain and forage of GA21 corn were comparable in their composition to that of the control corn line and to conventional corn. Results from the poultry feeding study showed that there were no differences in growth, feed efficiency, adjusted feed efficiency, and fat pad weights between chickens fed with GA21 grain or with parental control grain.

These data taken together demonstrate that Roundup Ready corn is as safe and nutritious as conventional corn for food and feed use. Dr. Cummins now points out the serious defects in the Monsanto study:

“The research group from Monsanto pointed out that substantial equivalence (*the idea that genetically modified (GM) crops are equivalent to crops that are not genetically modified in terms of nutrition and composition*) is crucial to the regulation of GM crops. Their research efforts included comparing GM corn containing primarily a gene that made the corn resistant to the herbicide glyphosate. The corn was then fed to chickens and the chicken were fed GM corn or corn that was not GM. The investigators believed that their results proved that the GM corn was substantially equivalent to corn that was not modified.”

"The investigators believed that their conclusions were valid even though GM corn was found to be about 9% lower in calcium content a difference that was statistically significant. The GM corn was also found to be statistically significantly different in the content of the amino acids serine and tyrosine from unmodified corn. The chickens fed GM corn or corn that was unmodified were not significantly different but the research report briefly and hidden mentions that the GM corn fed the chickens had never been exposed to the herbicide glyphosate. Major alterations in corn metabolism would only be triggered in the presence of the herbicide."

"The Monsanto researchers claimed that GM corn was not substantially different from unmodified corn even though the two were statistically significantly different! They seem to have convinced government regulators that statistical significance just doesn't count when you have faith in your company's product. The regulators and editors did not even wince when the experimental chickens were fed herbicide tolerant corn that had never been exposed to herbicide!"

"Statistical significance should count and the corn was clearly substantially different from unmodified corn. Feeding chickens GM corn that was not exposed to herbicide was clearly a strange thing [for Monsanto] to do."

"Baculovirus vectors efficiently transfer genes into human liver cells (Hofmann et al 1995; Boyce and Bucher 1996). The vectors transferred into human liver tissues most effectively in perfused liver tissue because serum components hampered virus transfer (Sandig et al 1996). Human conditions causing defects in complement should allow liver transfer of recombinant baculovirus. Inhibitors of complement facilitate baculovirus gene transfer (Hofmann and Strauss 1998). Hybrid baculovirus-adeno virus vectors have been used to deliver genes to human cells (Palombo et al 1998). Baculovirus vectors have been used to deliver hepatitis B to human liver efficiently to allow study of hepatitis B drug therapy (Delaney et al 1999)."

"In conclusion baculovirus vectors are being used to control insect pests because they are effective and persist for a long time in the environment. Baculovirus vectors are also being used in gene therapy of human liver. These areas of research seem to exist as two solitudes and the risks of one are not evaluated in the context of the other. The most disconcerting finding is the one showing that replication of the baculovirus is inherently unpredictable. However, there may be some that believe that we should all have unlabelled liver gene therapy with our salad."

Concluding Statement

"The experiments discussed in the above brief suggest that there should be great concern about the use of substantial equivalence to evaluate crops. First, because it is not a useful concept for recognizing and eliminating injurious toxins. Second, because the concept is not being used properly, even ignoring clear differences in composition. Last those employing the concept to approve GM crops seem unwilling to remove approved crops from the market when they are shown to be unsubstantially equivalent."

"Furthermore, the GM biopesticides seem to be approved or pushed for approval with inadequate safety evaluation and concern for their long term impact. The field of genetic engineering seems to be moving forward with undue haste and employing humans as experimental organisms. The profession would probably greatly improve its outlook if criminal charges could be laid against researchers and their university or company officials when injurious procedures effecting humans or the environment are implemented without full regards for the rights of humans to decline participation in the procedure or when foreseeable environmental damage is ignored. Charges could be laid based on the depraved indifference of researchers and the officials that direct them."

"Charges could be laid based on the depraved indifference of researchers and the officials that direct them."

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Toxic Shock!

California Allows Up To One Thousand Times More Glyphosate In Drinking Water Than Needed To Cause Breast Cancer In Women

by Jeff Prager

In late 2014 a story broke that revealed glyphosate — the chemical name of Roundup herbicide — multiplies the proliferation of breast cancer cells by 500% to 1300% even at exposures of just a few parts per trillion (ppt). The study, published in Food and Chemical Toxicology, is entitled, "**Glyphosate induces human breast cancer cells growth via estrogen receptors.**" You can read the abstract at: http://www.ncbi.nim.gov/pubmed/23756170

Here are the 3 pieces of scientific terminology you should have a working understanding of:

1. ppm = parts per million = 10 (-6) = number of parts out of a million

2. ppb = parts per billion = 10 (-9), which is 1,000 times smaller than ppm

3. ppt = parts per trillion = 10 (-12), which is 1,000 times smaller than ppb and 1,000,000 times smaller than ppm

The study found that breast cancer cell proliferation is accelerated by glyphosate in extremely low concentrations: ppt to ppb. The greatest effect was observed in the ppb range, including single-digit ppb such as even just 1 ppb.

This news, all by itself, sent shock waves across the internet. Women were asking things like: "*You mean to tell me that glyphosate residues on crops in just ppt or ppb concentrations can give me breast cancer?*" It doesn't exactly translate like that. It depends on how much you eat vs. your body mass (nanograms of glyphosate per kilogram of body weight) and genetic factors. But with ridiculously small amounts of this chemical now being correlated to cancer cell proliferation, you don't have to eat much at all in order to put yourself at risk. But it's not just eating glyphosate that's the problem. You're also drinking it. California allows 1,000 ppb of glyphosate in drinking water. In December of 1997, California released its Glyphosate in Drinking Water California Public Health Goal (PHG) document. The document openly admits:

"Glyphosate is a non-selective systemic herbicide used in agriculture, rights-of-way and aquatic systems. Exposure to glyphosate may occur from its normal use due to drift, residues in food crops and from runoff into potential drinking water sources."

It then goes on to state something borrowed straight from Monsanto's quack science team: "*Glyphosate is not mutagenic or teratogenic and there is no evidence for reproductive toxicity in multigeneration studies in rats.*"

This is a blatant lie and based on this blatant lie, California set an upper limit of 1.0 mg/L (or 1,000 ppb) for glyphosate in drinking water. Yes, that's 1,000 times higher than the amount now shown to cause a 500% to 1300% increase in cancer cell proliferation. What's even more shocking is that California's allowable exposure level is nearly 50% higher than the federal (EPA) level -- 700 ppb. Yes, California -- the state where more people are concerned about GMOs than seemingly anywhere else -- actually used Monsanto-sounding language in its "official" report that set a higher water contamination level than the federal government! And glyphosate carcinotoxicity was documented years earlier. Even though California released this document in 1997, the state was already willfully ignoring a growing body of scientific evidence documenting glyphosate toxicity which I'm reporting right here in this free PDF that you're lucky enough to be reading. For example, a study published two years earlier in 1995 in the Journal of Pesticide Reform (Volume 15, Number 3, Fall 1995) written by Caroline Cox concluded:

"Glyphosate-containing products are acutely toxic to animals, including humans. ...In animal studies, feeding of glyphosate for three months caused reduced weight gain, diarrhea, and salivary gland lesions. Lifetime feeding of glyphosate caused excess growth and death of liver cells, cataracts and lens degeneration, and increases in the frequency of thyroid, pancreas, and liver tumors. Glyphosate-containing products have caused genetic damage in human blood cells... reduced sperm counts in male rats... and caused an increase in fetal loss..."

In other words, California knew that glyphosate was harmful to humans. But the California government willfully ignored this evidence and even went out of its way to incorporate deceptive Monsanto spin into its "*Public Health Goal*" documents, thereby allowing 1,000 times higher levels of glyphosate in drinking water than we now know to cause cancer cell proliferation.

Ten Years Later, California Lowers Its Level By An Absurd 10%

Fast forward to 2007. After a public comment period which was no doubt dominated by disinfo-spewing Monsanto trolls, the state of California issued an updated Public Health Goal (PHG) document.

It concludes that the allowable glyphosate exposure for all Californians should be lowered to 900 ppb -- still nine hundred times higher than the amount needed to accelerate cancer cell growth as we see in the study I discussed previously. This 2007 document from the California government also borrows language that sounds like it's right out of Monsanto's P.R. department: "*Based on the genotoxicity and carcinogenicity study results, glyphosate is not likely to pose a cancer hazard to humans,*" it says.

Toxic Shock!

Now The Evidence Is Clear:
Monsanto's Chemicals Are Needlessly Killing Women

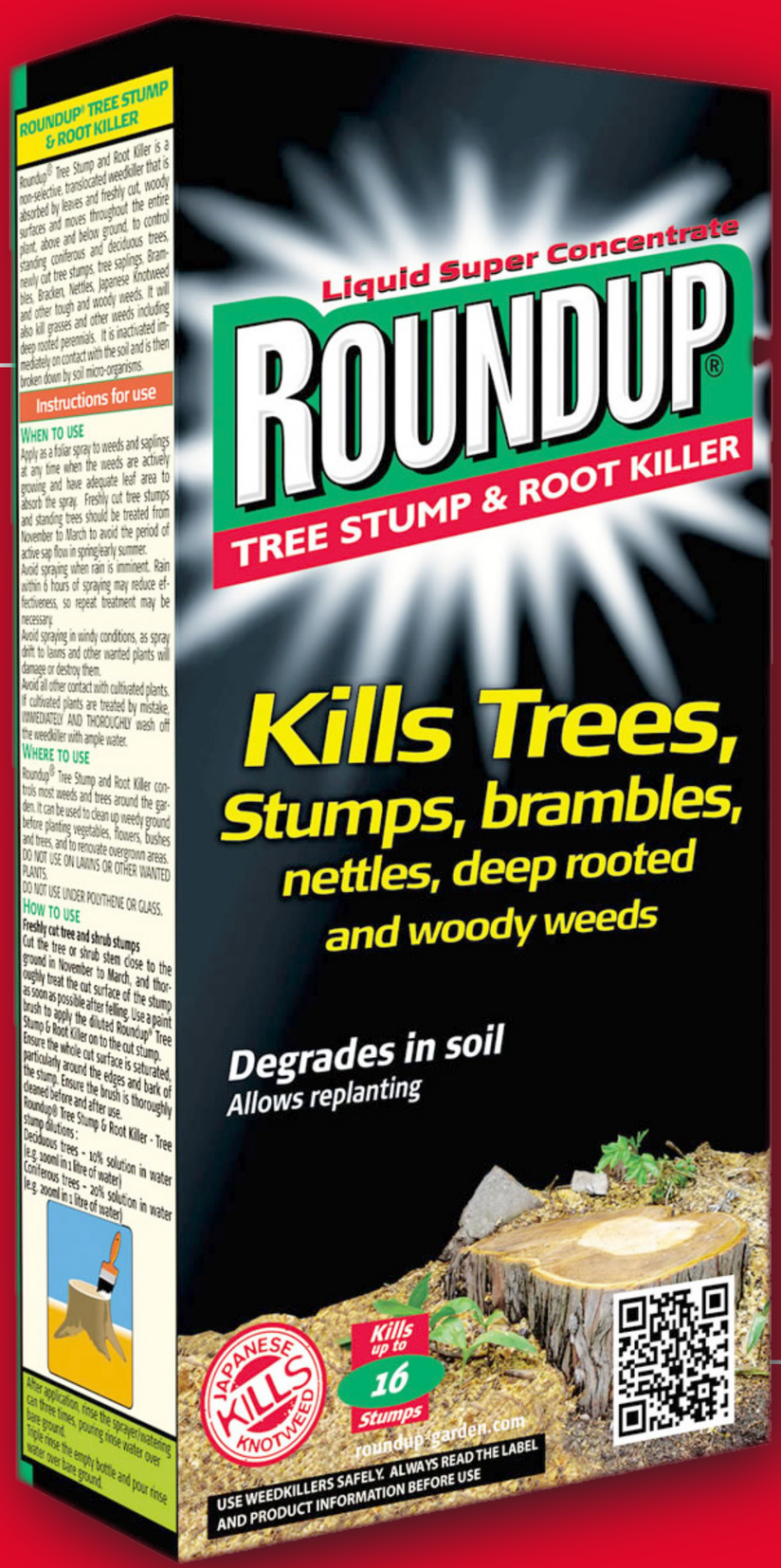
Now it's 2013. We've seen the horrific results of the GMO rat study revealing the growth of massive tumors in rats exposed to GMOs and Roundup (glyphosate). We've also now seen the "*parts per trillion*" study showing cancer cell proliferation being caused by ultra-low concentrations of glyphosate. We also know the biotech industry has gone to ridiculous lengths to spread disinfo on all of this solid and unimpeachable data to try to discredit scientists who speak out against GMOs and glyphosate, to get scientists blackballed from the industry, and to buy off politicians and members of the press to make sure there is no coverage granted to any scientific studies reporting the dangers of genetically modified crops and their related chemical herbicides.

Glyphosate Is The New
DDT, Dioxin, Agent Orange, PCBs And Aspartame
All Discontinued For Sale And/Or Production In The USA
But Not Cancer-Causing Glyphosate

Based on what we're seeing now, I believe glyphosate is the most toxic chemical that has ever been widely deployed across our food supply. Glyphosate is the new DDT, and it's contaminating our waterways, soils, food, water and most distressing, our bodies.

Furthermore, the California government has become fully responsible for casually allowing extremely high levels of glyphosate to contaminate the public drinking water, thereby causing tens of millions of Californians to be poisoned with concentrations of glyphosate that promote cancer cell growth. And what will the California government tell you now that the truth has come out? Now that they've allowed their own population to be exposed to a thousand times the concentration needed to accelerate the growth of cancer tumors?

"Run for the cure!" The one that doesn't exist. And don't label GMOs either for goodness sakes because we certainly don't have a desire to know our poisons and according to the California legislature we don't really have a need or a right to know whether we're eating deadly poison in our food. And of course we are.



Lifetime feeding of glyphosate causes excess growth and then death of liver cells, cataracts and lens degeneration, and increases the frequency of thyroid, pancreas, and liver tumors. Glyphosate-containing products have caused genetic damage in human blood cells, reduced sperm counts in male rats and caused an increase in fetal loss. Breast cancer not-withstanding.

Glyphosate Found At High Levels In Mothers' Breast Milk

Chemicals that destroy the natural world, like glyphosate, are being blasted into the earth at an unprecedented rate. Sales of Monsanto's Roundup, which contains glyphosate, spiked 73 percent in 2013. The rise of genetically modified crops is ushering in the mass application of immune system-destroying chemicals, as consequences are unveiled, one after another.

It's no wonder why the earth purges from time to time, disgusted by all the man-made concoctions that destroy life. Lava erupts from the ground and hail falls from the sky as the earth writhes in disdain.

Plant-killing glyphosate is so environmentally abundant now that it's showing up in urine and blood samples of individuals. The chemical is becoming a part of the human anatomy, circulating through and accumulating. Now researchers are discovering detectable levels of the weed killer in mothers' breast milk! How will newborns react to the weed killer at their most vulnerable, developing stage of life? How might a newborn's immune system be disturbed through disrupted gut microbe activity, as the weed killer enters their stomach and blood? What kind of resulting skin problems and learning disabilities does glyphosate encourage? And how does it affect the immune system which begins in the mucosal membranes between your mouth and your gut?

Glyphosate Is Bio-Accumulative, Passed Through Breast Milk To Newborns

Senior Monsanto scientist Dan Goldstein recently stated, "*If ingested, glyphosate is excreted rapidly, does not accumulate in body fat or tissues, and does not undergo metabolism in humans. Rather, it is excreted unchanged in the urine.*"

To a very strange extent that comment can be viewed as partially accurate. Glyphosate breaks down in the human body to its constituent elements. While we know Roundup® contains glyphosate we're not privy to all of the other chemical adjuvants and toxic elements contained in Rounup®. Trade secret you know. So "glyphosate" doesn't necessarily accumulate in everyone's body as glyphosate but as the constituent products of glyphsate.

This is far from the truth, since the discovery of glyphosate in breast milk proves its bioaccumulation. Furthermore, glyphosate has been found to disrupt the shikimate pathway of human gut microbes, essentially destroying positive gut flora, inhibiting the body's natural detoxification processes.

For years, Monsanto has claimed that their Roundup is safe because the human body excretes it. A new pilot study shows that glyphosate doesn't just go away; it persists in mothers and is passed to their kin through breast milk.

In the wake of these findings, the Organic Consumers Association is calling out for an outright ban on glyphosate. Director Ronnie Cummins stated, "This is another in a long line of studies showing the many ways in which glyphosate poses a real danger to human health. It's time for Americans to demand that the FDA, USDA and EPA ban this toxin for good."

He continued, "At the very least, the FDA must require labels on foods that contain this dangerous toxin. And the best way to do that is to require mandatory labelling of foods that contain genetically modified organisms, most of which derive from crops that require massive amounts of Monsanto's Roundup."

But this strategy may be nearly impossible, since the EPA claims that glyphosate is not bioaccumulative. To make matters worse, the US government recently raised allowable levels of the weed killer in food products. Plus, the glyphosate measured in breast milk falls within the 700 µg/l maximum contaminant level established by the US for glyphosate in drinking water.

30 percent of breast milk samples showed detectable levels of glyphosate.

The pilot study, conducted by Moms Across America and Sustainable Pulse, tested for glyphosate levels in American mothers' breast milk. What they found was startling by European standards -- concentrations of glyphosate in breast milk at 760 to 1600 times higher than pesticide limits set by European Drinking Water Directives.

In the small pilot study, 35 urine samples and 21 drinking water samples from across the US were measured. The results were compared with an EU study conducted by Friends of the Earth in 2013.

The urine samples of Americans were at least ten times more contaminated with glyphosate than Europeans. When samples of breast milk were analyzed, 30 percent showed detectable levels of glyphosate, which is theoretically passed on to newborns.

Virginia mother Jessica M., who tested positive for glyphosate in her breast milk, said, "*It is frightening to see any glyphosate in my body, especially in my breast milk that will then contaminate my son's growing body. It's particularly upsetting to test positive for glyphosate because I go to great lengths to eat organic and GMO free. I do not consume any meats or seafood and only very rarely eat dairy. This really shows me, and should show others, just how pervasive this toxin is in our food system.*"

Staggering And Astonishing Facts About Glyphosate® and Roundup® That You Need To Know

Presented below are ten sobering facts about Glyphosate, the key ingredient in Monsanto's RoundUp weedkiller, which the majority of Monsanto's seeds are genetically engineered to withstand:

• Glyphosate causes disease and biological / physiological disorders in crops Fifteen years of research by the USDA indicates that the chemical glyphosate, the key ingredient in RoundUp herbicide, is linked to fungal root disease in plants. See: http://www.reuters.com/article/2010/04/13/us-usa-gmos-regulators-idUSTRE63C2AJ20100413

There's also this Purdue Report about biological and physiological disorders: http://www.btny.purdue.edu/weedscience/2011/GlyphosatesImpact11.html

• Glyphosate is no longer effective at killing weeds. See: http://www.nytimes.com/2010/05/04/business/energy-environment/04weed.html

International Database on Glycines (Glyphosate family): http://www.weedscience.com/summary/MOA.aspx?MOAID=12
Iowa State: http://www.extension.iastate.edu/CropNews/2011/0120hartzler.htm
University of Arkansas: http://bumperscollege.uark.edu/test_cses2012/1946.php
National Academy of Sciences Report: http://www.nap.edu/catalog.php?record_id=12804

• Glyphosate use is increasing steadily According to the USGS, more than 88,000 tons of glyphosate were used in the United States in 2007, up from 11,000 tons in 1992. Since the advent of "super weeds," the use of glyphosate and other even stronger weed killers has risen significantly.
Article: http://www.reuters.com/article/2011/08/31/us-glyphosate-pollution-idUSTRE77U61720110831

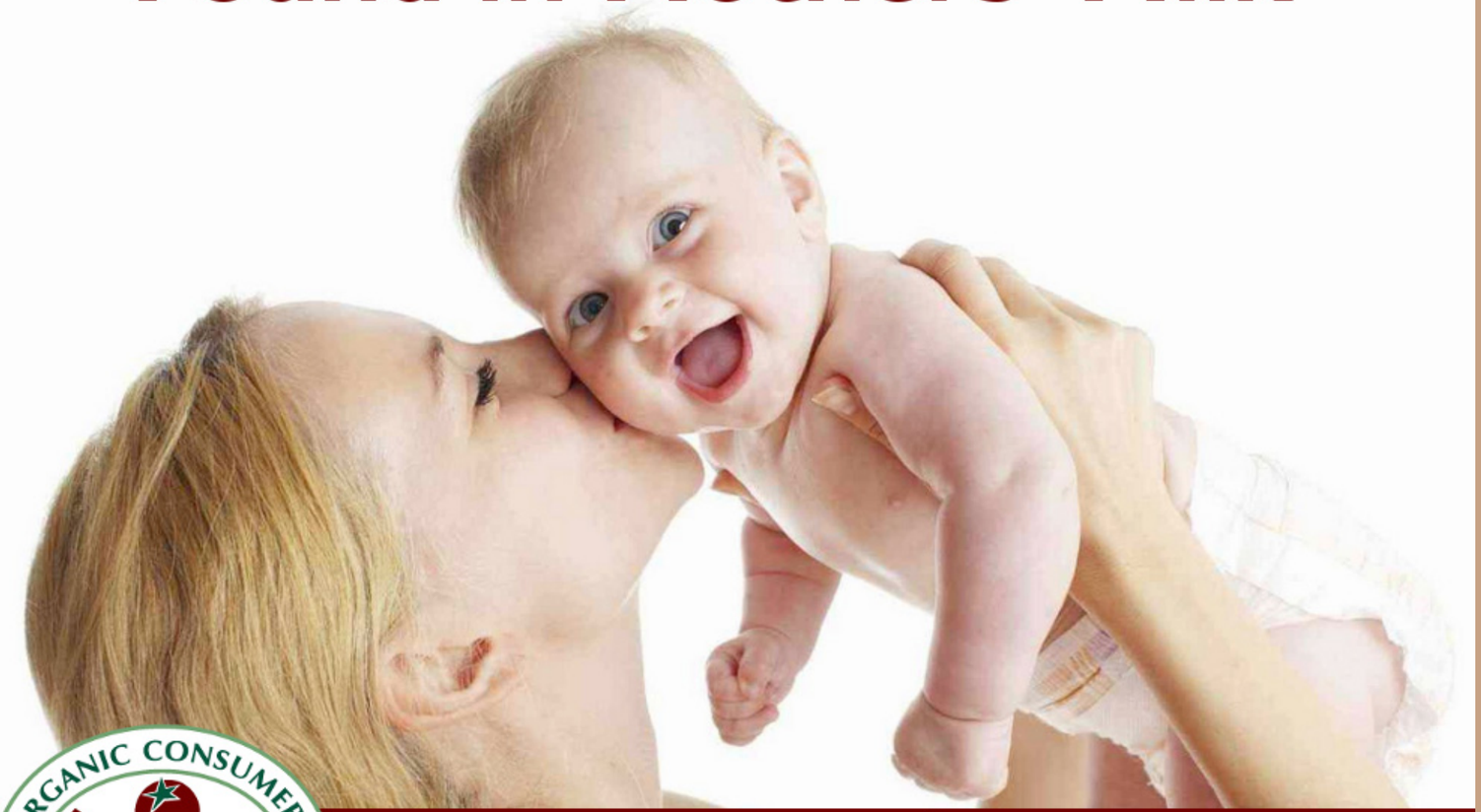
• Glyphosate is not breaking down as promised. In 1996, New York's attorney general sued Monsanto over the company's use of "*false and misleading advertising*" about RoundUp®. That case ended with Monsanto agreeing to stop calling Roundup "*biodegradable*," because it isn't and they pulled all ads claiming that Roundup was "*safer than table salt*," "*practically nontoxic*," and "*stayed where you put it*."

Two decades after the advent of "RoundUp Ready" crops and their dominance in the agricultural marketplace, the evidence of their falsehoods abound: multiple studies have found significant levels of glyphosate in streams, soil, air, rainwater, and groundwater:

Wastewater: http://toxics.usgs.gov/highlights/glyphosate_wastewater.html
Rain and Streams: http://www.usgs.gov/newsroom/article.asp?ID=2909
Groundwater: http://www.ncbi.nlm.nih.gov/pubmed/22101424
Soil: http://www.docstoc.com/docs/124999079/Effects-of-Glyphosate-and-Foliar-

Breaking News

Monsanto's Roundup Found in Mothers' Milk



ORGANIC CONSUMERS ASSOCIATION

Study suggests world's most widely used toxin accumulates in human tissue.


Are you
feeding me
GMOs?


Toxic

Amendments-on-Soil-Microorganisms
Atmosphere, Soil and Surface Water: http://environment.gov.ab.ca/info/library/6444.pdf
Mississippi and Iowa Streams: https://gsa.confex.com/gsa/2009AM/finalprogram/abstract_162346.htm
Mississippi Air and Rain: http://www.ncbi.nlm.nih.gov/pubmed/24549493
51 Midwestern Streams in 9 states: http://toxics.usgs.gov/highlights/glyphosate02.html

In our food a recent study found that Glyphosate residues in the main foods of the Western diet – sugar, wheat, and genetically modified corn and soy – inhibit critical enzymes in mammals which manifests slowly over time, as inflammation damages cellular systems throughout the body. Source: http://www.mdpi.com/1099-4300/15/4/1416
In humans (study #1):

No surprise, a study done in Germany in 2012 found glyphosate in all of the urine samples it took from non-agricultural workers in Berlin, at levels 5-20 times the limit for drinking water. Source: http://www.ithaka-journal.net/herbizide-im-urin?lang=en

In June 2013, another study found traces of glyphosate in the urine samples of individuals across 18 countries in Europe. Summary: http://gmoevidence.com/dr-hans-wolfgang-hoppe-glyphosate-found-in-human-urine-across-europe/

Original Study Report: http://gmoevidence.com/wp-content/uploads/2013/06/glyphosate_studyresults_june12.pdf

In January 2014, researchers from Germany and Egypt discovered that animals fed GM feed had much higher levels of glyphosate in their urine and organs than animals fed non-GM or organic feed, which translated into higher levels of the toxic chemical in humans as well. Source: http://omicsonline.org/open-access/detection-of-glyphosate-residues-in-animals-and-humans-2161-0525.1000210.pdf

• Glyphosate causes birth defects, tumors, and reproductive disorders in animals, as well as sharp declines in beneficial insects and often at dilutions far lower than the concentrations used in agricultural and even home garden spraying.

Study: http://www.ncbi.nlm.nih.gov/pubmed/20695457
Study: http://www.scribd.com/doc/57277946
Study: http://sustainablefoodtrust.org/2012/09/.pdf
Study: http://www.mlmp.org.pdf
Study: http://www.ncbi.nlm.nih.gov/pubmed/23820267
Study: http://onlinelibrary.wiley.com/abstract

A June 2011 report assembled by an international team of scientists revealed that studies done as early as the 1980s by biotech and ag-industry corporations (including Monsanto) all showed that Roundup's active ingredient glyphosate causes birth defects in laboratory animals … again, at very low exposures.

• Glyphosate is a genotoxic endocrine disruptor to human cells and gut bacteria
Human Cells: http://www.barnstablecounty.org/wp-content/uploads/2010/09/gasnier-toxicology-elsevier-262-184-191-glyphostae-ed-human-cell-lines2.pdf

Human Placental Cells: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1257596/?report=classic#b36-ehp0113-000716

Our gut bacteria was recently discovered to contain the very same metabolic pathway in plants that is being targeted and disrupted by Glyphosate—the shikimate Pathway—in direct opposition to Monsanto's claims that the human body did not contain this pathway: http://www.mdpi.com/1099-4300/15/4/1416

• Glyphosate is linked to cancer and deadly kidney disease in humans. Three studies have linked glyphosate exposure with non-Hodgkin's lymphoma. Glyphosate is the key ingredient in Monsanto's RoundUp weed-killer, along with other "inert" ingredients that are potentially even more dangerous than glyphosate alone.

2001: http://cebp.aacrjournals.org/content/10/11/1155.long
2002: http://www.ncbi.nlm.nih.gov/pubmed/12148884
2003: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1740618/

And a recent 2014 study linked glyphosate exposure to kidney disease in multiple countries:
http://www.lankabusinessonline.com/news/sri-lanka,-kidney-disease-linked-to-glysophate,-phosphate-fertilizer/2081217214

• Glyphosate causes DNA damage. Inhalation of glyphosate was observed to cause DNA damage after short exposure to concentrations that correspond to the 450-fold dilution of spraying most commonly used in agriculture. Study: http://www.ncbi.nlm.nih.gov/pubmed/22331240

• The EPA is still working on Glyphosate's human risk assessment. Although the EPA has found the time to establish a National Acceptable Daily Intake of glyphosate (5.5% per day; as cited in the study done on pregnant women), long-term human risk assessment studies are slow to emerge.
Glyphosate Detected in Pregnant Women: http://www.ncbi.nlm.nih.gov/pubmed/22261298
EPA Study Outline and Schedule: http://pesticidetruths.com/wp-content/uploads/2011/11/Reference-glyphosate-2009-12-00-Final-Work-Plan-EPA.pdf

• Glyphosate resistance is the primary purpose of genetic crop engineering. GM crops have been responsible for a 527 million pound increase in herbicide use in the United States over the first 16 years of commercial use of GM crops (1996 – 2011). Reuters Explains:
http://www.reuters.com/article/2012/10/02/us-usa-study-pesticides-idUSBRE89100X20121002

Compelling facts researched by Nature Magazine: http://www.washingtonpost.com/blogs/wonkblog/wp/2013/05/01/the-rise-of-genetically-modified-crops-in-two-charts/

Additional Reading

Why Glyphosate Should be Banned: A Review of its Hazards to Health and the Environment
Sirinathsinghji, E., Ho, Mae-Wan, Overview: http://permaculturenews.org/2012/11/01/why-glyphosate-should-be-banned-a-review-of-its-hazards-to-health-and-the-environment/

Full Report (ISIS Members only): http://www.i-sis.org.uk/error/login_error.php?location=Why_Glyphosate_Should_be_Banned.php

Glyphosate Fact Sheet from Beyond Pesticides
http://www.beyondpesticides.org/pesticides/factsheets/Glyphosate.pdf

Glyphosate Fact Sheet from Pesticide.org
http://www.pesticide.org/get-the-facts/pesticide-factsheets/factsheets/glyphosate

Glyphosate Fact Sheet from Mindfully.Org (by the way, one of the internet's most reliable web sites)
http://www.mindfully.org/Pesticide/Roundup-Glyphosate-Factsheet-Cox.htm

Ban GMOs Now!
Health & Environmental Hazards
Especially in the Light of the New Genetics

by Dr Mae-Wan Ho and Dr Eva Sirinathsinghji

From The Institute Of Science In Society

The industry-funded International Service for the Acquisition of Agri-biotech Applications (ISAAA) claims that the global area of genetically modified (GM) crops reached 170.3 m hectares (420 m acres) in 2012; a 100-fold increase since commercialization began in 1996; and "the fastest adopted crop technology in the history of modern agriculture" [1].

However, GM crops are still confined to 28 countries, with nearly 90 % planted in just five. USA's 69.5 m ha tops the list at 40.8 % of the total area; Brazil and Argentina with 36.6 and 23.9 m ha account for 21.5 % and 14.0 % respectively; and Canada and India with 11.6 and 10.8 m ha account for 6.8 % and 6.3 % respectively. Herbicide (glyphosate) tolerant crops comprise nearly 60 %, Bt crops 15% and stacked traits 25 %. The major crops are just three: herbicide tolerant soybean (47 %) maize (Bt 4%, stacked traits 23 %) and cotton (Bt 11 %, stacked traits 2%).

GM remains limited to two traits in three major crops that are largely kept out of most of the world.

One main reason is its inability to deliver really useful traits. As Geoffrey Lean of the Telegraph remarked in reviewing a new book by Prof Sir Gordon Conway, formerly President of the Rockefeller Foundation and Chief Scientific Adviser to the Department for International Development, and a known GM supporter [2}: "But what emerges from his book, One Billion Hungry….is how little – so far, at least – GM technology is contributing to beating hunger." In contrast, conventional breeding assisted by genetic markers has been turning out miracles in the meantime, as described in Conway's book. Scientists at Britain's National Institute of Agricultural Botany (NIAB) have just created new wheat hybrids that could increase yields by 30 %. But it is in Africa that major successes have been tumbling out. Nerica rice varieties up to four times as productive as traditional varieties with much shorter growing season, more protein, resist pests and diseases, thrive on poor soils, and withstand drought; also 30 varieties of drought-tolerant maize are boosting yield 20 to 30 % across 13 countries, climbing beans treble production in Central Africa, wheat varieties thriving on salty soils, plus a host of other wonders: blight-resistant potatoes, crops enriched with vitamin A, iron and other essential nutrients.

The other reason is that resistance to GM crops and GMOs (genetically modified organisms including transgenic trees, fish and livestock) has been growing simultaneously worldwide as the failures and hazards are coming to light behind the corporate propaganda.

GM crops are hardly grown in Europe even though the European Commission has given commercial approval for cultivation, showing every sign of caving in to the GM lobby. But at the end of May 2013, Monsanto, the largest producer of GM seeds, announced it is pulling out from Europe. Monsanto's Europe representative Brandon Mitchener told the press the company would no longer engage in any lobbying in Europe and would not apply for approval of any GM plants [3]. German Agriculture Ministry issued a revealing statement: "The promises of GM industry have not come true for European agriculture, nor have they for the agriculture in developing and emerging economies." Monsanto is the last company to depart Germany, if not Europe, following Bayer CropScience, BASF and Syngenta. On 17 July 2013, Monsanto announced it will withdraw all EU approval requests for new GMO crops [4], to concentrate on growing its conventional seeds business in Europe, and to secure EU approvals to import its GM crop varieties widely grown in the US and South America. So, the company has not given up on pushing GMOs on Europe after all. It was setting up a smokescreen to put us off our guard.

Monsanto has been in the news simultaneously for its unapproved glyphosate tolerant GM wheat that has turned up in a farmer's field in Oregon; and Japan and then South Korea suspended their wheat imports for fear of GM contamination, leading to a 4% drop in Monsanto's shares [5]. The shipments were eventually cancelled, which could cost US farmers billions [6].

In fact 8 European Union countries have imposed outright bans on crops approved: Austria, France, Germany, Hungary, Luxembourg, Greece, Bulgaria and Poland [7]. Switzerland has had a moratorium on GM crops since 2008, which was set to end in 2013. But in March 2013, the Swiss Parliament voted to prolong the moratorium ignoring the findings of their National Research Programme 59, which [8] "re-confirmed the safety of the commercial use of GM crops and recommended an end to the moratorium." Denmark gave up on GM crops after having allowed Monsanto to carry out field trials of GM maize since 2009 [9]. Italy is the latest to ban cultivation of GM maize (MON 810) citing environmental concerns [10]. In addition, regions and local administrations at every level in 37 European countries have declared themselves GMO-free. As of

2010, this comprises 169 main regions (prefectures, etc.); 123 intermediate regions (provinces, districts, etc.), 4 713 local governments (municipalities and communities up to areas of 1 m ha), and 31 357 individuals [11]; and the movement is growing rapidly.

Within the heartland of GMOs the USA, the failures of GM crops and the problems created are most visible and most acute [12] (GM Crops Facing Meltdown in the USA, SiS 46). A new study reveals that the US staple crop system has performed worse than non-GM Europe in yields, pesticide use, genetic diversity and resilience since GM crops were planted [13] (US Staple Crop System Failing from GM and Monoculture, SiS 59); with a dangerous downward trend in recent years. Meanwhile, a pitched battle is taking place to get GM crops out through GMO-labelling legislation that would unleash the power of consumers against the might of the biotech industry [14]. Close to 95 % of Americans support GM labelling. In October 2011, the Center for Food Safety filed a legal petition with the FDA to require labelling of all GM food. In 2012, 55 members of Congress wrote a letter to the FDA commissioner in support of the petition. The FDA has received over one million public comments supporting the petition, the largest response ever received by the agency. Meanwhile, 37 GM food labelling bills have been introduced in 21 states in 2013. In the latest move in Washington, Senator Barbara Boxer and Congressman Peter DeFazio have jointly sponsored new federal legislation that requires labelling of all GM food in the US. The Genetically Engineered Food Right-to-Know Act is the first national labelling bill to be introduced in Congress since 2010. The US Green Party has called Monsanto "a top risk to public health and the environment," and has urged a moratorium on GM food crops [15].

In November 2012, Peru imposed a 10 year ban on GMOs in the country, thanks to the effort of farmers from Parque de la Papa in Cusco, a community of 6 000 anxious to protect indigenous biodiversity especially of corn and potatoes on which their livelihood depends [16].

In the same month, Kenya banned import of all GMOs with immediate effect [13]. This followed a decision made by the cabinet on the basis of "inadequate research done on GMOs and scientific evidence provided to prove the safety of the foods".

On 1 June 2013, the new administration in Venezuela announced a new law to protect farmers against GM seeds [18]

On 22 July 2013, the Indian Supreme Court's expert panel of scientists called for a ban on herbicide tolerant crops for India [19].

A Critical Juncture

The rising opposition to GMOs has done little to diminish the aggressive expansionist agenda of the GM corporate empire. Mexico is a major target. US biotech firms Monsanto, DuPont and Dow have applied for permits to grow more than two million hectares of GM maize in northern Mexico [20]. Mexico is the birthplace of maize and a centre of biodiversity. Since 2009, the Mexican government has granted 177 permits for experimental plots of GM maize covering 2 664 hectares. Large-scale commercial release of GM maize has not yet been authorised; but GM contamination of native maize has already been discovered, as the result of what some regard as "a carefully and perversely planned strategy".

"Another killer chemical from Monsanto, Killer Chemical Central, manufacturers of (banned) Dioxon, (banned) PCBs, (banned) Agent Orange and (banned) DDT. This is a corporation whose business model is based on horror, human suffering and death."

~ Jeff Prager

The other major strategy of the GM corporate empire is seed monopoly and escalating seed costs. Conventional non-GM seeds are pushed out at the expense of GM seeds, thereby reducing farmers' choices [21]. The big four biotech seed companies – Monsanto DuPont/ Pioneer Hi-Bred, Syngenta, and Dow AgroSciences – now own 80 % of the US corn market and 70 % of soybean business. The costs of seeds have increased two to three fold since 1995. This is destroying the lives of farmers around the world; the most visible in India, where the introduction of GM cotton has coincided with an escalation of farm suicides ([22] Farmer Suicides and Bt Cotton Nightmare Unfolding in India, SiS 45). At the same time, farmers who want to return to conventional non-GM seed after experiencing increased pest resistance and crop failures find themselves unable to do so, on account of the limited availability of non-GM seeds [23].

Ban GMOs Now!

This is a dangerous situation for the future of food and farming, one that needs to be reversed as quickly as possible, particularly as GM agriculture is failing on all counts. That can only be achieved by a ban on GMOs, an action already taken by countries and local communities around the world. We need to join forces with them, to put an end to the GM corporate empire.

Ten years ago, 24 scientists from around the world formed an Independent Science Panel and produced a report [24] (The Case for A GM-Free Sustainable World, ISIS/TWN publication) summarizing compelling evidence on the hazards of GM crops and the benefits of organic agro-ecological farming, and called for a global ban on environmental releases of GMOs, and a shift to non-GM sustainable agriculture. This report was widely circulated, translated into several languages, and republished in the US a year later. It remains the most succinct and complete account on the subject; but crucial new evidence has come to light within the past decade that strengthens the case considerably.

First of all, decisive evidence has emerged on the unsustainability and destructiveness of conventional industrial agriculture, of which GM is the most extreme; in stark contrast to the proven successes of non-GM ecological farming: its productivity and resilience, environ-

mental and health benefits, and in particular, its enormous potential for saving energy and carbon emissions in mitigating and adapting to climate change. We presented all that in a comprehensive and definitive report published in 2008 ([25] Food Futures Now *Organic *Sustainable *Fossil Fuel Free , ISIS/TWN publication). Our report is completely in line with the International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD) report [26], which resulted from a three-year consultative process involving 900 participants and 110 countries around the world; a sure sign of the scientific consensus that has emerged around non-GM ecological farming as the way forward in food and farming.

To complete the case, we need to bring together all the damning evidence against GMOs on health and the environment, especially in the light of new discoveries in molecular genetics within the past ten years. That is the main reason for the present report.

GM agriculture is a recipe for disaster, as this report will make clear. It is also standing in the way of the shift to sustainable agriculture already taking place in local communities all over the world that can truly enable people to feed themselves in times of climate change. Future generations will not forgive us if we do not stop the GM takeover now. Please use this report, circulate it widely, and send it to your political representatives.

Executive Summary

Since the first commercial growing began in 1996, the global area of genetically modified (GM) crops is reported to have increased 100-fold. However, nearly 90 % are confined to 5 countries, with top grower the US accounting for more than 40 %. GM crops have been largely excluded from Europe and most developing countries because opposition has been growing simultaneously as widespread agronomical failures of the GM crops as well the health and environmental impacts are coming to light.

GM remains limited to three major crops – soybean, maize and cotton – and two traits: herbicide (mainly glyphosate) tolerance (HT) at nearly 60 % and insect resistance with toxins from the soil bacterium Bacillus thuringiensis (Bt) at 15 %, with the remaining stacked traits (HT and one or more Bt) at 25%.

The failures and hazards of glyphosate and glyphosate tolerant crops and Bt crops are reviewed respectively in Chapter 1 and Chapter 2. Chapter 3 reviews the range of hazards resulting from the uncontrollable, unpredictable process of genetic modification itself in the light of advances in molecular genetics within the past decade, which tells us why the technology cannot be safety applied to grow our crops or produce our food.

Glyphosate & Glyphosate Tolerant Crops

Glyphosate use has gone up sharply worldwide since the introduction of glyphosate-tolerant GM crops. Herbicide use per acre has doubled in the US within the past five years compared with the first five years of commercial GM crops cultivation, the increase almost entirely due to glyphosate herbicides. Glyphosate has contaminated land, water, air, and our food supply. Damning evidence of its serious harm to health and the environment has been piling up, but the maximum permitted levels are set to rise by 100-150 times in the European Union with further hikes of already unacceptably high levels in the US if Monsanto gets its way.

1. Scientific evidence accumulated over three decades documents miscarriages, birth defects, carcinogenesis, endocrine disruption, DNA damage, general toxicity to cells, neurotoxicity, and toxicity to liver and kidney at glyphosate levels well below recommended agricultural use.

2. The major adjuvant POEA in glyphosate Roundup formulations is by far the most cytotoxic for human cells, ahead of glyphosate and its metabolite. It also amplifies the toxic effects of glyphosate.

3. A recent review blames glyphosate for practically all modern diseases as its general chelating action affects numerous biological functions that require metal cofactors. It is the most pervasive environmental chemical pollutant that also inhibits enzymes involved in detoxification of xenobiotics, thereby increasing their toxicity. In addition, it kills beneficial gut bacteria that prevent pathogens from colonizing the gut and promotes the growth of the pathogenic bacteria, leading to autism and other diseases.

4. Rats fed Roundup contaminated and Roundup tolerant maize beyond the required 90 days showed a startling range of health impacts. Females were 2 to 3 times as likely to die as controls and much more likely to develop mammary tumours. In males, liver congestions and necrosis were 2.5 to 5.5 times as frequent as controls, while kidney diseases were 1.3-2.3 times controls. Males also develop kidney or skin tumours 4 times as often as the controls and up to 600 days earlier. The harmful effects were found in animals fed the GM maize that was not sprayed with Roundup, as well as those that were, indicating that the GM maize has its own toxicities apart from the herbicide.

5. Livestock illnesses from glyphosate tolerant GM feed including reproductive problems, diarrhoea, bloating, spontaneous abortions, reduced live births, inflamed digestive systems and nutrient deficiencies. Evidence has also emerged of chronic botulism in cattle and farmers as the result of glyphosate use.

6. Glyphosate is lethal to frogs and Roundup is worse; it increases toxic blooms, and accelerates the deterioration of water quality. It use also coincides with the demise of monarch butterflies.

7. Glyphosate poisons crops and soils by killing beneficial microorganisms and encouraging pathogens to flourish. Forty crop diseases are now linked to glyphosate use and the number is increasing.

8. Glyphosate-resistant weeds cover 120 million ha globally (61.8 m acres in the US) and continue to spread; it is a major factor accounting for the enormous increase in pesticide use since herbicide tolerant GM crops were introduced.

9. Contamination of ground water supplies, rain, and air has been documented in Spain and the US. Berlin city residents were found to have glyphosate concentrations above permitted EU drinking water levels.

Bt Crops

Bt crops were sold on the premise that they would increase yields and reduce pesticide use; instead they have resulted in too many crop failures, and the introduction of Bt cotton is now acknowledged to be responsible for the

escalation in farm suicides in India.

1. Bt crops' claim to reduce pesticide use is based on excluding the Bt produced in the crops in total 'pesticides applied'; but the Bt toxins leach from the plants and persist in soil and water, with negative impacts on health and the ecosystem comparable to conventional pesticides.

2. Fungicide use and insecticide treatment of corn and soybean have gone up dramatically since the introduction of Bt crops.

3. The breakdown of Bt traits due to target pest resistance and secondary pests has resulted in increasing use of conventional pesticides; and pesticide companies are reporting 5 to 50% increase in sales for 2012 and the first quarter of 2013.

4. Contrary to industry's claim that Bt is harmless to non-target species, independent studies showed that Bt toxins elicit immune response in mammals in some cases comparable to that due to cholera toxin. This is consistent with farm workers' reports of allergic symptoms affecting the eyes, skin and respiratory tract.

5. A new study found Bt proteins toxic to developing red blood cells as well as bone marrow cells in mice.

6. Toxicity to human kidney cells has been observed in vitro, consistent with in vivo experiments in lab animals showing toxicity to heart, kidney and liver.

7. Bt crops fail to control target pests due to insufficient expression of Bt toxins, thereby promoting the evolution of resistance.

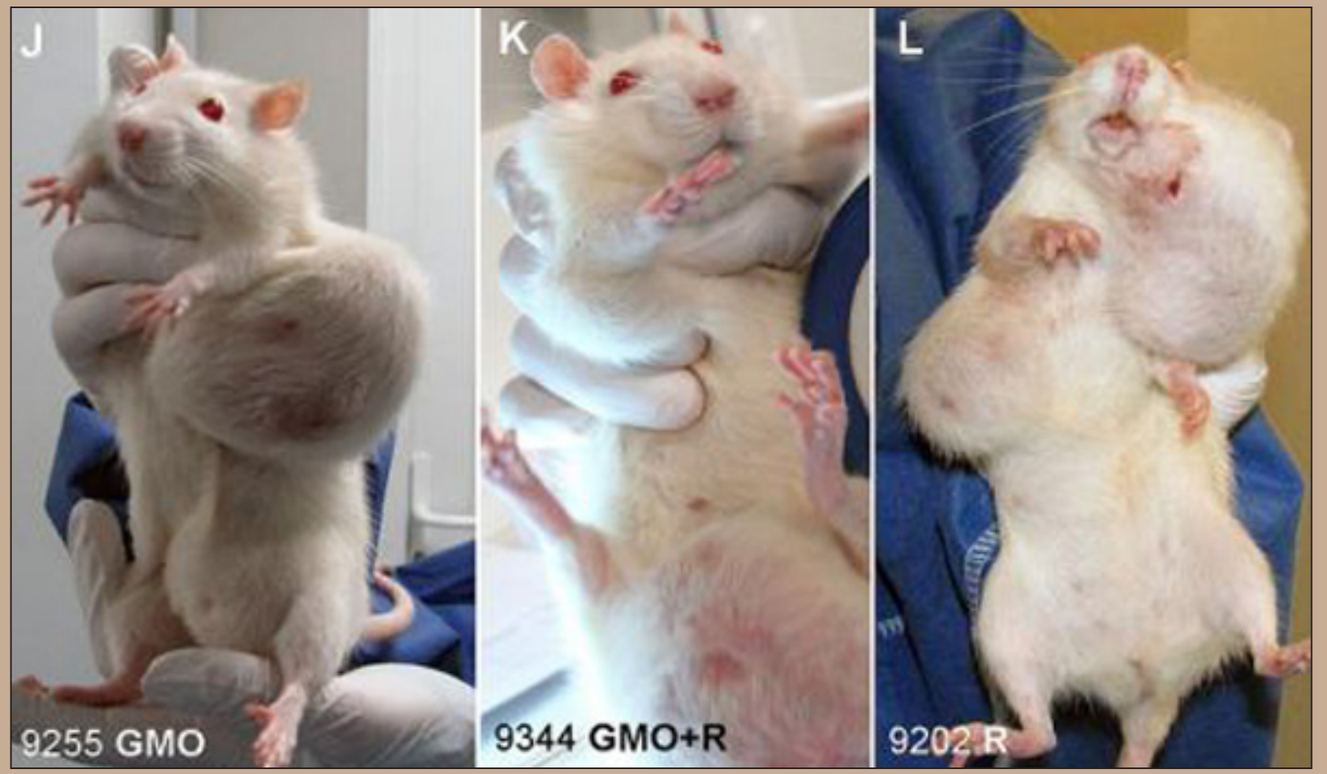
8. Bt crops promote the emergence of secondary pests when target pests are killed. Primary and secondary pests are already huge problems in the US, India and China, and are now hitting multiple crops in Brazil since Bt maize was introduced.

9. Stacked varieties containing multiple Bt toxins are predicted to hasten the evolution of multiple toxin resistance, as resistance to one toxin appears to accelerate the acquisition of resistance to further toxins.

10. Bt toxins harm non-target species including water fleas, lacewings, monarch butterflies, peacock butterflies and bees, which are showing worrying signs of population decline across the world.

11. Bt toxins leach into the soil via the root of Bt crops where they can persist for 180 days; this has been linked to the emergence of new plant diseases and reduced crop yields.

12. Bt toxins also persist in aquatic environments, contaminating streams and water columns and harming important aquatic organisms such as the caddisfly.



The Not-So-New Genetics: And The Horrors Of Genetic Modification

The rationale and impetus for genetic engineering and genetic modification was the 'central dogma' of molecular biology that assumed DNA carries all the instructions for making an organism. This is contrary to the reality of the fluid and responsive genome that already has come to light since the early 1980s. Instead of linear causal chains leading from DNA to RNA to protein and downstream biological functions, complex feed-forward and feed-back cycles interconnect organism and environment at all levels, marking and changing RNA and DNA down the generations. In order to survive, the organism needs to engage in natural genetic modification in real time, an exquisitely precise molecular dance of life with RNA and DNA responding to and participating fully in 'downstream' biological functions. That is why organisms and ecosystems are particularly vulnerable to the crude, artificial genetically modified RNA and DNA created by human genetic engineers. It is also why genetic modification can probably never be safe.

1. Genetic modification done by human genetic engineers is anything but precise; it is uncontrollable and unpredictable, introducing many collateral damage to the host genome as well as new transcripts, proteins and metabolites that could be harmful.

2. GM feed with very different transgenes have been shown to be harmful to a wide range of species, by farmers in the field and independent scientists working in the lab, indicating that genetic modification itself is unsafe.

3. Genetic modification done by human genetic engineers is different from natural genetic modification done by organisms themselves for the following reasons: it relies on making unnatural GM constructs designed to cross species barriers and jump into genomes; it combines and transfers genes between species that would never have exchanged genes in nature; GM constructs tend to be unstable and hence more prone to further horizontal gene transfer after it has integrated into the genome.

4. Horizontal gene transfer and recombination is a major route for creating new viruses and bacteria that cause diseases and spreading drug and antibiotic resistance. Transgenic DNA is especially dangerous because the GM constructs are already combinations of sequences from diverse bacteria and viruses that cause diseases, and contain antibiotic resistance marker genes.

5. There is experimental evidence that transgenes are much more likely to spread and to transfer horizontally.

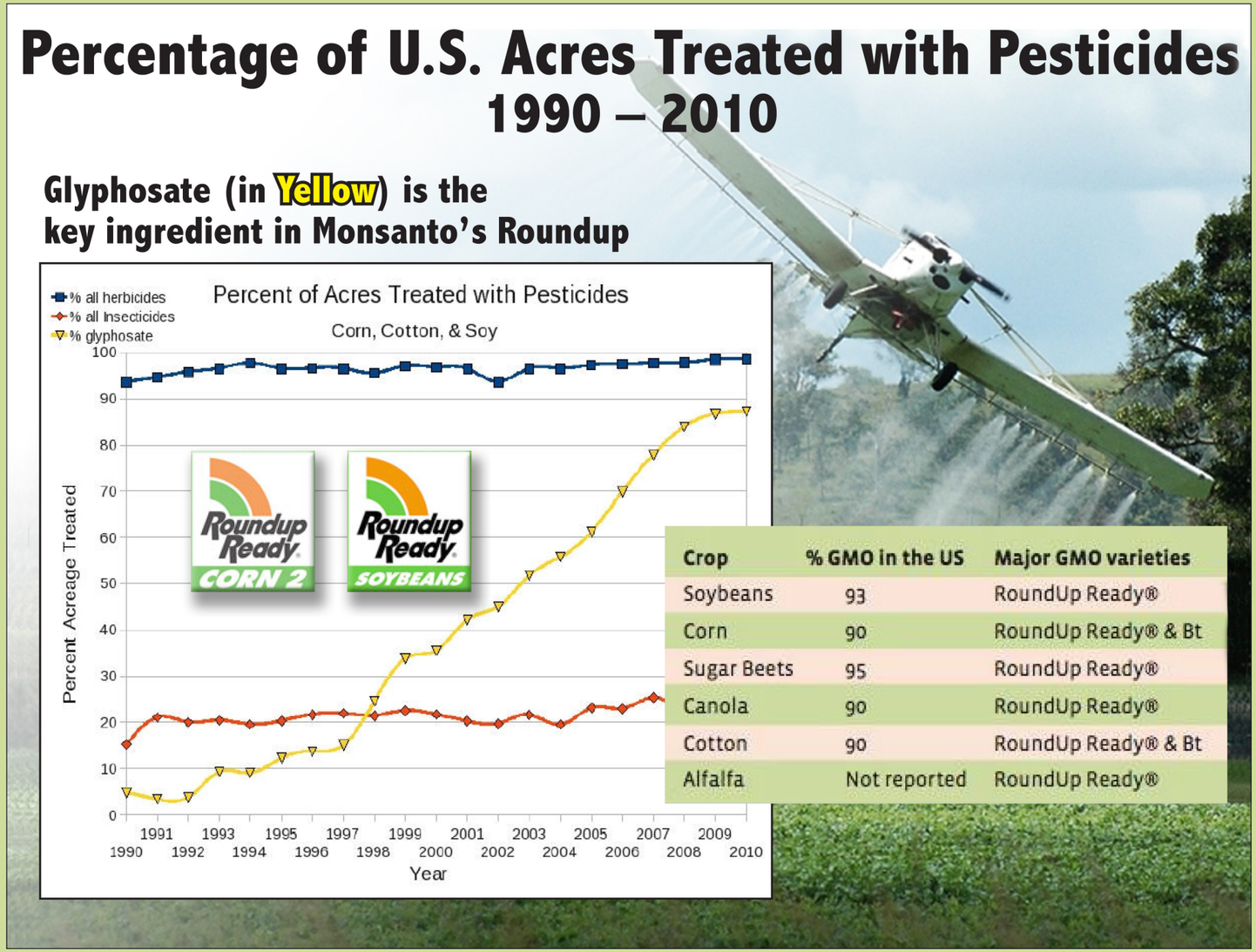
6. The instability of the GM construct is reflected in the instability of transgenic varieties due to both transgene silencing and the loss of transgenes, for which abundant evidence exists. Transgenic instability makes a mockery

of 'event-specific' characterization and risk assessment, because any change in transgene expression, or worse, rearrangement or movement of the transgenic DNA insert(s) would create another transgenic plant different from the one that was characterized and risk assessed. And it matters little how thoroughly the original characterization and risk assessment may have been done. Unstable transgenic lines are illegal, they should not be growing commercially, and they are not eligible for patent protection.

7. There is abundant evidence for horizontal transfer of transgenic DNA from plant to bacteria in the lab and it is well known that transgenic DNA can persist in debris and residue in the soil long after the crops have been cultivated. At least 87 species (2 % of all known species) of bacteria can take up foreign DNA and integrate it into their genome; the frequency of that happening being greatly increased when a short homologous anchor sequence is present.

8. The frequency at which transgenic DNA transfers horizontal has been routinely underestimated because the overwhelming majority of natural bacteria cannot be cultured. Using direct detection methods without the need to culture, substantial gene transfers were observed on the surface of intact leaves as well as on rotting damaged leaves.

9. In the only monitoring experiment carried out with appropriate molecular probes so far, China has detected the spread of a GM antibiotic resistance gene to bacteria in all of its major rivers; suggesting that horizontal gene transfer has contributed to the recent rise in antibiotic resistance in animals and humans in the country.



10. GM DNA has been found to survive digestion in the gut of mice, the rumen of sheep and duodenum of cattle and to enter the blood stream.

11. In the only feeding trial carried out on humans, the complete 2 266 bp of the epsps transgene in Roundup Ready soybean flour was recovered from the colostomy bag in 6 out of 7 ileostomy subjects. In 3 out of 7 subjects, bacteria cultured from the contents of the colostomy bag were positive for the GM soya transgene, showing that horizontal transfer of the transgene had occurred; but no bacteria were positive for any natural soybean genes.

12. The gastrointestinal tract of mammals is a hotspot for horizontal gene transfer between bacteria, transfer beginning in the mouth.

13. Evidence is emerging that genomes of higher plants and animals may be even softer targets for horizontal gene transfer than genomes of bacteria.

14. The CaMV 35S promoter, most widely used in commercial GM crops, is known to have a fragmentation hotspot, which makes it prone to horizontal gene transfer; in addition. it is promiscuously active in bacteria, fungi, as well as human cells. Recent evidence also suggests that the promoter may enhance multiplication of disease-associated viruses including HIV and cytomegalovirus through the induction of proteins required for transcription of the viruses. It also overlaps with a viral gene that interferes with gene silencing, an essential function in plants and animals that protects them against viruses.

15. The Agrobacterium vector, most widely used for creating GM plants is now known to transfer genes also to fungi and human cells, and to share genetic signals for gene transfer with common bacteria in the environment. In addition, the Agrobacterium bacteria as well as it gene transfer vector tend to remain in the GM crops created, thereby constituting a ready route for horizontal gene transfer to all organisms interacting with the GM crops, or come into contact with the soil on which GM crops are growing or have been grown.

16. In 2008, Agrobacterium was linked to the outbreak of Morgellons disease. The Centers for Disease Control in the US launched an investigation, which concluded in 2012, with the finding: "no common underlying medical condition or infection source was identified". But they had failed to investigate the involvement of Agrobacterium.

17. New GM crops that produce double-stranded RNA (dsRNA) for specific gene-silencing are hazardous because many off-target effects in the RNA interference process are now known, and cannot be controlled. Furthermore, small dsRNA in food plants were found to survive digestion in the human gut and to enter the bloodstream where they are transported to different tissues and cells to silence genes.

18. Evidence accumulated over the past 50 years have revealed nucleic acids (both DNA and RNA) circulating in the bloodstream of humans and other animals that are actively secreted by cells for intercommunication. The nucleic acids are taken up by target cells to silence genes in the case of double-stranded microRNA (miRNA), and may be integrated into the cells' genome, in the case of DNA. The profile of the circulating nucleic acids change according to states of health and disease. Cancer cells use the system to spread cancer around the body. This nucleic acid intercom leaves the body very vulnerable to genetically modified nucleic acids that can take over the

New Study Concludes GMO Deleterious for Health
GMO found yet again as deleterious for health in new study.

The rats were fed an ordinary rat chow found to contain GMOs on PCR analysis
using probes for the cauliflower mosaic virus 35S promoter and a gene control element
in more than 80% of commercial GM crops grown with potential health hazards predicted since 1999

CaMV 35S Promoter In GM Feed That Sickened Rats Transferred Into Rat Blood, Liver, And Brain Cells

by Dr Mae-Wan Ho
Institute of Science in Society

Wednesday, January 7, 2015

Researchers led by Hanaa Oraby at Egypt's National Research Center in Cairo are not the first to look for horizontal transfer of genetically modified (GM) DNA into animal cells, but certainly among the first to do an experiment aimed at detecting it and succeeded [1]. Horizontal gene transfer is the direct uptake of DNA (or RNA) into cells and integration of the sequence into the cell's genome. Some of us regard horizontal gene transfer as the most serious hidden hazard of genetically modified organisms (GMOs) released into the environment ([2] Horizontal Gene Transfer – The Hidden Hazards of Genetic Engineering (ISIS special report). But a prevailing culture of denial by vested interests and regulators has obstructed proper investigation until very recently (see [3] Horizontal Transfer of GM DNA Widespread, SiS 64).

A GMO is an organism with synthetic foreign DNA gene sequences inserted into its genome in a laboratory process of artificial genetic modification that bypasses normal reproduction. Part of the foreign DNA is a control element called a promoter that is necessary for expressing the foreign genes. The most widely used is the cauliflower mosaic virus (CaMV) 35S promoter (which is what enables the virus to hijack the cell for making endless copies of the virus). The CaMV 35S promoter is now in more than 80 % of all GM plants [4], and is the first test for the presence of GMOs in unknown samples.

Effects of long term use of glyphosate on crop (wheat) health. Left planting not treated with glyphosate and glyphosate treated wheat on the right.

Probing For CaMV 35S Promoter In The Rat Diet And In Rat Tissues

The Cairo researchers used three pairs of primers – specific short anchoring sequences that bind by specific base-pairing to the opposite ends of the DNA segment of interest – so as to amplify different segments from the CaMV 35S promoter with PCR (polymerase chain reaction). The amplified segments can then be isolated and detected on electrophoresis. The primers together amplify nearly 80 % of the entire promoter sequence. The experimental diet was an ordinary lab chow containing 60 % yellow maize and 34 % soybean, but unlabelled as to whether it is GM or not. The presence of GM material in the diet was ascertained using PCR assay with the three pairs of primers, which all gave the expected positive results, indicating that the diet contained GM material (up to a maximum of 94 %, if both the soybean and maize were completely GM).

The experimental animals consisted of 29 male Wistar albino rats immediately after weaning (age three to four weeks), which were divided into two main groups. One was fed on the lab chow containing GM ingredients for three months, and were further divided into three subgroups of 5, 5, and 7 animals, euthanized after 30, 60, and 90 days. The other control group was fed on a balanced non-GM diet for the same period and euthanized at the end of the experiment.

The lab chow diet used all through this experiment gave positive results when screened with primers for CaMV 35S promoter. The expected 195 bp (base pairs) amplified product was detected in all samples of the GM diet, but was absent in the control diet made up with non-GM material to match the nutritional content of the GM diet. As further confirmation, the PCR product obtained from the GM diet was sequenced, and shown to have 100 % identity with the CaMV 35S promoter at nucleotide coordinate 7190-7380 of the CaMV on sequence alignment analysis using the GenBank database. It also showed 100 % sequence identity with a number of binary vectors used for transferring genes in the lab that also contain the CaMV 35S promoter.

PCR analysis of the different tissues showed amplified sequence segments of the expected sizes for the three pairs of primers – 70, 88 and 195 bp – in some of the DNA samples of blood, liver and brain of rats fed the GM diet after 30, 60 and 90 days. None of the three primers gave amplification product in DNA samples of tissues from the controls fed the non-GM diet.

The 195 bp segment amplified from DNA samples of liver and brain in rats fed GM diet was subjected to DNA sequencing, and comparison with GenBank database revealed 100 % identity with the CaMV whole genome at the same nucleotide coordinates 7190-7384 for the 35S promoter. Furthermore, it also showed 100 % identity with the PCR segment ampli-

fied from the GM diet, and with the binary vectors segments that are 100 % identical to the PCR product from the GM diet.

Feeding rats with GM diet for 30, 60, and 90 days increased the mean transfer frequency of GM target sequences significantly from 0 in the controls to 8 + 0.0000 %, 12.3 + 1.2018 % and 16.7 + 2.4529 % respectively. Thus, there is a cumulative effect with time of exposure.

Bearing in mind that the three primer pairs together amplify nearly 80 % of the entire CaMV 35S promoter, and in some animals, the three segments were all amplified in the same sample, it suggests that the whole CaMV 35S promoter may have been transferred into the genome of those animals. Considering that even a promoter containing only 46 bp of the 5' sequence from the CaMV 35S promoter was previously reported to be sufficient for accurate initiation of gene transcription for gene expression [5], it is highly likely that the transferred CaMV35S promoter sequence would alter the activity of some genes in the host cell genome that may have harmful consequences (see later).

There was no significant difference in the rate of transfer into blood, liver, or brain tissues. Moreover, the frequency of uptake for the larger segments was greater than that for the smaller segments; thus, the transfer frequency of the 70 bp segment was the lowest at 1.09 + 0.4161 %, the 88 bp at 2.09 + 0.7318 %, and the 159 bp at 3.8 + 0.8069 %. This finding is consistent with previous researchers who postulated that the shorter the fragment, the lower the uptake efficiency [6].

GM Fed Rats Suffered Severe Damages To Liver, Kidney And Testis

In a separate report written by some of the same researchers in Cairo, the same GM diet was fed to identical rats in a post-market safety assessment of GMOs [7]. Biochemical, histopathological, and cytogenetic analyses on liver, kidney, and testis revealed that the GM diet fed for 30, 60 and 90 days suffered significant deleterious effects.
A total of 30 rats were fed the GM diet, 10 each for 30 days, 60 days and 90 days. The controls were on a wheat-based non-GM nutritionally matched diet for similar periods of time.

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) enzyme activities were measured in blood serum as indicators of liver cell damage. Creatinine and uric acid levels were determined also in blood serum as indicators of kidney function. Malondialdehyde in liver cells resulting from lipid peroxidation is a biomarker of oxidative stress. In addition, specimens of liver, kidney and testis were dissected immediately after the rats were euthanized and sectioned for histopathological and histochemical investigations. Cytogenetic and DNA damage analyses were carried out on testis and liver. Chromosome analysis was done on germ cells from the testis. Sperms were examined for morphological abnormalities and DNA fragmentation was determined in liver cells.
The results were unambiguous.

Histopathology Of Liver, Kidney And Testis

Liver cells showed slight damage in rats fed GM diet for 30 days, with damage increasing after 60 and 90 days. The effects start as a slight dilatation and congestion of the central vein (supplying the liver) and fragmentation of the nucleus in some cells. After 60 days, mild cellular infiltration (from the blood) was observed. After 90 days, the blood sinusoids (spaces) also showed slight dilatation and congestion (Figure 1).

Figure 1 Liver sections: a, control; b, 30 day GM-fed; c, 60 day GM-fed; d 90 day GM fed (see text for details)
Kidney sections show damaging effects of the GM diet evident even after the first 3o days as interstitial haemorrhage (blood in spaces between cells) and a widening of the tubules. This got worse in 60 and 90 days (Figure 2).

Figure 2 Kidney sections: a, control; b, 30 day GM-fed; c, 60 day GM-fed; d 90 day GM fed (see text for details)

The testis of rats fed on GM food for 30 days showed mild thickening of the basement membrane of the seminiferous tubules (where germ cells develop) with gaps appearing between the germinal epithelium of some tubules. At 60 and 90 days, an increase in the connective tissue component and in the number of Leidig cells (in the connective tissue), with a disarrangement of the germinal epithelium (Figure 3).

Figure 3 Testis sections: a, control; b, 30 day GM-fed; c, 60 day GM-fed; d 90 day GM fed (see text for details)

Protein content in liver tissues decreased significantly after 30 or 90 days, indicating dysfunction of some hepatocytes. Abnormal cellular activity in the kidney was also confirmed by a statistically significant increase in the protein content. Consistent with the liver and kidney damages seen, AST and ALT activity increased in the serum of experimental rats by 33 to 107 % and 33 to 92 % respectively. Blood creatine and uric acid concentrations significantly increased by 15 to 315 % and 37 to 96 % respectively. MDA concentrations in liver, as an indicator of oxidative stress, increased significantly in all animals fed GM diet by 286 to as high as 940%.

Mitotic index (as a measure of cell division) was significantly reduced in the 60 and 90 days fed rats from 8.8 + 0.326 % in controls to 8.4 + 0.221 % (30 days), 6.8 + 0.466 % (60 days) and 6.6 + 0.266 % (90 days). Concomitantly, there was a significant increase in chromosomal aberrations, from 0.4 + 0.163 % in controls to 6.6 + 0.221 %, 13.8 + 0.326 % and 8.0 + 0.632 % respectively for 30, 60 and 90 day GM fed rats. The frequency of morphologically abnormal sperm increased by up to two-fold, from 3.33 +0.35 % to 5.83 + 0.60 %, 7.8 + 0.65 % and 6.6 + 0.24 %. At the same time DNA fragmentation went up from 11.83 + 0.7 % in controls to 19.0 + 1.2 %, 28.3 + 1.6 % and 24.3+ 0.7% respectively.

The researchers concluded the results [7] "indicate that there are health hazards linked to the ingestion of diets containing genetically modified components."

However, the investigations have not gone further into the mechanisms whereby the genetically modified components were hazardous to health; nor do the results directly implicate the CaMV 35S promoter found transferred to rat blood, liver and brain in the other report [1]. It will be useful to review the potential hazards of the CaMV 35S promoter, which were first pointed out 15 years ago.

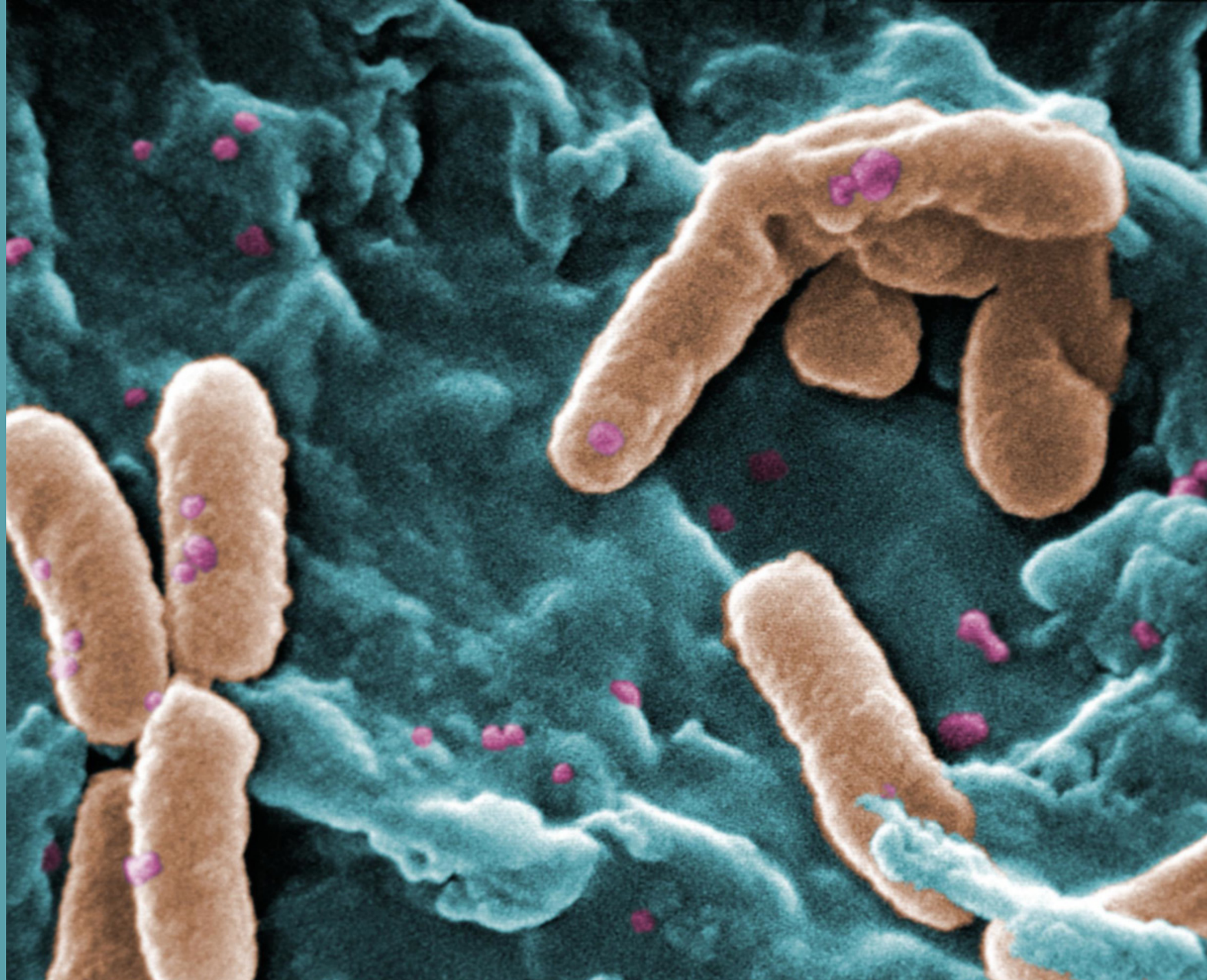
Predicted Hazards Of Cauliflower Mosaic Virus 35S Promoter

When first deployed, geneticists assumed that the CaMV 35S promoter would only work in plants, as the complete virus (wrapped in its protein coat) specifically infects only plant cells. But it soon transpired that the isolated piece of promoter DNA without its coat is extremely promiscuous, and works in cells across kingdoms of plants and animals, as well as bacteria. We issued a serious warning against its use in 1999 [8] Cauliflower Mosaic Viral Promoter – A Recipe for Disaster (ISIS scientific publication) when it was found to have a recombination hotspot where it tends to fragment and join, which makes it prone to unintended (horizontal) gene transfer into cells of all organisms exposed to the GMO, including bacteria, fungi, pollinators, wild animals and humans (see [9] CaMV 35S promoter fragmentation hotspot confirmed, and it is active in animals (ISIS scientific publication). What that implies is the CaMV 35S promoter can break loose from the plant genome DNA and jump into the genome of all those other cells, with the potential to mutate, activate or inactivate genes (including those leading to cancer), reactivate dormant viruses, or create new viruses by recombination (gene shuffling) [8, 10] (Hazards of Transgenic Plants Containing the Cauliflower Mosaic Viral Promoter, ISIS scientific publication) But our warnings were met with abuse and denial and ultimately ignored.

Since then, evidence has emerged that the CaMV 35S promoter may enhance the multiplication of disease-associated viruses including HIV and cytomegalovirus through the induction of proteins required for transcription of the viruses [11] (New Evidence Links CaMV 35S Promoter to HIV Transcription, ISIS scientific publication). Further, the CaMV 35S promoter overlaps with a virus gene, the product of which is toxic to plants and likely also to animals [12]. For a more detailed description on the risks of the CaMV 35S promoter and indeed on GMOs in general, see [13] and final chapter in [14] Ban GMOs Now, ISIS Report.

Conclusions

GMOs are once again found to be deleterious for health in a feeding trial that last no longer than 90 days. And within that time, the most widespread piece of transgenic DNA found in the GM diet, the CaMV 35S promoter, was found transferred horizontally into the animals' tissues at high frequencies. The CaMV 35S promoter is not the only hazardous piece of transgenic DNA, there are similar aggressive promoters designed to make genes express out of context, as well as genes coding for antibiotics and other dangerous functions, together with numerous recombination hotspots that enhance horizontal gene transfer; all of which contribute to making all GMOs unsafe. That is indeed the conclusion from research carried out by scientists independent of the industry up to now, which fully corroborates what farmers have been witnessing in their livestock and doctors in their patients for years [14]. People need to take immediate action to ban GMOs from their own home and local communities. Governments should recall all GMOs from the market. And companies and regulators should face prosecution for causing damages to health and criminal negligence.



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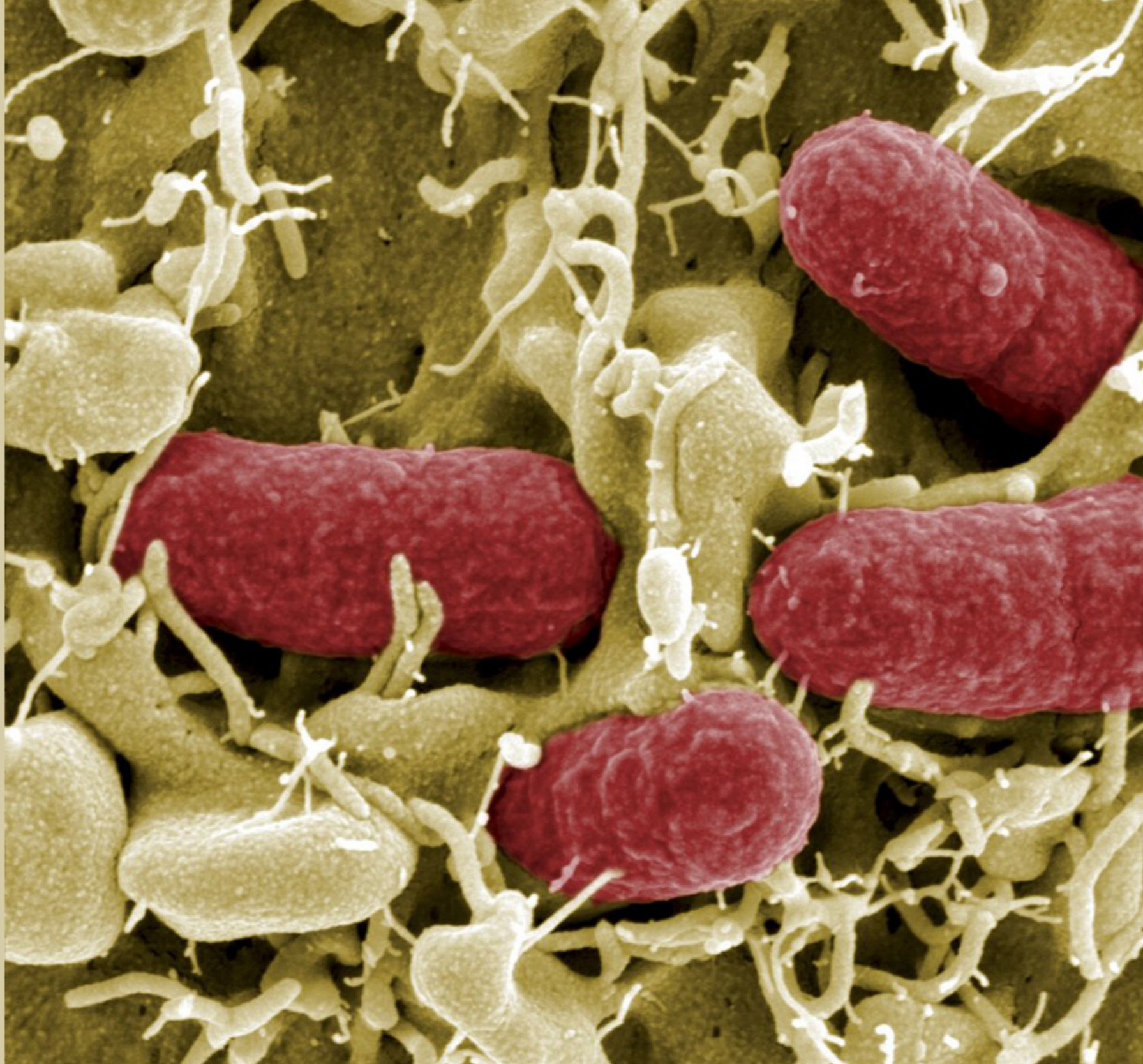

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The Institute Of Science In Society

The Institute of Science in Society (ISIS) was co-founded in 1999 by scientists Mae-Wan Ho and Peter Saunders to provide critical yet accessible and reliable information to the public and policy makers. ISIS aims to reclaim science for the public good; to promote a contemporary, holistic science of the organism and sustainable systems; and influence social and policy changes towards a sustainable, equitable world. ISIS is a partner organisation of the Third World Network based in Penang, Malaysia, and works informally with many scientists who are members of ISIS or of the Independent Science Panel that ISIS initiated (see below).

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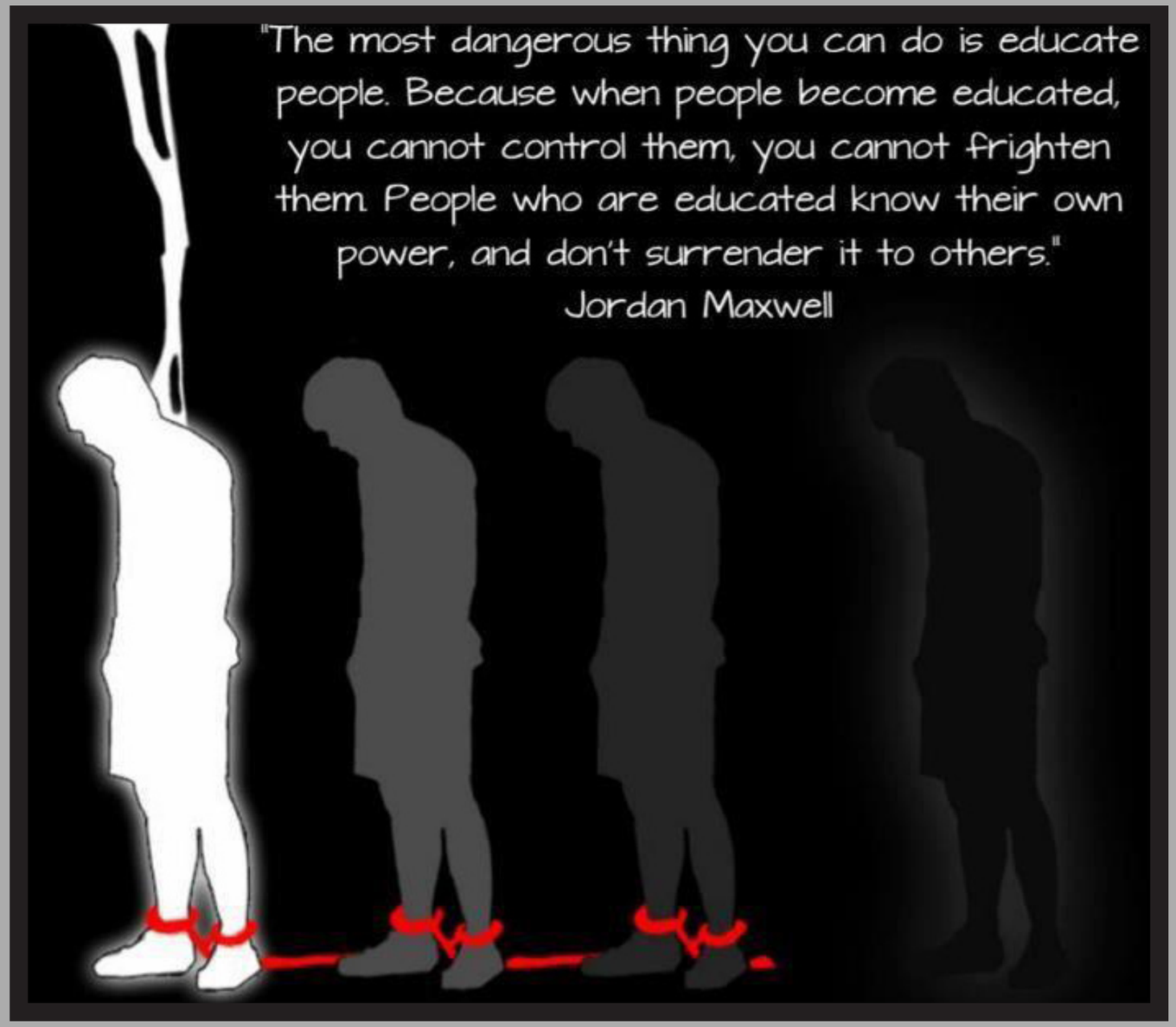


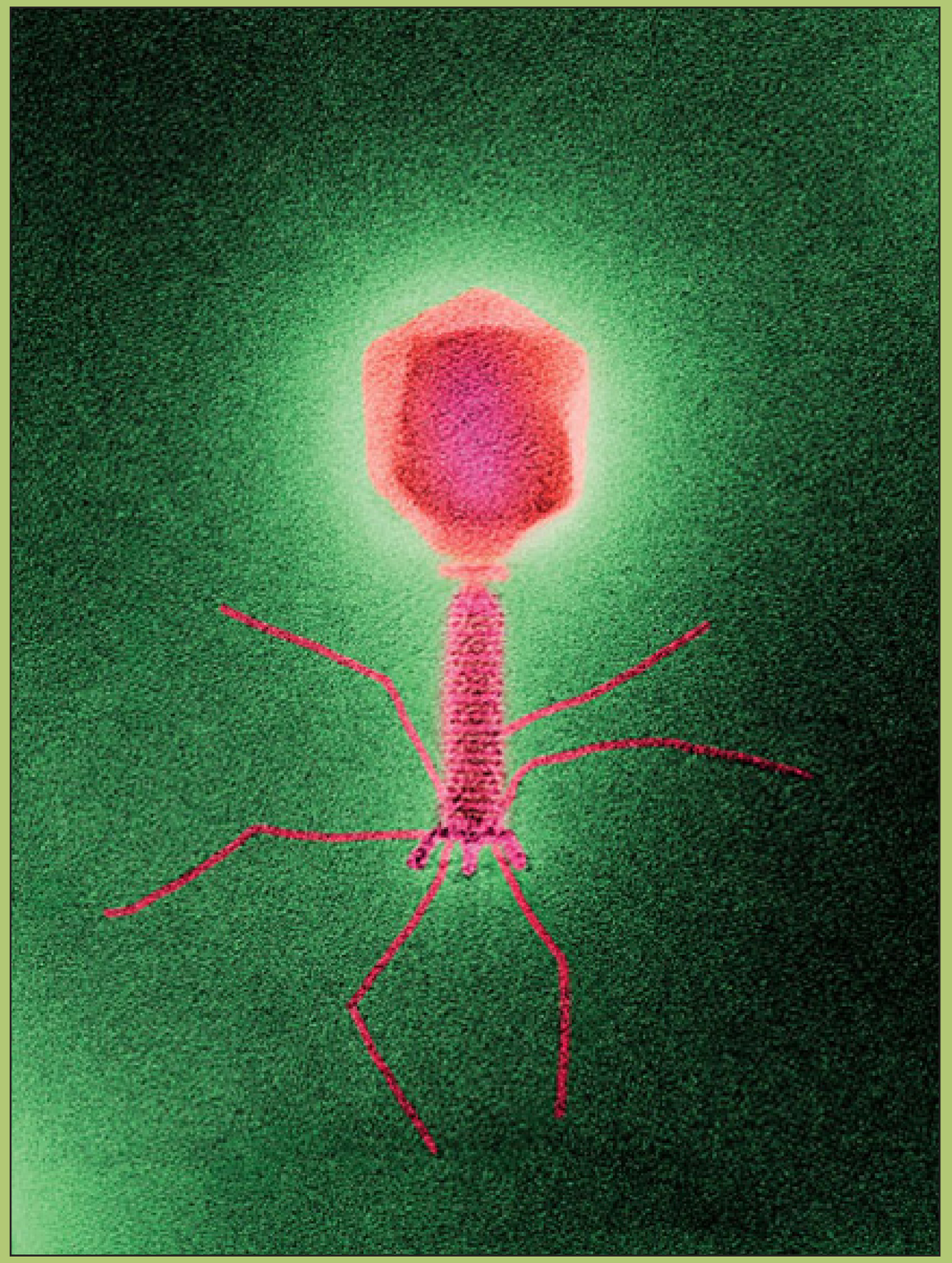
plines. Its report, The Case for a GM-Free Sustainable World, calling for a ban on GM crops and a comprehensive shift to sustainable agriculture was presented in the UK Parliament and European Parliament, circulated worldwide, and translated into 5 or more languages.

Sustainable World Global Initiative, launched April 2005, http://www.i-sis.org.uk/SustainableWorldInitiativeF.php, held its first international conference 14/15 July 2005 in UK Parliament, followed by a weekend workshop 21 January 2006, out of which came a proposal for an innovative food and energy self-sufficient 'Dream Farm 2' for demonstration/education/research purposes. Its first report, Which Energies?, appeared in 2006, followed by a second definitive report, Food Futures Now (2008) showing how organic agriculture and localized food and energy systems can provide food and energy security and free us from fossil fuels. The third and final report, Green Energies - 100% Renewable by 2050 (2009) was also launched in UK Parliament November 2009, and struck a chord among politicians and opinion formers. It marksthe turning point in the world's commitment to green renewable energies.Reclaiming Beauty and Truth in Science and Art, was launched in a unique art/science event 26-27 March 2011, when a wholefoods factory was transformed overnight into an art gallery and music/lecture hall around the theme of 'quantum jazz', the sublime aesthetics of quantum coherence in living systems and the living universe http://www.i-sis.org.uk/Avant_Garde_ArtScience_Event.php. The event was marked by a commemorative volume of essays and artworks, Celebrating ISIS, Quantum Jazz Biology *Medicine*Art, a Quantum Jazz Art DVD of artworks with a special selection of music, plus four DVDs of performances and interviews at the actual event itself. Our second act was an extended art/science/music festival, Colours of Water, 12-28 March 2013, a resounding success featuring an amazing cast of scientists, artists, musician, and other social leaders from around the world, all inspired by water and aiming to raise awareness on sustainable water use and conservation. (http://www.i-sis.org.uk/coloursofwater/). Surg Clin North Am. 2011 Aug;91(4):771-85, viii. doi: 10.1016/j.suc.2011.05.001.

Bacteriophage

These bacteria-infecting viruses *(pictured at right)*, phages for short, are the most abundant life-form on the planet, their number far exceeding that of stars in the universe. Trillions inhabit each of us.

A bacteriophage is a virus that infects and replicates within a bacterium. The term is derived from "bacteria" and the Greek 'phagein', "to devour". Bacteriophages are composed of proteins that encapsulate a DNA or RNA genome, and may have relatively simple or elaborate structures. Their genomes may encode as few as four genes, and as many as hundreds of genes. Phages replicate within the bacterium following the injection of their genome into its cytoplasm. Bacteriophages are among the most common and diverse entities in the biosphere. Phages are widely distributed in locations populated by bacterial hosts, such as soil or the intestines of animals. One of the densest natural sources for phages and other viruses is sea water, where up to 9×108 virions per milliliter have been found in microbial mats at the surface and up to 70% of marine bacteria may be infected by phages. They have been used for over 90 years as an alternative to antibiotics in the former Soviet Union and Central Europe, as well as in France. They are seen as a possible therapy against multi-drug-resistant strains of many bacteria.

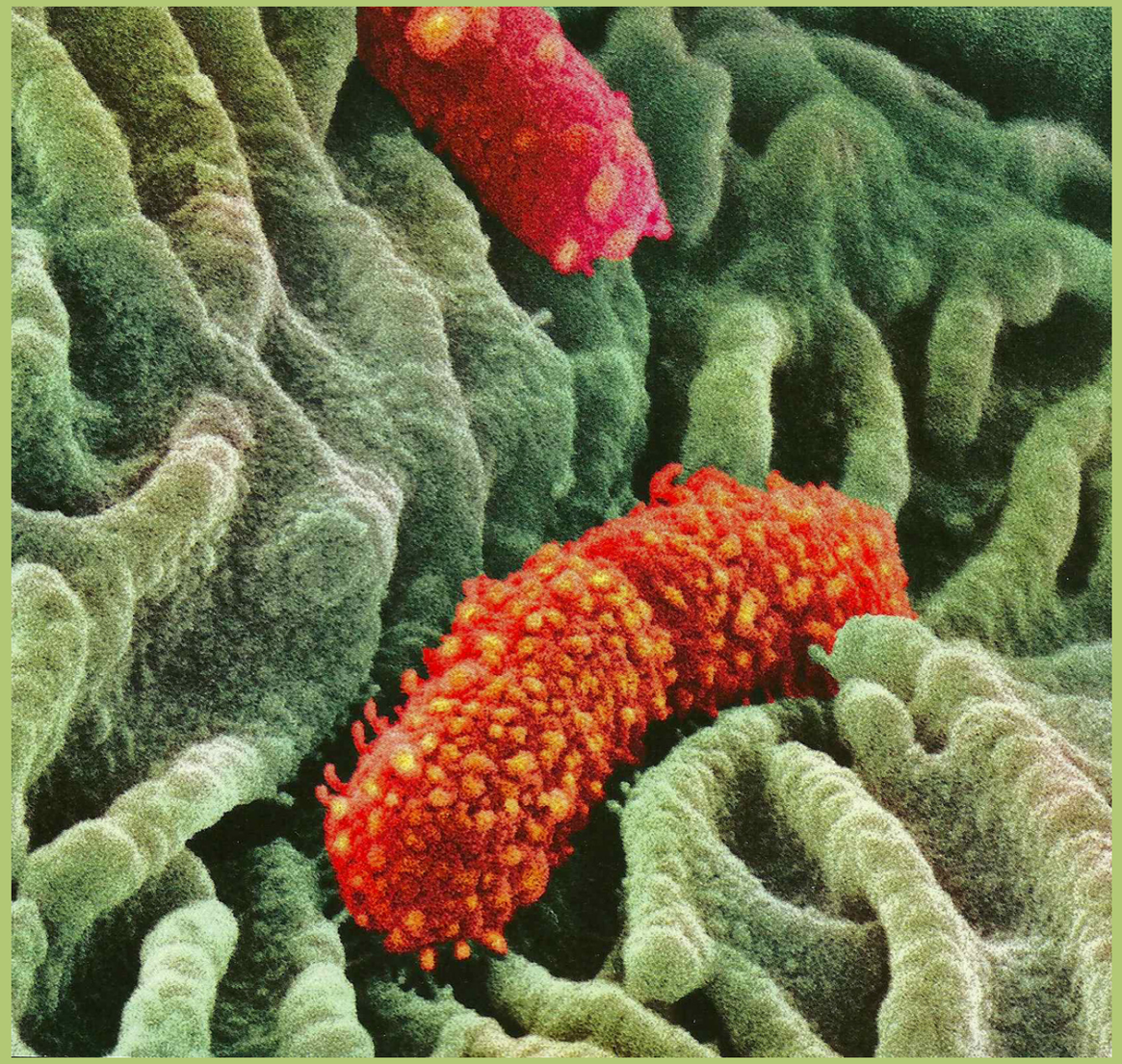


There's Usually A Reason For Everything

by Jeff Prager

This uncontested, published, peer reviewed report is included here to help the reader understand several aspects of the GMO contribution to human illnesses and disorders of every shape and size. We won't be discussing the effects of glyphosate and other environmental chemicals that affect other mammals, birds, rodents or any of the 1.5 million known and named species. This report will also help to describe the fact that the science of the gut microbiome is new and we know very little about how the gut microbiome is affected by anything—food, vitamins, vaccines, GMO food, food additives, chemical pollution—and anything else that might affect it. And oc course we know just as little about how the gut microbiome affects everything else. In fact, we're just learning about our external microbiome, the bacteria that live on our skin.

There are calculated to be somewhere between 10 and 100 trillion bacteria in your gut—over 1000 different types—and internal organs. There are even bacteria living in your heart and lungs. Your gut bacteria is alone is estimated to weigh between 2 and 4 pounds and interestingly, your gut bacteria are responsible for manufacturing certain amino acids that we can't get anywhere else. Regardless of what we eat, we require these gut bacteria to make these chemicals or we'll get sick and possibly even die. So it is critically important that you understand how gut bacteria can be affected, how glyphosate uses the shikimate pathway in your gut bacteria to function (*humans don't have a shikimate pathway so glyphosate was said to be safe but your trillions of gut bacteria, your entire microbiome, has and uses the shikimate pathway*). I hope you'll also learn how glyphosate chelate's minerals and deprives your body of nutrients that are necessary to live a healthy life. I sincerely hope this peer reviewed report helps you because it really helped me.



In a previous post, it was shown that microbes from the gut (*above, in red*) can send factors to the brain, which stimulate BDNF and other signals to make new brain cells, or otherwise. These signals are part of a large network of endocrine cells in the gut sending signals into the blood. These signals can effect the huge vagus nerve and effect changes in the brain. They also regulate local GI function.

Contributions Of Intestinal Bacteria To Nutrition And Metabolism In The Critically Ill

by Morowitz MJ1, Carlisle EM, Alverdy JC.

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Abstract

Important advances in the study of bacteria associated with the human gastrointestinal tract have significant implications for clinicians striving to meet the metabolic and nutritional needs of critically ill patients. This article offers a broad overview of the importance of the host-microbe relationship, discusses what is currently known about the role of gut microbes in nutrition and metabolism in the healthy human host, reviews how gut microbes are affected by critical illness, and discusses interventions that have already been used to manipulate the gut microbiome in patients in the intensive care unit.

Important advances in the study of bacteria associated with the human gastrointestinal tract have significant implications for clinicians striving to meet the metabolic and nutritional needs of critically ill patients. A transition from culture-based to culture-independent studies of the intestinal microbiota has ushered in a new era of laboratory and clinical studies in this field. These studies are helping to clarify the important role of bacteria in carbohydrate metabolism, and are providing new evidence that highlights the role of bacteria in protein and lipid homeostasis. We know that during periods of caloric excess or deprivation, microbial populations in the GI tract are clearly altered; however the molecular etiology for such changes remains elusive. Similarly, little is known about how microbial ecology changes before, during, and after critical illness. Nevertheless, several approaches, e.g. probiotic administration, have been employed to manipulate gut microbial communities in the ICU. In this review we offer a broad overview of the importance of the host-microbe relationship, discuss what is currently known about the role of gut microbes in nutrition and metabolism in the healthy human host, review how gut microbes are impacted by critical illness, and discuss interventions that have already been utilized to manipulate the gut microbiome in ICU patients.

MICROBES AND NUTRITION DURING CRITICAL ILLNESS

It has been known for decades that intestinal bacteria make important contributions to human metabolism and physiology. Perhaps the example best known to clinicians is the microbial synthesis of the essential nutrient vitamin B12 — the enzymes required for B12 synthesis are possessed by bacteria but not by plants or animals [1]. However, research from the past decade has conclusively established that the host-microbe relationship in humans is far more complex than previously appreciated. The implications of this research for assessing and meeting the nutritional needs of critically ill patients are substantial.

The goals of this review are: (i) to offer a broad overview of the importance of the host-microbe relationship, (ii) to detail what is known about the host-microbe relationship with regard to nutrition and metabolism in the healthy host, (iii) to review the scarce existing literature about how microbial ecology changes during critical illness, and (iv) to discuss specific interventions that have been used to manipulate the gut flora to improve patient nutrition and outcomes in the intensive care unit (ICU).

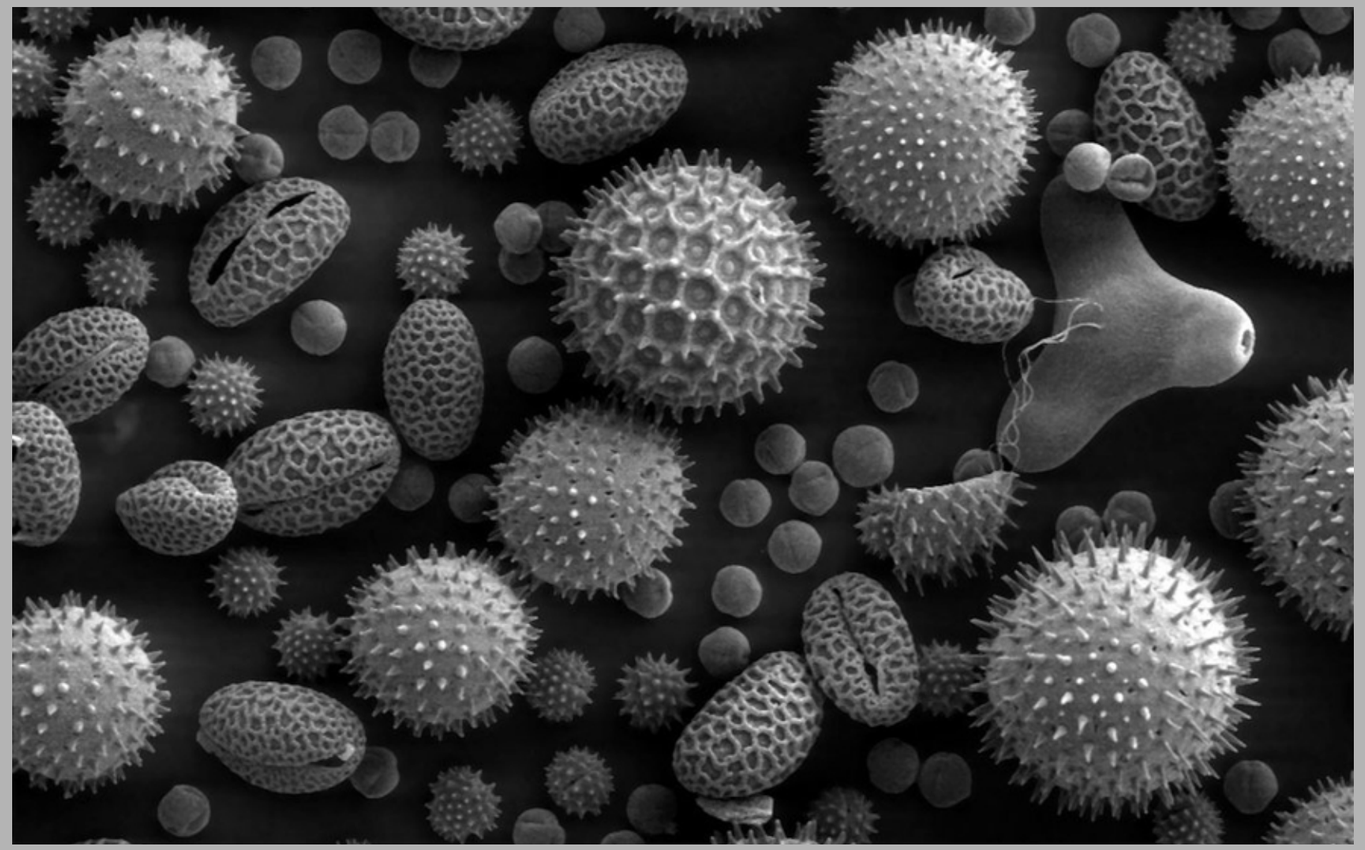
REVOLUTIONARY ADVANCES IN UNDERSTANDING THE HUMAN MICROBIOME

An understanding of the complex relationship between humans and our microbes dates back at least to Pasteur. However, until very recently, the ability of microbiologists and clinicians to characterize and dissect this relationship was hampered by the reality that only a minority of microbes on the planet (and in the human body) can be cultured, isolated, and systematically studied in the laboratory [2]. As a result, most clinical focus on bacteria and

viruses has been directed toward the statistical minority of organisms that cause clinical disease and can be easily isolated in culture.

Over 25 years ago, microbial ecologists conclusively demonstrated that bacterial DNA can be used to identify which organisms are present in a complex biological sample without dependence on cultivating those organisms in the laboratory [3]. Until recently, these culture-independent techniques to characterize microbial diversity were relatively restricted to studies of ocean and soil samples. Over the past decade, concerted efforts have been made to use these techniques to undertake comprehensive molecular surveys of the organisms associated with humans. These efforts have benefited from remarkable advances in DNA sequencing technologies, as well as from well-funded initiatives such as the NIH Human Microbiome Project [4, 5] and its European counterpart MetaHIT [6].

Perhaps the foremost lesson of these recent efforts has been that all humans, both healthy and critically ill, are intimately associated with a vast population of microbial organisms. Uncertainty remains regarding the precise number of bacteria in the human body, but it is generally agreed that there at least 10 bacterial cells for every 1 human cell [7]. This has led authorities in the field to describe humans as "superorganisms" composed of both human and microbial cells [8]. Although clinicians have not historically thought about their patients in this way, it is easy to recognize the evolutionary logic of a symbiotic relationship between humans and microbes. By supporting lifelong colonization by organisms that possess a diverse set of metabolic capabilities, the host effectively augments its own genome; this is a much more efficient arrangement than waiting for humans to evolve new metabolic capacities on their own [9]. In return for their contributions, microbes associated with the body are rewarded with a relatively safe, predictable, and nutrient-rich niche for colonization. As will be discussed in subsequent sections, the impact of critical illness on this symbiotic relationship remains poorly understood.



Genetically engineered to process metals, microbes may assist in processing and mining asteroid materials.

All epithelial surfaces that interface with the external world harbor microbes, but the most dense microbial communities are those in the distal intestinal tract. Recent estimates suggest that 10 to 100 trillion microbes (including up to 1000 species) reside in this location [8, 10]. Remarkably, although more than 70 bacterial divisions (deep evolutionary lineages) are known to exist on the planet, human gut microbial communities are dominated by just four lineages. Two dominant divisions, the Bacteroidetes and the Firmicutes, comprise over 95% of the total community; most of these organisms are strict anaerobes such as the Bacteroides and Clostridium species [11]. The remainder of human gut microbes are often from two other divisions: Actinobacteria (e.g., Bifidobacterium species) and Proteobacteria. The phylum Proteobacteria contains the gram-negative enterics that despite being well known to clinicians, represent only a fraction of the gut microbial community [11]. The dominance of these four bacterial phyla and the relative absence of all other phyla suggests that, under normal circumstances, the human-microbe relationship is highly selective and highly stable. Throughout most of a person's life, this relationship is either symbiotic (mutually beneficial) or commensal (providing benefit to one member without harming the other); pathogenic host-microbe interactions are indeed the exception rather than the rule [9].

There is currently enormous interest in characterizing the clinical relevance of the human microbiome (defined as the collective set of microbial genomes associated with the human body). In addition to the GI tract, important sites of colonization also under study include the skin, oropharynx, respiratory tract, and genitourinary tract. A primary objective of current research is to better define the basic features of the human microbiome, e.g., how do microbial communities change over time in a given individual and how much interindividual variability is observed in various microbial communities? An equally important objective is to identify associations between the microbiome and human health and disease [12].

SPECIFIC CONTRIBUTIONS OF THE GUT MICROBIOTA TO HUMAN METABOLISM

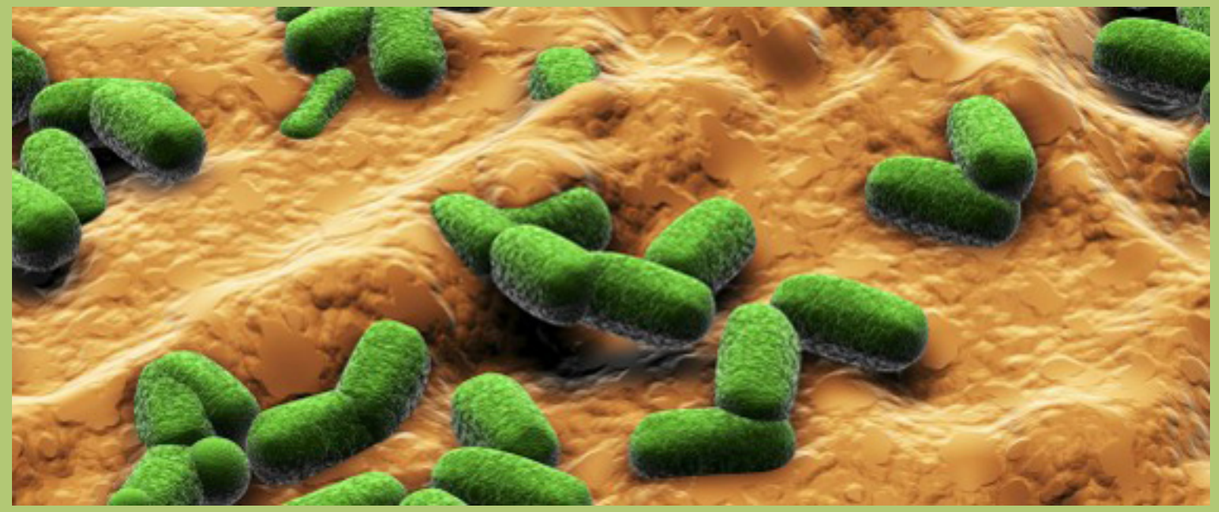
A particularly compelling example of the importance of the gut microbiota to host metabolism is provided by comparing the nutritional status of germ-free (GF) and conventionally raised laboratory animals. Numerous investigators have demonstrated that conventionally raised animals require up to 30% less caloric intake to maintain their body weight [9]. This remarkable observation is not only surprising; it is also counterintuitive since one might reasonably expect that bacteria and their human host may compete for a limited supply of ingested nutrients. In this section, we summarize what is known about how microbes directly impact human nutrition.

Microbiota and carbohydrates

The sophisticated relationship that has evolved between the human GI tract and gut microbiota allows for efficient utilization of dietary carbohydrates. In the proximal GI tract, simple sugars such as glucose are absorbed, and disaccharides (e.g., lactose) are hydrolyzed into their corresponding monosaccharide components such that they too can be absorbed [9]. However, a significant portion of dietary carbohydrates, including complex plant-derived polysaccharides and unhydrolyzed starch, normally passes undigested through to the distal GI tract [13]. Here, dense microbial populations (up to 1011 cells per gram of colonic matter) are present that are well-equipped to hydrolyze complex carbohydrates. Many of the enzymes required to utilize these dietary substrates are not encoded in the human genome; by contrast, the microbiome, which contains approximately 100x more genes than the human genome, is highly enriched in such enzymes [9].

Utilization of complex polysaccharides via fermentation by anaerobic bacteria in the large intestine results in the accumulation of short chain fatty acids (SCFA) [14]. The principal SCFAs seen in the colon, acetate, propionate, and butyrate, have inherent nutritional value, but also impact gut epithelial physiology in other ways. They are ab-

sorbed by passive diffusion across the colonic epithelium, and are subsequently utilized by different organs. Acetate, the SCFA produced in highest concentration, is used by skeletal and cardiac muscle and can be used by adipocytes for lipogenesis. Butyrate is metabolized primarily in the gut epithelium to yield ketone bodies or CO2 [9]. Interestingly, the colonic epithelium derives up to 70% of its energy needs directly from butyrate. Propionate metabolism is poorly understood but appears to involve transport to the liver by the portal circulation. It is believed that SCFAs also impact water absorption, local blood flow, and epithelial proliferation in the large intestine [9].

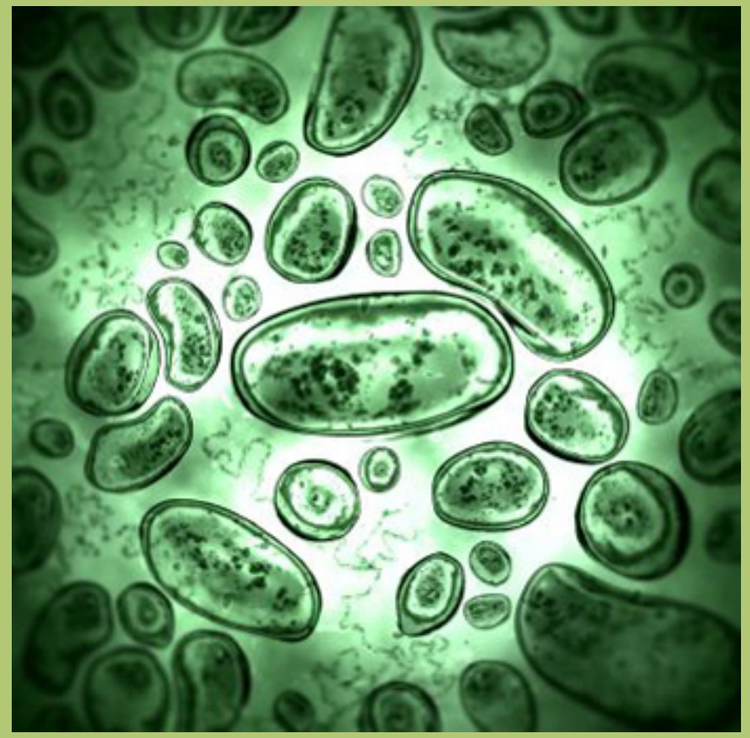


Genomic analysis of gut bacteria offers vivid examples of the role of microbes in nutrient utilization. For example, in 2003, Xu, et al. published the complete genome sequence of the gram-negative anaerobe Bacteroides thetaiotaomicron, a prominent member of the normal intestinal microbiota [10]. Annotation and analysis of the genome revealed a sophisticated apparatus for acquiring and digesting otherwise unusable dietary polysaccharides. This apparatus, including a complex, multi-component, multi-enzyme complex starch utilization system (SUS), consists of over 230 glycoside hydrolase and 15 polysaccharide lyase genes [15]. The genomic analysis demonstrated that B. thetaiotaomicron has evolved the remarkable capacity to sense the availability of carbohydrates in its microenvironment, and that it also has the ability to forage and utilize host-derived glycans (e.g., mucin and heparin). Mechanistic studies in gnotobiotic animals further demonstrated that, when B. thetaiotaomicron senses a scarcity of fucose in the intestinal lumen, it actually induces the gut epithelium to upregulate expression of fucosylated glycans that can be used by the bacteria as an energy source without harming the host [16]. This body of work illustrates how the remarkable host-microbe symbiosis can be teased apart by pairing genomic sequencing efforts with creative in vivo laboratory studies.

Microbiota and protein metabolism

In contrast to carbohydrates, relatively little attention has been paid to the relationship between the intestinal microbiota and nitrogen balance in humans. This is partly because conventional wisdom states that all essential amino acid requirements in humans must be supplied by the diet [17]; however, emerging evidence indicates that gut microbes can impact nitrogen balance by de novo synthesis of amino acids and intestinal urea recycling. These contributions are most pronounced in ruminant animals that, amazingly, can live on a protein-free diet because their microbiota is capable of synthesizing most or all amino acids required for survival.

Microbial synthesis of essential amino acids has been notoriously difficult to measure in humans, but studies with radiolabelled tracers, e.g., 13C and 15N, indicate that the intestinal microbiota makes a measurable contribution to the pool of essential amino acids. A series of experiments involving labeled inorganic nitrogen suggests that up to 20% of circulating lysine and threonine in nonruminant mammals, including adult humans, is synthesized by gut microbes [18, 19]. Similarly, Raj, et al. demonstrated that gut microbial synthesis of leucine in adult men was approximately 20% of the dietary amount [17]. Interestingly, another study demonstrated that several substrates required for microbial synthesis of essential amino acids are derived from dietary carbohydrates [20]. Taken together, these studies provide compelling evidence that gut microbes contribute to the circulating pool of essential amino acids. More work is needed to define these contributions in both healthy and undernourished humans.



The intestinal microbiota also contributes to nitrogen balance by participating in urea nitrogen salvaging (UNS) [21, 22]. Elevated urease expression in gut microbes results in metabolism of urea in the GI tract into ammonia and carbon dioxide. Some of the ammonia can be utilized for microbial synthesis of amino acids. Perhaps more importantly, the nitrogen generated during this process (urea nitrogen) can re-enter the host circulation and serve as a substrate for synthetic processes [23]. Interestingly, reduced urea recycling has been reported in GF animals [24] and in humans receiving antibiotic therapy [25]. Furthermore, several reports indicate that regulation of UNS is important in settings of low N intake and high N demand (e.g., during pregnancy and during periods of rapid somatic growth in infancy) [26–28]. While still relatively preliminary, these studies underscore the relationship between gut microbes and protein metabolism that will likely be further described through on-going characterization of the human microbiome.

MICROBIOTA AND LIPID METABOLISM

Until recently, few studies of the association between lipid metabolism and the microbiome existed. However, important research by Jeffrey Gordon, Fredrick Backhed, and colleagues suggests that the body's supply of triglycerides, a prominent source of energy during critical illness [29], is tightly linked to the intestinal microbiota. These findings have enormous potential relevance for research in a wide range of disease states, including metabolic disorders such as obesity (see below) and cardiovascular disease.

This line of inquiry began with comparisons of lipid metabolism in GF and conventionally-raised adult mice. By use of x-ray absorptiometry and epididymal fat pad weight analysis, it was demonstrated that wild-type (WT) animals contained 42% more total body fat than GF animals, despite a higher metabolic rate and a reduced daily consumption of standard chow [30]. To mechanistically evaluate this finding, the authors transferred the microbiota of WT animals to GF animals. A rapid increase (within 10 days) of total body fat content and epididymal fat weight was noted despite no significant difference in total body weight. Intriguingly, colonization of GF mice with just a single gut microbe (B. thetaiotaocmicron, discussed above) also yielded a significant increase in total body fat content, although the increase in fat content was less than that seen with transfer of the complete mouse microbiota. Further work in this model suggested that the microbiota stimulates increased hepatic triglyceride production and promotes storage of adipocyte triglycerides by suppressing the activity of a circulating inhibitor of lipoprotein lipase [30].

These pioneering studies have led to a sustained effort to understand the relationship between the microbiota and adiposity. In one interesting experiment, GF mice were colonized with gut bacteria from humans fed with a typical Western diet

(high fat, high carbohydrate), and a similar increase in adiposity was seen in the GF mice [31]. Other experiments that analyzed the lipids present in the serum and adipose tissue of WT and GF mice show that WT animals had elevated levels of 18 phosphatidylcholine species and decreased levels of nine triglyceride species relative to GF animals [32]. Alternatively, in the adipose tissue the concentration of most phosphatidylcholine compounds was similar between the two groups, but an increased concentration of triglycerides was detected in WT animals. Even more between group differences were detected in the liver lipid profiles. For example, in addition to numerous differences in cholesteryl ester and phosphatidylcholine species, WT mice had a significant increase in 95 types of liver triglycerides. The translational relevance of these findings must still be defined, but these results provide clues to the role of microbes in lipid metabolism.

Vitamins

Most human diets provide a robust supply of vitamins, the essential human nutrients that must be obtained from exogenous sources. However, it has long been recognized that gut microbes also contribute to vitamin synthesis. The magnitude of this contribution in healthy and unhealthy patients is currently poorly understood.

It has been known for nearly a century that ruminants have no dietary requirement for water-soluble vitamins as a consequence of the dense microbial populations in the rumen, and that GF laboratory animals require dietary supplements of vitamins that are not needed by their WT counterparts [33]. Several bacterial genera that are common in the distal intestine (e.g., Bacteroides, Bifidobacterium, and Enterococcus) are known to synthesize vitamins. Thiamine, folate, biotin, riboflavin, and pantothenic acid are water-soluble vitamins that are plentiful in the diet, but that are also synthesized by gut bacteria. Likewise, it has been estimated that up to half of the daily Vitamin K requirement is provided by gut bacteria [33]. Interestingly, the molecular structure of bacterially synthesized vitamins is not always identical to the dietary forms of the vitamins. In fact, several specialized epithelial transporters have been recognized to participate specifically in the absorption of vitamins derived from gut bacteria [34]. Perhaps the relative ease in replenishing vitamin stores in ICU patients has minimized enthusiasm for aggressive investigation of how bacterial vitamin biosynthesis is altered in hospitalized patients.

LESSONS LEARNED FROM STUDIES OF NUTRIENT EXCESS AND DEPRIVATION

Studying the relationship between the gut microbiota and energy balance in the extreme states of obesity and starvation may improve our ability to assess and satisfy nutritional needs in the ICU.

OBESITY

Studies of energy balance in conventional and GF animals led to the hypothesis that the microbial ecology of the GI tract contributes to the pathogenesis of obesity [35]. Although it is widely acknowledged that excessive caloric intake is the root cause of obesity, it is reasonable to question whether an individual's metabolic response to caloric excess might vary according to the gut microbiota. Much of the work in this area has relied upon a rodent model of obesity in which animals homozygous for a mutation in the leptin gene (ob/ob) harbor a fully penetrant obese phenotype [36]. Early studies utilizing 16S ribosomal RNA based genetic sequencing identified that obese animals have a markedly decreased abundance of Bacteroidetes organisms (such as B. thetaiotaomicron) and a corresponding increase in Firmicutes [36]. Obese mice also possessed an abundance of methanogenic organisms from the domain Archaea, and it is believed that these organisms can aid in bacterial fermentation in the gut via removal of H2 [37]. The microbial differences observed in these experiments were division wide,

Macrophages attacking e. coli

i.e., not skewed by the presence or absence of a single species. Further, the differences could not be explained by differences in food consumption. Of central importance, corresponding studies have shown similar features of the gut microbes in obese humans [38, 39].

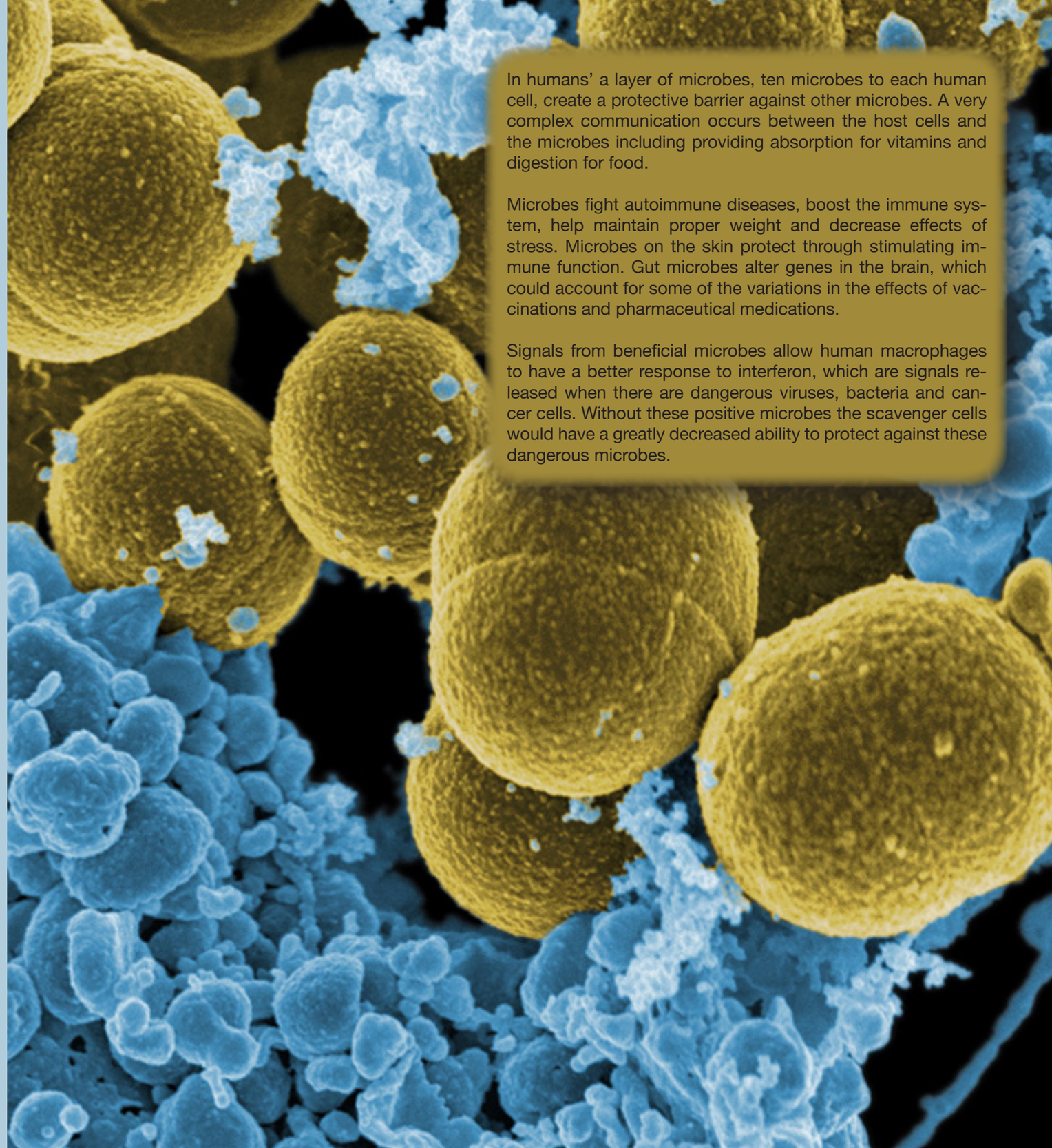
Why would a microbial community enriched in Firmicutes promote obesity? Recent work has suggested that the microbiota of obese individuals has an increased capacity to harvest energy from the diet [35]. Landmark papers, utilizing high-throughput metagenomic sequencing platforms to identify as many genes as possible from all members of a mixed population of bacteria, from Gordon, Turnbaugh, Ley and colleagues, have conclusively demonstrated that the metabolic potential of the gut microbiome varies according to the microbial community composition. Molecular analysis of the microbiota of lean and obese mice demonstrated that the obese microbiome is markedly enriched in genes enabling breakdown of dietary polysaccharides, e.g., glucosidases, galactosidases, and amylases, and genes encoding proteins that transport and metabolize the products of polysaccharide metabolism [37]. Biochemical and bomb calorimetry analyses in the same experiments demonstrated increased concentrations of SCFA's (indicating a higher degree of bacterial fermentation) and significantly less energy remaining in the feces of obese mice relative to their lean counterparts [37]. Finally, these phenotypic traits were transmissible; colonization of GF animals with the microbiota of obese animals led to higher weight gain than colonization with microbiota from lean WT mice.

Turnbaugh, et al. have advanced these ideas even further by demonstrating that the microbiome associated with diet-induced obesity (DIO) (in contrast to the ob/ob mutant model) is also rich in Firmicutes species and is similarly efficient at extracting energy from the diet [31]. This set of experiments utilized a mouse model of DIO in which conversion to a high fat/high sugar (Western) diet reliably produces increased total body weight and increased epididymal fat content. The authors demonstrated that DIO alters gut microbial ecology by supporting the growth of Firmicutes species, and, in this case, they detected a specific association between obesity and the abundance of a class of organisms (Mollicutes) from the Firmicutes division that has also been identified in humans. Transplantation of cecal contents from DIO mice, similar to experiments with the ob/ob mice, yielded higher increases in body weight and fat than when cecal contents were transplanted from lean, WT animals. Here, again, metagenomic analyses were used to prove that the gut microbiome of animals fed a Western diet is enriched in genes encoding proteins related to energy harvest, including phosphotransferase proteins that enable the transport of simple sugars such as glucose and fructose.

A critical lesson from this body of work is that alterations in the microbiome of obese individuals are reversible. Early on, Ley, et al. demonstrated that the ratio of Firmicutes to Bacteroidetes species decreases over time in humans on either a fat-restricted or carbohydrate-restricted diet [39]. This was subsequently supported by Turnbaugh's findings that the bloom in Mollicutes seen in DIO was reversible with dietary manipulation [31]. Additional studies monitoring changes in the microbiota after surgical and non-surgical weight loss interventions have produced similar findings [40–42].

FASTING

Because caloric excess and obesity are associated with an altered gut microbiota, a corollary hypothesis is that the mirror-image pattern of alterations would be observed during periods of nutrient deprivation. This question is central to the issue of whether the host-microbe relationship might be exploited to improve the nutritional status of critically ill patients. Surprisingly, relatively little is known about the impact of short and long term fasting on the gut microbiota.



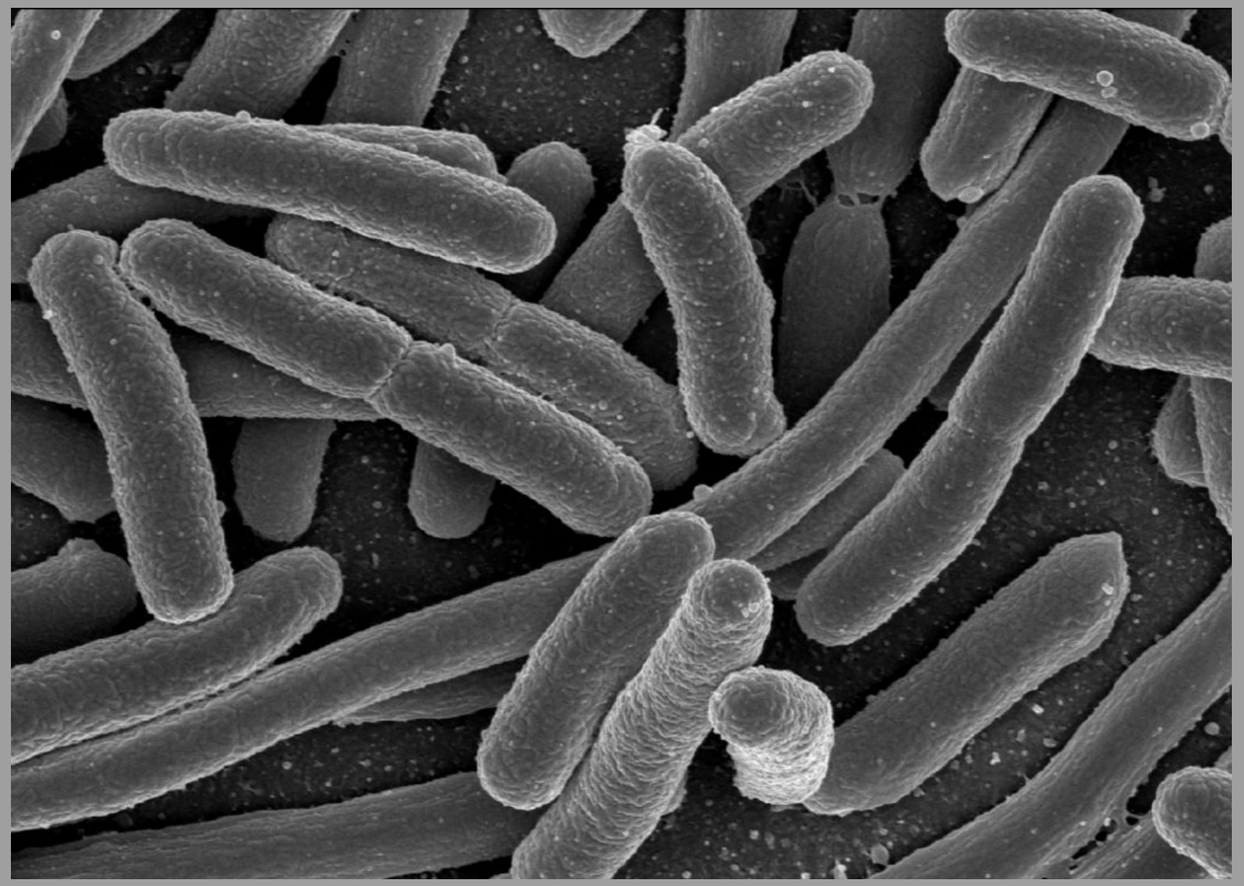
In humans' a layer of microbes, ten microbes to each human cell, create a protective barrier against other microbes. A very complex communication occurs between the host cells and the microbes including providing absorption for vitamins and digestion for food.

Microbes fight autoimmune diseases, boost the immune system, help maintain proper weight and decrease effects of stress. Microbes on the skin protect through stimulating immune function. Gut microbes alter genes in the brain, which could account for some of the variations in the effects of vaccinations and pharmaceutical medications.

Signals from beneficial microbes allow human macrophages to have a better response to interferon, which are signals released when there are dangerous viruses, bacteria and cancer cells. Without these positive microbes the scavenger cells would have a greatly decreased ability to protect against these dangerous microbes.

In 1968, Tennant, et al. demonstrated that GF mice do not survive as long as WT mice during starvation despite similar patterns of starvation-induced weight loss. However, this group did not characterize the microbiota of the WT animals [43]. In 1974, Tannock and Savage used a culture-based approach to characterize the intestinal bacteria of mice exposed to a stress model that included deprivation of food, water, and bedding for 48 hours[44]. They concluded that stressed animals had a reduction in Lactobacilli and total mucosal-associated bacteria relative to control animals, but maintained a similar number of colonic anaerobes. In 1989, Deitch, et al. similarly reported that starvation induced a decrease in Lactobacilli in the murine GI tract, however they noted a bloom of gram-negative enteric organisms. Subsequently, several studies have contrasted gut microbes in newborn animals receiving either enteral or parenteral nutrition. These studies suggest that TPN-fed animals have an increased relative abundance of potential pathogens, such as Clostridium perfringens, that can forage on glycans lining the gut epithelium [45, 46]. However, it is not known if these findings can be extended to critically ill adults that have shifted abruptly from the fed to the fasting state.

Two recent studies harnessed the power of high-throughput DNA sequencing to profile changes in microbial ecology during fasting in animal models. Crawford, et al. performed a fascinating study of myocardial ketone body metabolism by the intestinal microbiota during nutrient deprivation [47]. After a 24 hour fast, the authors observed a significant increase in the abundance of Bacteroidetes species and a corresponding decrease in Firmicutes; this is the converse of what was observed in models of caloric excess. They proceeded to provide convincing evidence that the microbiota plays an integral role in fasting-induced hepatic ketogenesis, an important energy source during stress and starvation. In GF animals, ketogenesis was markedly reduced, and it was shown that myocardial metabolism was redirected towards glucose utilization. To understand further how microbial ecology is altered during fasting, Costello, et al. performed an innovative study in which they studied the Burmese python, a vertebrate that consumes large meals between long intervals of fasting [48]. These authors also demonstrated an abundance of Bacteroidetes during fasting that shifted towards a post-prandial abundance of Firmicutes. Species that were enriched in the post-prandial state included Clostridium and Lactobacillus. These innovative studies serve as a foundation to study gut microbes in hospitalized patients that are not candidates for enteral nutrition.



EscherichiaColi: Scanning electron micrograph of Escherichia coli, grown in culture and adhered to a cover slip. Escherichia coli, one of the many species of bacteria present in the human gut

WHAT HAPPENS TO THE MICROBIOME DURING CRITICAL ILLNESS?

High-throughput culture-independent techniques have not yet been widely applied to study how the human microbiome changes during critical illness. However, several clinical trials have evaluated strategies to manipulate the gut flora without thoroughly assessing the microbiome before or after therapy. Given the emerging evidence that the microbiota contributes to normal physiology, it stands to reason that therapeutic attempts to eradicate pathogens might be coupled with attempts to restore the "normal" microbiota. For example, the above discussion suggests that optimizing the balance between Bacteroidetes and Firmicutes is a promising, but untested, strategy to improve energy balance among the critically ill.

To date, evaluations of the microbial ecology of the ICU have largely been restricted to culture-based studies. Not surprisingly, studies frequently demonstrate that patients admitted to the ICU are rapidly colonized with opportunistic pathogens [49–52]. It has also been shown that pathogens detected by routine surveillance of the airways or the GI tract can serve as harbingers of an ensuing clinical infection by that organism [53, 54]. Frequently encountered organisms in skin, oropharyngeal, endotracheal, and fecal samples from critically ill patients include the gram-negative enterics as well as species of Candida, Pseudomonas, and Staphylococcus. However, it is critical to emphasize that the fate of commensal organisms, many of which serve beneficial purposes, in the ICU is poorly understood. For this reason, a trial with prospective monitoring of the microbiome in ICU patients with comprehensive culture-independent techniques is needed.

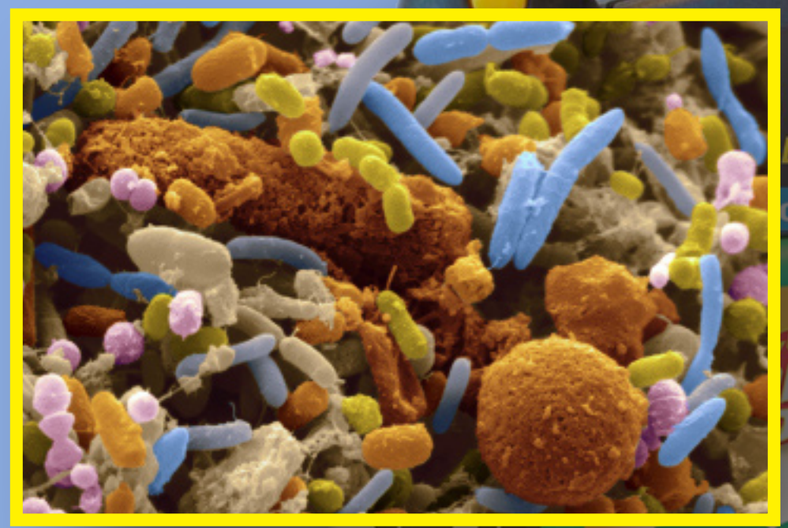
Although we lack a comprehensive molecular readout of gut microbes in the ICU, several human and animal studies provide clues about how the microbiota is altered by common ICU exposures. Several excellent studies have demonstrated that the pervasive, site-specific, and drug-specific effects of antibiotic therapy on the microbiota can be long-lasting [55–57]. Multiple host factors relevant to the critically ill, including epithelial inflammation and hypoxia, are also known to perturb the microbiota and encourage the overgrowth of pathogens [58, 59]. Some of the most commonly used pharmaceutical agents in the ICU, including acid suppression therapies, vasopressors, and opioids, are known to impact the human microbiota [60, 61]. Finally, our group was the first to demonstrate that the use of total parenteral nutrition or enteral nutrition with processed liquid diets dramatically alters the intestinal microbiota such that bacterial translocation to extraintestinal sites is promoted. As the effects of artificial nutrition, polypharmacy, and the selective pressures of extreme physiologic stress and injury accumulate over the course of critical illness, their impact on the ecologic health of the intestinal microbiota is likely to have a major untoward effect on recovery. Clinical interventions that can preserve gut microbial communities such that a benefit in overall recovery is realized will require more in-depth analysis of the direct impact of these interventions on the gut flora.

SELECTIVE MANIPULATION OF THE GUT MICROBIOTA IN THE ICU

If one accepts that a "healthy" intestinal microbiota serves important biological functions, then it is reasonable to hypothesize that gut microbial communities can be manipulated or "optimized" during critical illness to increase the chances of achieving desired clinical outcomes. In theory, manipulation of the gut microbiota could be used to improve energy balance and decrease the incidence of infectious complications. A fundamental problem with clinical application of this theory has been that we lack a detailed understanding of if and how the microbiome is

altered during critical illness. As a result, interventions in this field have been introduced with a limited scientific foundation. Nonetheless, several strategies to optimize the microbiome have now been evaluated clinically. Some, such as the recent description of fecal transplantation for Clostridium difficile colitis [62], will not be discussed here. Others with obvious relevance to nutrition are discussed.

Over the past two decades, several clinical trials have documented that selective decontamination of the gastrointestinal tract and/or the oropharynx improves outcomes in critically ill patients while simultaneously promoting the growth of antibiotic resistant bacteria [63]. Accepted approaches to decontamination consist of administering a regimen of broad-spectrum nonabsorbable antibiotics that theoretically spares the colonic anaerobes, and instead targets yeast, gram-negative pathogens (e.g., the Enterobacteriaceae and Pseudomonas aeruginosa), and gram-positive pathogens (e.g., Staphylococcus aureus) in the oral cavity or the GI tract. These protocols drastically alter the ICU microbiota [63], and by extension decrease both mortality and the incidence of infectious complications such as ventilator-associated pneumonia [51, 64, 65]. Importantly, although these landmark studies serve as proof of principle that the intestinal microbiota can be manipulated in the ICU to achieve desirable outcomes, no studies utilized molecular techniques to profile the ICU microbiome before, during, or after decontamination. As a result, a precise understanding of how decontamination protocols work is lacking. Nevertheless, enthusiasm for decontamination protocols has diminished due to unacceptable increases in drug-resistant bacterial strains within the ICU.



PROBIOTICS

The administration of probiotics and prebiotics represents an increasingly popular alternative to gut decontamination protocols. Probiotics are defined as live microorganisms that confer health benefits upon humans and animals that ingest them in adequate amounts [66]; prebiotics are nondigestible food ingredients that confer health benefits by selectively inducing the growth of probiotic species [67]. Commonly, probiotics and prebiotics are administered together as a food or dietary supplement known as a synbiotic [67]. Although trials in a wide range of clinical settings have demonstrated great promise regarding the safety and efficacy of these supplements [67]), many critical issues pertaining to their usage remain unresolved. Interestingly, despite the fact that they are often used to treat patients with disease, probiotics and prebiotics are viewed by regulatory agencies as nutritional supplements rather than as pharmaceutical agents or biohazards. This definition has allowed for lax oversight in the field which has resulted in the commercial use of the terms probiotics and prebiotics even when scientific criteria for the terms have not been met [67].

The practice of administering live microbes with putative health benefits to unhealthy patients dates back to the early twentieth century. Much of the early work in the field was performed at the Pasteur Institute in Paris, where Nobel laureate Eli Metchnikoff and others advanced the notion of a differential gut microbiota in health and disease [68]. These scientists hypothesized that the protective effects of specific diets in some regions of Europe could be attributed to the diet-induced growth of beneficial microbes. Interestingly, this led almost instantly to commercial attempts to capitalize upon these ideas, hence the development of probiotics. The most commonly used probiotic species are nonpathogenic yeasts and organisms from the genera Lactobacillus and Bifidobacterium [69]. The most commonly used prebiotics are the naturally occurring oligosaccharides known as fructans that are normally found in foods such as garlic, artichokes, and bananas [67]. Another well-studied class of prebiotics is resistant starches, such as those found in unripe bananas and raw potatoes. As knowledge of the intestinal microbiome expands, it is likely that many more potential probiotic species and prebiotic supplements will be identified. The long list of clinical diagnoses that have been treated with probiotics and/or prebiotics ranges from intestinal infections (e.g., rotavirus infection) to extraintestinal infections (e.g., urinary infections) (cite) to allergic disorders (e.g., asthma); in other cases, these agents have been used prophylactically, e.g., to prevent colon cancer[66]. The strongest clinical data comes from trials of probiotics and prebiotics in the treatment of

intestinal infections, inflammatory bowel disease, and irritable bowel syndrome [69]. Despite their widespread usage, knowledge of the putative mechanism of action of probiotics and prebiotics is limited. Most mechanistic studies in this area have centered upon production of antimicrobial substances to inhibit colonization by pathogens, enhance the mucosal barrier function, and downregulate mucosal inflammation [69]. It is particularly interesting that, despite the growing awareness of how gut microbes contribute to energy balance and despite the administration of probiotics/prebiotics as nutritional supplements, little research on this topic has focused on how these agents specifically impact nutrition, metabolism, or energy balance.

Several studies have been conducted to test the hypothesis that outcomes in critically ill patients can be improved by administering probiotics and prebiotics. These studies, including a randomized trial comparing the effects of early enteral nutrition with and without prebiotic supplementation, indicate that the incidence of sepsis and multi-organ dysfunction syndrome among patients with severe pancreatitis is lower after treatment with probiotics/prebiotics [70]. However, in 2008, the Dutch Acute Pancreatitis Study Group released results of a well-publicized multicenter, randomized, controlled study demonstrating increased mortality among patients with severe acute pancreatitis that received probiotic prophylaxis.

The increased mortality was attributed to a high incidence of intestinal ischemia, although a direct link between the probiotic and bowel ischemia was not proven [71]. A subsequent meta-analysis concluded that probiotics do not influence mortality in the treatment of acute pancreatitis [72], however, the results of the Dutch study have raised important questions about the whether and how probiotics should be administered to vulnerable populations. Nonetheless, several other studies conducted in surgical and medical ICUs, document improved outcomes after probiotic administration following trauma, liver transplant, and ICU admission for severe sepsis [73].

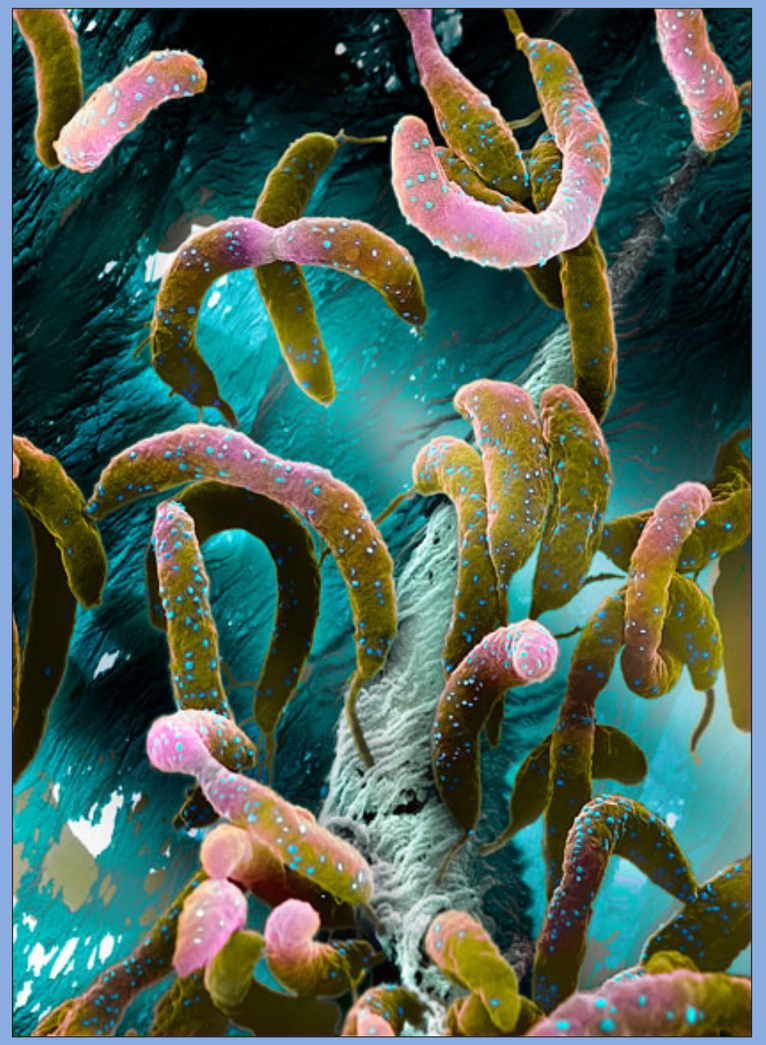
As noted, data regarding the safety and efficacy of probiotic and prebiotic administration are limited. Potential safety issues involved with manipulation of the microbiota with probiotics/prebiotics include probiotic-induced disease and antibiotic resistance [73]. Even if questions remain about efficacy and optimal route of delivery, it is generally accepted that probiotic administration in healthy individuals is safe. However, there is little understanding of how to approach these issues in the ICU. While probiotics have indeed been safely administered to vulnerable hospitalized populations such as neonates and transplant recipients, the significance of the results of the Dutch pancreatitis study cannot be overemphasized. They serve as a powerful reminder of the seemingly obvious fact that administering live microbial organisms to unhealthy patients might be dangerous, particularly when so little is known about the putative mechanism of action. The importance of exercising caution is further underscored by the scant federal regulation of commercial interests in this area.

MODULATING THE LOCAL GUT MICROENVIRONMENT

Another possible approach to improve outcomes for critically ill patients is to manipulate the intestinal microenvironment to maintain the local microbial ecology of the GI tract indirectly. It is well established that the use of vasoactive pressors, antibiotics, and highly processed nutrients will change not only the local microbiota, but also pH, oxygen tension, SCFA production, and various critical micronutrients that maintain the health of normal intestinal microbes. Our group and others have shown that maintenance of a more acidic intestinal pH through the course of surgical injury and administration of oral pH solutions enhance local intestinal immunity and prevent lethal gut-derived sepsis [74]). Most recently we have shown that surgical injury causes a rapid depletion of mucus phosphate, thereby inducing certain strains of pathogenic bacteria to upregulate their virulence against the intestinal epithelial barrier [75]. Most bacteria that cause serious infections in ICU patients are equipped with exquisite sensory mechanisms to detect the level of local phosphate concentration.

Phosphate concentration is a key trigger by which bacteria activate their virulence machinery to, in some cases, cause lethal sepsis. When phosphate levels are high at sites of local microbial colonization, such as the intestinal mucus, microbes use the PhoB phosphosensory/phosphoregulatory system to repress virulence activation. However, during phosphate depletion, the PhoB system is derepressed and virulence is activated even to the point of tissue invasion, immune activation, and organ failure [75]. The PhoB and analogous systems are highly conserved among microbes and offer an opportunity for clinicians to understand the precise host signals that trigger microbes to transform from indolent colonizers to lethal pathogens rapidly. We have shown in animal studies that maintenance of local phosphate concentration can suppress virulence activation among highly pathogenic bacteria such as P. aeruginosa even during periods of severe physiologic stress [74].

This also appears to be the case for other pathogens such as C. albicans and E. faecalis (unpublished observations). Therefore, providing therapies at the microenvironmental level could be a novel approach to create molecular diplomacy between pathogen and host through the course of severe physiologic stress such as that which occurs during human critical illness.



Caulobacter crescentus, above, is a Gram-negative, oligotrophic bacterium widely distributed in fresh water lakes and streams. Caulobacter is an important model organism for studying the regulation of the cell cycle, asymmetric cell division, and cellular differentiation.

CONCLUSIONS

The intersection between the microbiome, nutrition, and critical illness will undoubtedly grow more interesting in the coming years. While the studies discussed in this paper provide clear evidence that gut microbes contribute to human nutrition and metabolism, it is too early to know if this information will be translated into meaningful improvements in current practice patterns.

However, it is easy to identify clinical scenarios in critical care that are likely to be impacted by this growing field of study; these topics include achieving positive nitrogen balance, managing hyperglycemia and cholestasis, and reducing the incidence of infectious complications during critical illness.

At present, a few concluding points can be safely made. First, it is apparent that future evaluations of human nutritional status during critical illness should include consideration of the gut microbiota. Second, it will be important to conduct the necessary studies to understand how the microbial ecology of the human body is altered during critical illness. Third, opportunities to manipulate the gut microbes in hospitalized patients are already presenting themselves, and the efficacy of such interventions must be rigorously evaluated by multidisciplinary teams of clinicians and scientists with a solid understanding of microbial behavior.

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Geobacter

Geobacter (*pictured at right)* is a genus of proteobacteria. Geobacter are an anaerobic respiration bacterial species which have capabilities that make them useful in bioremediation. The geobacter was found to be the first organism with the ability to oxidize organic compounds and metals, including iron, radioactive metals and petroleum compounds into environmentally benign carbon dioxide while using iron oxide or other available metals as electron acceptor.

Research on the potential of Geobacter is underway and on-going. Geobacter's ability to consume oil-based pollutants and radioactive material with carbon dioxide as waste byproduct has already been used in environmental clean-up for underground petroleum spills and for the precipitation of uranium out of groundwater. Geobacter metabolize the material by creating pili between itself and the food material. It has been shown that species of Geobacter are able to cooperate in metabolizing a mixture of chemicals that neither could process alone. Provided with ethanol and sodium fumarate, G. metallireducens broke down the ethanol generating an excess of electrons which were passed to G. sulfurreducens via "nanowires" grown between the species, enabling G. sulfurreducens to break down the fumarate ions.

The production of electricity during this process has also led scientists to theorize that Geobacter could act as a natural battery. This natural battery could use renewable biomass such as compost materials, or be used to convert human and animal solid waste into electricity. There are also potential applications in the field of nanotechnology for the creation of microbial nanowires in very small circuits and electronic devices. The nanowires could also be connected, creating a microscopic power grid.

The Big Six:
A Profile of Corporate Power in Seeds, Agrochemicals & Biotech

By Hope Shand

Sixteen years after GE crops made their commercial debut in the US, what are the benefits for farmers, diversity and society? The following article, adapted, in part, from ETC Group's **Who Will Control the Green Economy?**, *provides an update on current trends in industrial agriculture and examines the giant firms that control "the first link" in the corporate food chain.*[1]

The Big Six Seed, Biotech & Agrochemical Corporations
Business-friendly court decisions in the 1980s opened the door to exclusive monopoly rights on seeds and other life forms, propelling an unprecedented wave of seed industry concentration. In recent decades, the seed industry has experienced a faster rate of market concentration than any other farm input sector.[2] Monsanto may be the largest, most notorious and conspicuous of all the biotech Gene Giants, but it's important to look at the bigger picture.

The Big Six: The world's six largest seed/agrochemical/biotech firms (BASF, Bayer, Dow Agrosciences, DuPont, Monsanto, Syngenta) have a dangerous chokehold on the global agricultural research agenda. Together these six companies account for almost $50 billion per annum in sales of seeds, biotech traits and agrochemicals; they spend about $4.7 billion annually on ag R&D. After taking over the first link in the industrial food chain – commercial seeds – the Big Six corporations now determine, to an astonishing degree, the current priorities and future direction of agriculture research worldwide.

The Big Six agenda promotes genetic engineering, chemical dependence and monopoly patents that thwart both public and private sector alternatives and innovation. According to agricultural economists, some U.S. farmers adopted industry's genetically engineered (GE) seeds and companion chemicals faster than any agricultural technology in history.

The undisputed commercial success of GE seeds in the U.S. and a handful of other countries illustrates the paradox of new technologies that are introduced in oligopolistic markets with minimal government regulation and oversight: that is, such products don't have to be technically superior (i.e. they don't have to work) or be socially useful in order to be profitable. Although the biotech industry's public relations machine has perpetuated the myth that biotech is spurring agricultural productivity worldwide and feeding hungry people, the reality is far different. Proprietary, high-tech seeds are neither accessible nor suitable to the needs of most of the world's farmers – the small-scale producers who are responsible for feeding the vast majority of the world's population, safeguarding biodiversity, and providing our best hope of confronting climate chaos.

Big Six Tech Cartels: It's important to examine the combined power and influence of the Big Six because these corporations aren't just competitors – *they are also collaborators* – in tightly concentrated markets. The Big Six are forging

World's Top 10 Seed Companies

Rank / Company (headquarters) | US$ Millions, 2009 | Market Share

1. Monsanto (USA) |$7,297 | 27%
2. DuPont (Pioneer) (USA) / $4,641 | 17%
3. Syngenta (Switzerland) | $2,564 | 9%
4. Groupe Limagrain (France) | $1,252 | 5%
5. Land O' Lakes/Winfield Solutions (USA) | $1,100 | 4%
6. KWS AG (Germany) | $997 | 4%
7. Bayer CropScience (Germany) | $700 | 3%
8. Dow AgroSciences (USA) | $635 | 2%
9. Sakata (Japan) | $491 | 2%
10. DLF-Trifolium A/S (Denmark) | $385 | 1%

Total Top 10 $20,062 | 73%

Sources: ETC Group

MONSANTO

BAYER

Limagrain

DOW

DUPONT

syngenta

Conclusion:

There is no social benefit when six corporations are allowed tp monopolize the very basis of the world's food supply. The Big Six are all about industry profits, not diversity, sustainability or food security.

In reality, the Big Six takeover of the first link in the industrial food chain offers a very incomplete picture of today's food and farming landscape.

In December 2012 Pesticide Action Network (PAN) Asia & the Pacific hosted a Permanent People's Tribunal in Bangalore, India where the Big Six pesticide and biotech firms were brought to trial for human rights violations. In the words of Javier Souza, chair of PAN International:

"It is time that the global community takes notice of the extent of the harm to humanity and the planet caused by agrochemical transnational corporations and takes actions to hold them to account"

Link: HeritageFarmCompanion_BigSix-1.pdf

Aluminum and Glyphosate Can Synergistically Induce Pineal Gland Pathology: Connection to Gut Dysbiosis and Neurological Disease

by Stephanie Seneff1*, Nancy Swanson2, Chen Li1

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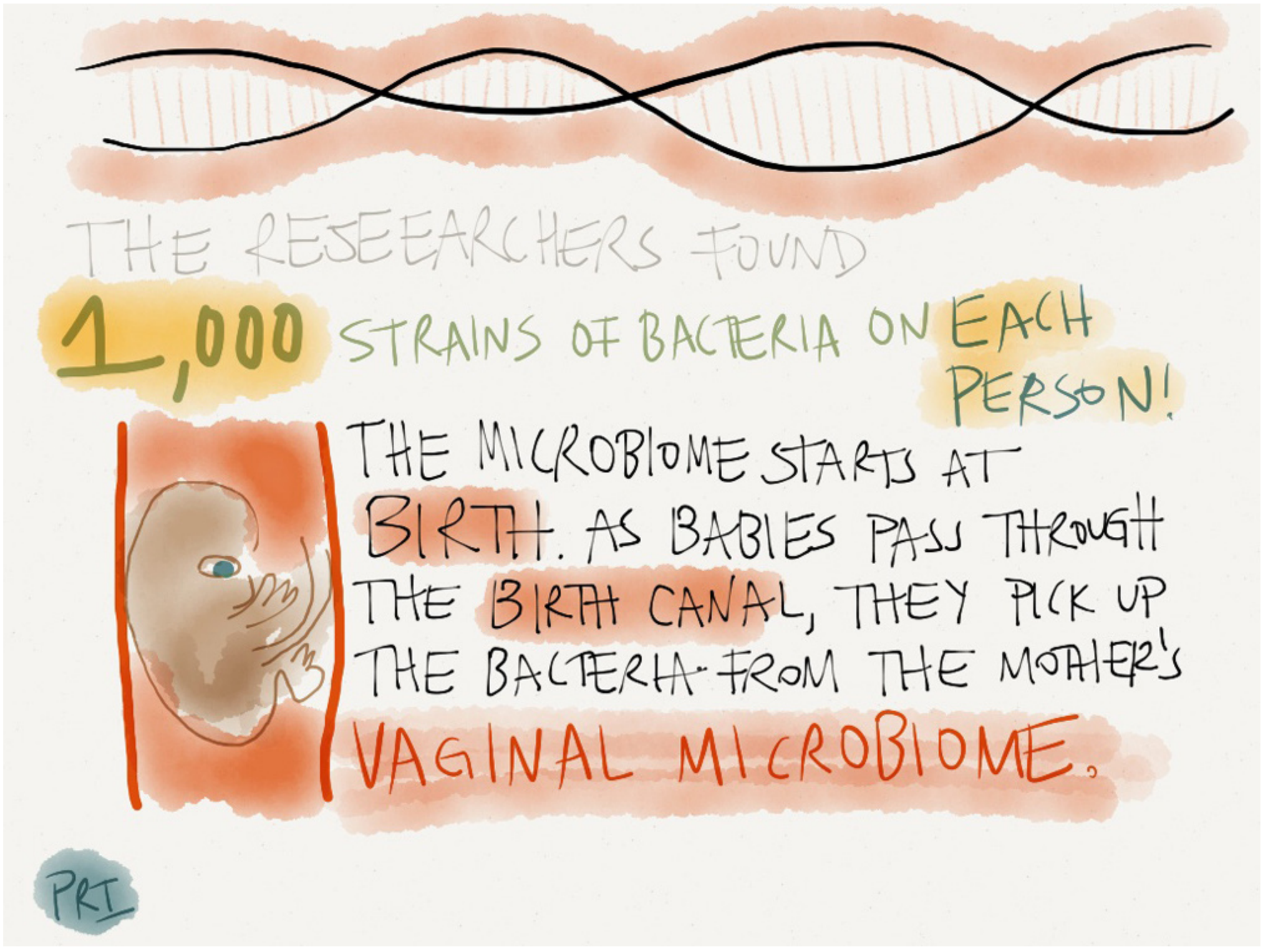
Received 17 October 2014; revised 10 November 2014; accepted 10 December 2014

Abstract

Many neurological diseases, including autism, depression, dementia, anxiety disorder and Parkinson's disease, are associated with abnormal sleep patterns, which are directly linked to pineal gland dysfunction. The pineal gland is highly susceptible to environmental toxicants. Two pervasive substances in modern industrialized nations are aluminum and glyphosate, the active ingredient in the herbicide, Roundup®. In this paper, we show how these two toxicants work synergistically to induce neurological damage. Glyphosate disrupts gut bacteria, leading to an overgrowth of Clostridium difficile. Its toxic product, p-cresol, is linked to autism in both human and mousemmodels. p-Cresol enhances uptake of aluminum via transferrin. Anemia, a result of both aluminum disruption of heme and impaired heme synthesis by glyphosate, leads to hypoxia, which induces increased pineal gland transferrin synthesis. Premature birth is associated with hypoxic stress and with substantial increased risk to the subsequent development of autism, linking hypoxia to autism. Glyphosate chelates aluminum, allowing ingested aluminum to bypass the gut barrier. This leads to anemia-induced hypoxia, promoting neurotoxicity and damaging the pineal gland. Both glyphosate and aluminum disrupt cytochrome P450 enzymes, which are involved in melatonin metabolism. Furthermore, melatonin is derived from tryptophan, whose synthesis in plants and microbes is blocked by glyphosate. We also demonstrate a plausible role for vitamin D3 dysbiosis in impaired gut function and impaired serotonin synthesis. This paper proposes that impairedsulfate supply to the brain mediates the damage induced by the synergistic action of aluminum and glyphosate on the pineal gland and related midbrain nuclei.

Conclusion

In this paper, we have developed the argument that glyphosate, the active ingredient in the herbicide, Roundup, and aluminum, a pervasive toxic metal in our environment, operate synergistically to induce dysfunction in the pineal gland leading to the sleep disorder that is characteristic of multiple neurological diseases, including autism, ADHD, depression, Alzheimer's disease, ALS, anxiety disorder and Parkinson's disease. We further argue that impaired supply of melatonin and sulfate to the brain as a consequence of pineal damage can explain how the disrupted sleep can lead to more general neurological damage, and we propose that this is a significant component of the disease process. The steady increase in glyphosate usage on corn and soy crops aligns remarkably well with the increase in sleep disorder and in autism, as well as other neurological diseases. We have shown how disruption of CYP enzymes and promotion of anemia and hypoxia, due to both aluminum and glyphosate, and disruption of gut bacteria by glyphosate, can cause a pathology leading to deficiencies in both melatonin and sulfate in the cerebrospinal fluid that is characteristic of autism and Alzheimer's disease. Insufficient sulfate leads to impaired lysosomal recycling of cellular debris, and insufficient melatonin leads to sleep disorder,vascular disease and impaired protection from ROS damage in the brain.


THE RESEEARCHERS FOUND
1,000 STRAINS OF BACTERIA ON EACH PERSON!
THE MICROBIOME STARTS AT BIRTH. AS BABIES PASS THROUGH THE BIRTH CANAL, THEY PICK UP THE BACTERIA FROM THE MOTHER'S VAGINAL MICROBIOME.
PRI

The oral and intratracheal toxicities of ROUNDUP and its components to rats

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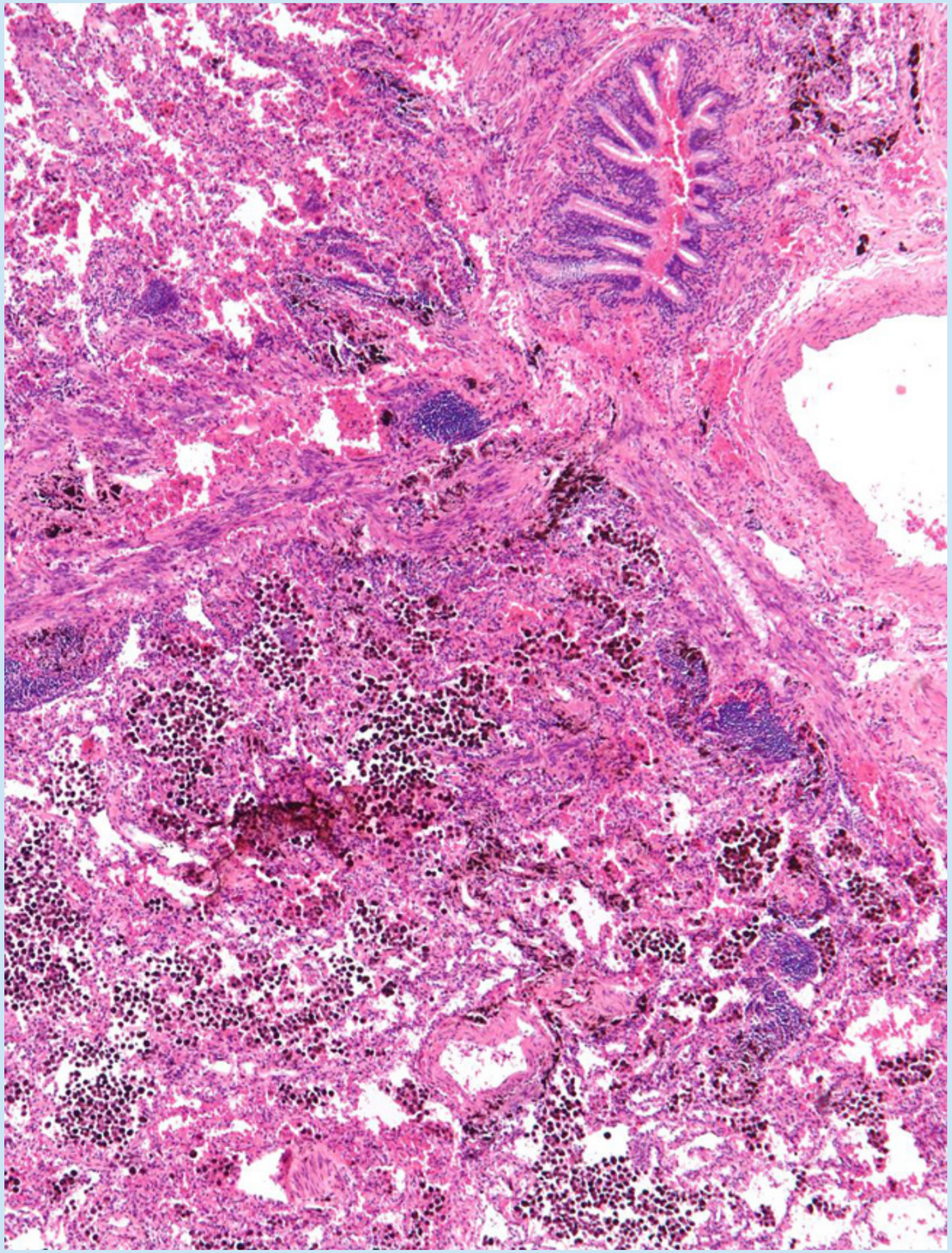
Author information

1Department of Pharmacy, Faculty of Allied Health Sciences, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia.

Abstract

The toxicities of ROUNDUP and its component chemicals, glyphosate (N-phosphonomethylglycine) and polyoxyethyleneamine (POEA), were determined at 0, 1, 3, 6 and 24 h following administration to rats. The intratracheal administration of glyphosate (0.2 g/kg), POEA (0.1 g/kg), a mixture of glyphosate (0.2 g/kg) + POEA (0.1 g/kg), or ROUNDUP (containing 0.2 g/kg glyphosate and 0.1 g/kg POEA) elicited immediate respiratory effects which were more severe and which lasted longer in the groups receiving the POEA-containing preparations than in the glyphosate alone group. By 1 h, all test preparations had caused deaths, but more occurred from the POEA-containing preparations than from glyphosate. The po administration of POEA (1 g/kg), the mixture of glyphosate (2 g/kg) +POEA (1 g/kg), or ROUNDUP (containing 2 g/kg glyphosate and 1 g/kg POEA) produced diarrhea and blood-stained weeping from noses. Death was only seen from POEA at 24 h. Glyphosate (2 g/kg po) produced transient diarrhea without nose bleeds; POEA caused diarrhea at 1 h; and the mixture of POEA + glyphosate produced diarrhea later that increased in severity with time. Bloody nose secretions were seen only with the preparations that contained POEA. No deaths, respiratory effects or bloody nose secretions occurred in controls given saline. Both POEA and glyphosate caused lung hemorrhages and lung epithelial cell damage with po or intratracheal exposures. These results indicate POEA and preparations that contained POEA were more toxic than glyphosate: http://www.ncbi.nlm.nih.gov/pubmed/9167243

Both POEA and glyphosate
caused lung hemorrhages (seen at right)
and lung epithelial cell damage



Hepatoma tissue culture (HTC) cells as a model for investigating the effects of low concentrations of herbicide on cell structure and function.

by Malatesta M1, Perdoni F, Santin G, Battistelli S, Muller S, Biggiogera M.

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Abstract

Previous studies on mice fed genetically modified (GM) soybean demonstrated modifications of the mitochondrial functions and of the transcription/splicing pathways in hepatocytes. The cause(s) of these alterations could not be conclusively established but, since the GM soybean used is tolerant to glyphosate and was treated with the glyphosate-containing herbicide Roundup , the possibility exists that the effects observed may be due to herbicide residues. In order to verify this hypothesis, we treated HTC cells with 1-10mM Roundup and analysed cellular features by flow cytometry, fluorescence and electron microscopy. Under these experimental conditions, the death rate and the general morphology of HTC cells were not affected, as well as most of the cytoplasmic organelles. However, in HTC-treated cells, lysosome density increased and mitochondrial membranes modified indicating a decline in the respiratory activity. Moreover, nuclei underwent morpho-functional modifications suggestive of a decreased transcriptional/splicing activity. Although we cannot exclude that other factors than the presence of the herbicide residues could be responsible for the cellular modifications described in GM-fed mice, the concordance of the effects induced by low concentrations of Roundup on HTC cells suggests that the presence of Roundup residues could be one of the factors interfering with multiple metabolic pathways: http://www.ncbi.nlm.nih.gov/pubmed/18835430

the concordance of the effects induced by low concentrations of Roundup on HTC cells suggests that the presence of Roundup residues could be one of the factors interfering with multiple metabolic pathways

Sea urchin embryo, DNA-damaged cell cycle checkpoint and the mechanisms initiating cancer development

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Abstract

Cell division is an essential process for heredity, maintenance and evolution of the whole living kingdom. Sea urchin early development represents an excellent experimental model for the analysis of cell cycle checkpoint mechanisms since embryonic cells contain a functional DNA-damage checkpoint and since the whole sea urchin genome is sequenced. The DNA-damaged checkpoint is responsible for an arrest in the cell cycle when DNA is damaged or incorrectly replicated, for activation of the DNA repair mechanism, and for commitment to cell death by apoptosis in the case of failure to repair. New insights in cancer biology lead to two fundamental concepts about the very first origin of cancerogenesis. Cancers result from dysfunction of DNA-damaged checkpoints and cancers appear as a result of normal stem cell (NCS) transformation into a cancer stem cell (CSC). The second aspect suggests a new definition of “cancer”, since CSC can be detected well before any clinical evidence. Since early development starts from the zygote, which is a primary stem cell, sea urchin early development allows analysis of the early steps of the cancerization process. Although sea urchins do not develop cancers, the model is alternative and complementary to stem cells which are not easy to isolate, do not divide in a short time and do not divide synchronously. In the field of toxicology and incidence on human health, the sea urchin experimental model allows assessment of cancer risk from single or combined molecules long before any epidemiologic evidence is available. Sea urchin embryos were used to test the worldwide used pesticide Roundup that contains glyphosate as the active herbicide agent; it was shown to activate the DNA-damage checkpoint of the first cell cycle of development. The model therefore allows considerable increase in risk evaluation of new products in the field of cancer and offers a tool for the discovery of molecular markers for early diagnostic in cancer biology. Prevention and early diagnosis are two decisive elements of human cancer therapy: http://www.ncbi.nlm.nih.gov/pubmed/18157084

Sea urchin embryos were used to test the worldwide used pesticide Roundup that contains glyphosate as the active herbicide agent; it was shown to activate the DNA-damage checkpoint of the first cell cycle of development of cancer

Cytotoxicity on human cells of Cry1Ab and Cry1Ac Bt insecticidal toxins alone or with a glyphosate-based herbicide

by Mesnage R1, Clair E, Gress S, Then C, Székács A, Séralini GE.

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Abstract

The study of combined effects of pesticides represents a challenge for toxicology. In the case of the new growing generation of genetically modified (GM) plants with stacked traits, glyphosate-based herbicides (like Roundup) residues are present in the Roundup-tolerant edible plants (especially corns) and mixed with modified Bt insecticidal toxins that are produced by the GM plants themselves. The potential side effects of these combined pesticides on human cells are investigated in this work. Here we have tested for the very first time Cry1Ab and Cry1Ac Bt toxins (10 ppb to 100 ppm) on the human embryonic kidney cell line 293, as well as their combined actions with Roundup, within 24 h, on three biomarkers of cell death: measurements of mitochondrial succinate dehydrogenase, adenylate kinase release by membrane alterations and caspase 3/7 inductions. Cry1Ab caused cell death from 100 ppm. For Cry1Ac, under such conditions, no effects were detected. The Roundup tested alone from 1 to 20 000 ppm is necrotic and apoptotic from 50 ppm, far below agricultural dilutions (50% lethal concentration 57.5 ppm). The only measured significant combined effect was that Cry1Ab and Cry1Ac reduced caspases 3/7 activations induced by Roundup; this could delay the activation of apoptosis. There was the same tendency for the other markers. In these results, we argue that modified Bt toxins are not inert on nontarget human cells, and that they can present combined side-effects with other residues of pesticides specific to GM plants: http://www.ncbi.nlm.nih.gov/pubmed/22337346

In these results, we argue that modified Bt toxins are not inert on nontarget human cells, and that they can present combined side-effects with other residues of pesticides specific to GM plants

Impairment of carbon metabolism induced by the herbicide glyphosate

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Author information

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Abstract

The herbicide glyphosate reduces plant growth and causes plant death by inhibiting the biosynthesis of aromatic amino acids. The objective of this work was to determine whether glyphosate-treated plants show a carbon metabolism pattern comparable to that of plants treated with herbicides that inhibit branched-chain amino acid biosynthesis. Glyphosate-treated plants showed impaired carbon metabolism with an accumulation of carbohydrates in the leaves and roots. The growth inhibition detected after glyphosate treatment suggested impaired metabolism that impedes the utilization of available carbohydrates or energy at the expected rate. These effects were common to both types of amino acid biosynthesis inhibitors. Under aerobic conditions, ethanolic fermentative metabolism was enhanced in the roots of glyphosate-treated plants. This fermentative response was not related to changes in the respiratory rate or to a limitation of the energy charge. This response, which was similar for both types of herbicides, might be considered a general response to stress conditions: http://www.ncbi.nlm.nih.gov/pubmed/21944839

The herbicide glyphosate reduces plant growth and causes plant death by inhibiting the biosynthesis of aromatic amino acids

A commercial formulation of glyphosate inhibits proliferation and differentiation to adipocytes and induces apoptosis in 3T3-L1 fibroblasts

by Martini CN1, Gabrielli M, Vila Mdel C.

Author information

1Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Pabellón 2, Ciudad Universitaria, 1428 Buenos Aires, Argentina.

Abstract

Glyphosate-based herbicides are extensively used for weed control all over the world. Therefore, it is important to investigate the putative toxic effects of these formulations which include not only glyphosate itself but also surfactants that may also be toxic. 3T3-L1 fibroblasts are a useful tool to study adipocyte differentiation, this cell line can be induced to differentiate by addition of a differentiation mixture containing insulin, dexamethasone and 3-isobutyl-1-methylxanthine. We used this cell line to investigate the effect of a commercial formulation of glyphosate (GF) on proliferation, survival and differentiation. It was found that treatment of exponentially growing cells with GF for 48h inhibited proliferation in a dose-dependent manner. In addition, treatment with GF dilution 1:2000 during 24 or 48h inhibited proliferation and increased cell death, as evaluated by trypan blue-exclusion, in a time-dependent manner. We showed that treatment of 3T3-L1 fibroblasts with GF increased caspase-3 like activity and annexin-V positive cells as evaluated by flow cytometric analysis, which are both indicative of induction of apoptosis. It was also found that after the removal of GF, remaining cells were able to restore proliferation. On the other hand, GF treatment severely inhibited the differentiation of 3T3-L1 fibroblasts to adipocytes. According to our results, a glyphosate-based herbicide inhibits proliferation and differentiation in this mammalian cell line and induces apoptosis suggesting GF-mediated cellular damage. Thus, GF is a potential risk factor for human health and the environment: http://www.ncbi.nlm.nih.gov/pubmed/22546541

According to our results, a glyphosate-based herbicide inhibits proliferation and differentiation in this mammalian cell line and induces apoptosis suggesting GF-mediated cellular damage. Thus, Glyphosate is a potential risk factor for human health and the environment

A step further toward glyphosate-induced epidermal cell death: involvement of mitochondrial and oxidative mechanisms

by Heu C1, Elie-Caille C, Mougey V, Launay S, Nicod L

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Abstract

A deregulation of programmed cell death mechanisms in human epidermis leads to skin pathologies. We previously showed that glyphosate, an extensively used herbicide, provoked cytotoxic effects on cultured human keratinocytes, affecting their antioxidant capacities and impairing morphological and functional cell characteristics. The aim of the present study, carried out on the human epidermal cell line HaCaT, was to examine the part of apoptosis plays in the cytotoxic effects of glyphosate and the intracellular mechanisms involved in the apoptotic events. We have conducted different incubation periods to reveal the specific events in glyphosate-induced cell death. We observed an increase in the number of early apoptotic cells at a low cytotoxicity level (15%), and then, a decrease, in favor of late apoptotic and necrotic cell rates for more severe cytotoxicity conditions. At the same time, we showed that the glyphosate-induced mitochondrial membrane potential disruption could be a cause of apoptosis in keratinocyte cultures: http://www.ncbi.nlm.nih.gov/pubmed/22522424

A deregulation of programmed cell death mechanisms in human epidermis leads to skin pathologies. We previously showed that glyphosate, an extensively used herbicide, provoked cytotoxic effects on cultured human keratinocytes. At the same time, we showed that the glyphosate-induced mitochondrial membrane potential disruption could be a cause of apoptosis in keratinocyte cultures

Glyphosate-Based Herbicides Potently Affect Cardiovascular System in Mammals: Review of the Literature

by Gress S1, Lemoine S, Séralini GE, Puddu PE.

Author information

1EA 4650 Signalisation, électrophysiologie et imagerie des lésions d'ischémie-reperfusion myocardique, Institute of Biology, University of Caen, Esplanade de la Paix, 14032, Caen Cedex, France.

Abstract

In glyphosate (G)-based herbicides (GBHs), the declared active principle G is mixed with several adjuvants that help it to penetrate the plants' cell membranes and its stabilization and liposolubility. Its utilization is growing with genetically modified organisms engineered to tolerate GBH. Millions of farmers suffer poisoning and death in developing countries, and occupational exposures and suicide make GBH toxicity a worldwide concern. As GBH is found in human plasma, widespread hospital facilities for measuring it should be encouraged. Plasma determination is an essential prerequisite for risk assessment in GBH intoxication. Only when standard ECGs were performed, at least one abnormal ECG was detected in the large majority of cases after intoxication. QTc prolongation and arrhythmias along with first-degree atrioventricular block were observed after GBH intoxication. Thus, life-threatening arrhythmias might be the cause of death in GBH intoxication. Cardiac cellular effects of GBH were reviewed along with few case reports in men and scanty larger studies. We observed in two mammalian species (rats and rabbits) direct cardiac electrophysiological changes, conduction blocks and arrhythmias among GBH-mediated effects. Plasmatic (and urine) level determinations of G and electrocardiographic Holter monitoring seem warranted to ascertain whether cardiovascular risk among agro-alimentary workers might be defined: http://www.ncbi.nlm.nih.gov/pubmed/25245870

We observed in two mammalian species
(rats and rabbits)
direct cardiac electrophysiological changes,
conduction blocks and arrhythmias among
GBH-mediated effects.

Mixtures of glyphosate and surfactant TN20 accelerate cell death via mitochondrial damage-induced apoptosis and necrosis

byKim YH1, Hong JR, Gil HW, Song HY, Hong SY

Author information

1Department of Immunology, College of Medicine, Soonchunhyang University, Cheonan, Republic of Korea.

Abstract

Glyphosate, a common herbicide, is not toxic under normal exposure circumstances. However, this chemical, when combined with a surfactant, is cytotoxic. In this study, the mechanism of the additive effect of glyphosate and TN-20, a common surfactant in glyphosate herbicides, was investigated. After exposure of rat H9c2 cells to glyphosate and TN-20 mixtures, following assays were performed: flow cytometry to determine the proportion of cells that underwent apoptosis and necrosis; western blotting to determine expression of mitochondrial proteins (Bcl-2 and Bax); immunological methods to evaluate translocation of cytochrome C; luminometric measurements to determine activity of caspases 3/7 and 9; and tetramethyl rhodamine methyl ester assay to measure mitochondrial membrane potentials. Bcl-1 intensity decreased while Bax intensity increased with exposure to increasing TN-20 and/or glyphosate concentrations. Caspase activity increased and mitochondrial membrane potential decreased only when the cells were exposed to a mixture of both TN-20 and glyphosate, but not after exposure to either one of these compounds. The results support the possibility that mixtures of glyphosate and TN-20 aggravate mitochondrial damage and induce apoptosis and necrosis. Throughout this process, TN-20 seems to disrupt the integrity of the cellular barrier to glyphosate uptake, promoting glyphosate-mediated toxicity: http://www.ncbi.nlm.nih.gov/pubmed/23099315

The results support the possibility that
mixtures of glyphosate and IN-20 aggravate
mitochondrial damage and induce apoptosis and
necrosis. Throughout this process, IN-20 seems to
disrupt the integrity of the cellular barrier
to glyphosate uptake, promoting
glyphosate-mediated toxicity

Glyphosate-Based Herbicides Potently Affect Cardiovascular System in Mammals: Review of the Literature.

by Gress S1, Lemoine S, Séralini GE, Puddu PE.
Cardiovascular Toxicology • September 23, 2014

Author information

1EA 4650 Signalisation, électrophysiologie et imagerie des lésions d'ischémie-reperfusion myocardique, Institute of Biology, University of Caen, Esplanade de la Paix, 14032, Caen Cedex, France.

Abstract

In glyphosate (G)-based herbicides (GBHs), the declared active principle G is mixed with several adjuvants that help it to penetrate the plants' cell membranes and its stabilization and liposolubility. Its utilization is growing with genetically modified organisms engineered to tolerate GBH. Millions of farmers suffer poisoning and death in developing countries, and occupational exposures and suicide make GBH toxicity a worldwide concern. As GBH is found in human plasma, widespread hospital facilities for measuring it should be encouraged. Plasma determination is an essential prerequisite for risk assessment in GBH intoxication. Only when standard ECGs were performed, at least one abnormal ECG was detected in the large majority of cases after intoxication. QTc prolongation and arrhythmias along with first-degree atrioventricular block were observed after GBH intoxication. Thus, life-threatening arrhythmias might be the cause of death in GBH intoxication. Cardiac cellular effects of GBH were reviewed along with few case reports in men and scanty larger studies. We observed in two mammalian species (rats and rabbits) direct cardiac electrophysiological changes, conduction blocks and arrhythmias among GBH-mediated effects. Plasmatic (and urine) level determinations of G and electrocardiographic Holter monitoring seem warranted to ascertain whether cardiovascular risk among agro-alimentary workers might be defined: http://www.ncbi.nlm.nih.gov/pubmed/25245870

In this study "We observed in two mammalian species (rats and rabbits) direct cardiac electrophysiological changes, conduction blocks and arrhythmias among GBH-mediated effects."

Glyphosate-rich air samples induce IL-33, TSLP and generate IL-13 dependent airway inflammation.

by Kumar S1, Khodoun M2, Kettleson EM1, McKnight C3, Reponen T1, Grinshpun SA1, Adhikari A4.

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4. Department of Environmental Health, College of Medicine, University of Cincinnati, OH 45267, USA; Department of Environmental Health Sciences, Jiann-Ping Hsu College of Public Health, Georgia Southern University, Statesboro, GA 30460, USA. Electronic address: aadhikari@georgiasouthern.edu.

Abstract

Several low weight molecules have often been implicated in the induction of occupational asthma. Glyphosate, a small molecule herbicide, is widely used in the world. There is a controversy regarding a role of glyphosate in developing asthma and rhinitis among farmers, the mechanism of which is unexplored. The aim of this study was to explore the mechanisms of glyphosate induced pulmonary pathology by utilizing murine models and real environmental samples. C57BL/6, TLR4-/-, and IL-13-/- mice inhaled extracts of glyphosate-rich air samples collected on farms during spraying of herbicides or inhaled different doses of glyphosate and ovalbumin. The cellular response, humoral response, and lung function of exposed mice were evaluated. Exposure to glyphosate-rich air samples as well as glyphosate alone to the lungs increased: eosinophil and neutrophil counts, mast cell degranulation, and production of IL-33, TSLP, IL-13, and IL-5. In contrast, in vivo systemic IL-4 production was not increased. Co-administration of ovalbumin with glyphosate did not substantially change the inflammatory immune response. However, IL-13-deficiency resulted in diminished inflammatory response but did not have a significant effect on airway resistance upon methacholine challenge after 7 or 21 days of glyphosate exposure. Glyphosate-rich farm air samples as well as glyphosate alone were found to induce pulmonary IL-13-dependent inflammation and promote Th2 type cytokines, but not IL-4 for glyphosate alone. This study, for the first time, provides evidence for the mechanism of glyphosate-induced occupational lung disease: http://www.ncbi.nlm.nih.gov/pubmed/25172162

This study, "for the first time, provides evidence for the mechanism of glyphosate-induced occupational lung disease."

Effect of glyphosate on the sperm quality of zebrafish

by Danio rerio.Lopes FM1, Varela Junior AS2, Corcini CD3, da Silva AC4, Guazzelli VG5, Tavares G6, da Rosa

Abstract

Glyphosate is a systemic, non-selective herbicide widely used in agriculture worldwide. It acts as an inhibitor of the enzyme 5-enolpyruvylshikimate-3-phosphate synthase by interrupting the synthesis of essential aromatic amino acids. This pathway is not present in animals, although some studies have shown that the herbicide glyphosate can affect fish reproduction. In this study, the effect of glyphosate on sperm quality of the fish Danio rerio was investigated after 24 and 96 h of exposure at concentrations of 5mg/L and 10mg/L. The spermatic cell concentration, sperm motility and motility period were measured employing conventional microscopy. The mitochondrial functionality, membrane integrity and DNA integrity were measured by fluorescence microscopy using specific probes. No significant differences in sperm concentration were observed; however, sperm motility and the motility period were reduced after exposure to both glyphosate concentrations during both exposure periods. The mitochondrial functionality and membrane and DNA integrity were also reduced at the highest concentration during both exposure periods. The results showed that glyphosate can induce harmful effects on reproductive parameters in D. rerio and that this change would reduce the fertility rate of these animals: http://www.ncbi.nlm.nih.gov/pubmed/25089920

"The results showed "that glyphosate can induce harmful effects on reproductive parameters in D. rerio and that this change would reduce the fertility rate of these animals."

Major pesticides are more toxic to human cells than their declared active principles

Mesnage R1, Defarge N1, Spiroux de Vendômois J2, Séralini GE1.

Author information

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2CRIIGEN, 40 rue Monceau, 75008 Paris, France.

Abstract

Pesticides are used throughout the world as mixtures called formulations. They contain adjuvants, which are often kept confidential and are called inerts by the manufacturing companies, plus a declared active principle, which is usually tested alone. We tested the toxicity of 9 pesticides, comparing active principles and their formulations, on three human cell lines (HepG2, HEK293, and JEG3). Glyphosate, isoproturon, fluroxypyr, pirimicarb, imidacloprid, acetamiprid, tebuconazole, epoxiconazole, and prochloraz constitute, respectively, the active principles of 3 major herbicides, 3 insecticides, and 3 fungicides. We measured mitochondrial activities, membrane degradations, and caspases 3/7 activities. Fungicides were the most toxic from concentrations 300-600 times lower than agricultural dilutions, followed by herbicides and then insecticides, with very similar profiles in all cell types. Despite its relatively benign reputation, Roundup was among the most toxic herbicides and insecticides tested. Most importantly, 8 formulations out of 9 were up to one thousand times more toxic than their active principles. Our results challenge the relevance of the acceptable daily intake for pesticides because this norm is calculated from the toxicity of the active principle alone. Chronic tests on pesticides may not reflect relevant environmental exposures if only one ingredient of these mixtures is tested alone: http://www.ncbi.nlm.nih.gov/pubmed/24719846

"RoundupTM was among the most toxic herbicides and insecticides tested. Most importantly, 8 formulations out of 9 were up to one thousand times more toxic than their active principles."

Glyphosate, hard water and nephrotoxic metals: are they the culprits behind the epidemic of chronic kidney disease of unknown etiology in Sri Lanka?

by Jayasumana C1, Gunatilake S2, Senanayake P3.

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3. Hela Suwaya Organization, Malabe 10115, Sri Lanka. helasuwaya@gmail.com.

Abstract

The current chronic kidney disease epidemic, the major health issue in the rice paddy farming areas in Sri Lanka has been the subject of many scientific and political debates over the last decade. Although there is no agreement among scientists about the etiology of the disease, a majority of them has concluded that this is a toxic nephropathy. None of the hypotheses put forward so far could explain coherently the totality of clinical, biochemical, histopathological findings, and the unique geographical distribution of the disease and its appearance in the mid-1990s. A strong association between the consumption of hard water and the occurrence of this special kidney disease has been observed, but the relationship has not been explained consistently. Here, we have hypothesized the association of using glyphosate, the most widely used herbicide in the disease endemic area and its unique metal chelating properties. The possible role played by glyphosate-metal complexes in this epidemic has not been given any serious consideration by investigators for the last two decades. Furthermore, it may explain similar kidney disease epidemics observed in Andra Pradesh (India) and Central America. Although glyphosate alone does not cause an epidemic of chronic kidney disease, it seems to have acquired the ability to destroy the renal tissues of thousands of farmers when it forms complexes with a localized geo environmental factor (hardness) and nephrotoxic metals: http://www.ncbi.nlm.nih.gov/pubmed/24562182

"Although glyphosate alone does not cause an epidemic of chronic kidney disease, it seems to have acquired the ability to destroy the renal tissues of thousands of farmers when it forms complexes with a localized geoenvironmental factor

Glyphosate commercial formulation causes cytotoxicity, oxidative effects, and apoptosis on human cells: differences with its active ingredient

by Chaufan G1, Coalova I, Ríos de Molina Mdel C.

Author information

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Abstract

In the present study, the effects on oxidative balance and cellular end points of glyphosate, aminomethylphosphonic acid (AMPA), and a glyphosate formulation (G formulation) were examined in HepG2 cell line, at dilution levels far below agricultural recommendations. Our results show that G formulation had toxic effects while no effects were found with acid glyphosate and AMPA treatments. Glyphosate formulation exposure produced an increase in reactive oxygen species, nitrotyrosine formation, superoxide dismutase activity, and glutathione (GSH) levels, while no effects were observed for catalase and GSH-S-transferase activities. Also, G formulation triggered caspase 3/7 activation and hence induced apoptosis pathway in this cell line. Aminomethylphosphonic acid exposure produced an increase in GSH levels while no differences were observed in other antioxidant parameters. No effects were observed when the cells were exposed to acid glyphosate. These results confirm that G formulations have adjuvants working together with the active ingredient and causing toxic effects that are not seen with acid glyphosate: http://www.ncbi.nlm.nih.gov/pubmed/24434723

"These results confirm that Glyphosate formulations have adjuvants working together with the active ingredient and causing toxic effects that are not seen with acid glyphosate"

Glyphosate and its Formulations Toxicity, Occupational and Environmental Exposure

by Kwiatkowska M1, Pawe J2, Bukowska B2.

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Abstract

Glyphosate (N-(phosphonomethyl)glycine) is an active ingredient of the most widely used herbicide formulations in protecting agricultural and horticultural crops. Numerous results (mostly published in the years 2010-2013) concerning the action of glyphosate and its formulations in the recent decade were analyzed. Initial reports about alleged biodegradability of glyphosate in the environment turned out to be wrong. It has been shown that glyphosate remains in the soil and can reach people by spreading along with groundwater. Recent publications have shown that glyphosate is detected at low concentrations in the human blood. Publications cited in this article, which indicate a possible induction of neoplastic changes by glyphosate formulation, have raised great concern and controversy in the scientific world. Presenting adverse effects of glyphosate and its formulations we focused on the role of glyphosate formulations in hormonal disorders by impeding the expression of steroidogenic acute regulatory protein and the inhibition of aromatase activity. The impact of glyphosate on oxygen reactive species formation, changes in redox system and the effect on necrosis and apoptosis in various types of cells was shown. We also revealed that glyphosate as a phosphonate herbicide does not inhibit directly the activity of acetylcholinesterase. Based on numerous studies it was noted that commercial formulations of glyphosate exhibit higher toxicity than that of the active substance itself. The discussed problems clearly show the need to evaluate the toxicity of glyphosate and its formulations and related potential threat to humans.

"It has been shown that glyphosate remains in the soil and can reach people by spreading along with groundwater. Based on numerous studies it was noted that commercial formulations of glyphosate exhibit higher toxicity than that of the active substance itself. The impact of glyphosate on oxygen reactive species formation, changes in redox system and the effect on necrosis and apoptosis in various types of cells was shown."

Glyphosate induces human breast cancer cell growth via estrogen receptors

by Thongprakaisang, Thiantanawat A, Rangkadilok N, Suriyo T, Satayavivad J.

Abstract

Glyphosate is an active ingredient of the most widely used herbicide and it is believed to be less toxic than other pesticides. However, several recent studies showed its potential adverse health effects to humans as it may be an endocrine disruptor. This study focuses on the effects of pure glyphosate on estrogen receptors (ERs) mediated transcriptional activity and their expressions. Glyphosate exerted proliferative effects only in human hormone-dependent breast cancer, T47D cells, but not in hormone-independent breast cancer, MDA-MB231 cells, at 10 $^{-12}$ to 10 M in estrogen withdrawal condition. The proliferative concentrations of glyphosate that induced the activation of estrogen response element (ERE) transcription activity were 5-13 fold of control in T47D-KBluc cells and this activation was inhibited by an estrogen antagonist, ICI 182780, indicating that the estrogenic activity of glyphosate was mediated via ERs. Furthermore, glyphosate also altered both ER and expression. These results indicated that low and environmentally relevant concentrations of glyphosate possessed estrogenic activity. Glyphosate-based herbicides are widely used for soybean cultivation, and our results also found that there was an additive estrogenic effect between glyphosate and genistein, a phytoestrogen in soybeans. However, these additive effects of glyphosate contamination in soybeans need further animal study: http://www.ncbi.nlm.nih.gov/pubmed/23756170

"These results indicated that low and environmentally relevant concentrations of glyphosate possessed estrogenic activity. Glyphosate exerted proliferative effects only in human hormone-dependent breast cancer, T47D cells"

Glyphosate-induced stiffening of HaCaT keratinocytes, a Peak Force Tapping study on living cells.

by Heu C1, Berquand A, Elie-Caille C, Nicod L.

Abstract

The skin is the first physiological barrier, with a complex constitution, that provides defensive functions against multiple physical and chemical aggressions. Glyphosate is an extensively used herbicide that has been shown to increase the risk of cancer. Moreover there is increasing evidence suggesting that the mechanical phenotype plays an important role in malignant transformation. Atomic force microscopy (AFM) has emerged within the last decade as a powerful tool for providing a nanometer-scale resolution imaging of biological samples. Peak Force Tapping (PFT) is a newly released AFM-based investigation technique allowing extraction of chemical and mechanical properties from a wide range of samples at a relatively high speed and a high resolution. The present work uses the PFT technology to investigate HaCaT keratinocytes, a human epidermal cell line, and offers an original approach to study chemically-induced changes in the cellular mechanical properties under near-physiological conditions. These experiments indicate glyphosate induces cell membrane stiffening, and the appearance of cytoskeleton structures at a subcellular level, for low cytotoxic concentrations whereas cells exposed to IC50 (inhibitory concentration 50%) treatment exhibit control-like mechanical behavior despite obvious membrane damages. Quercetin, a well-known antioxidant, reverses the glyphosate-induced mechanical phenotype: http://www.ncbi.nlm.nih.gov/pubmed/22369932

"These experiments indicate glyphosate induces cell membrane stiffening, and the appearance of cytoskeleton structures at a subcellular level, for low cytotoxic concentrations whereas cells exposed to IC50 t reatment exhibit control-like mechanical behavior despite obvious membrane damages."

Cytotoxic and DNA-damaging properties of glyphosate and Roundup in human-derived buccal epithelial cells.

by Koller VJ, Fürhacker M, Nersesyan A, Mišík M, Eisenbauer M, Knasmueller S.

Abstract

Glyphosate (G) is the largest selling herbicide worldwide; the most common formulations (Roundup, R) contain polyoxyethyleneamine as main surfactant. Recent findings indicate that G exposure may cause DNA damage and cancer in humans. Aim of this investigation was to study the cytotoxic and genotoxic properties of G and R (UltraMax) in a buccal epithelial cell line (TR146), as workers are exposed via inhalation to the herbicide. R induced acute cytotoxic effects at concentrations > 40 mg/l after 20 min, which were due to membrane damage and impairment of mitochondrial functions. With G, increased release of extracellular lactate dehydrogenase indicative for membrane damage was observed at doses > 80 mg/l. Both G and R induced DNA migration in single-cell gel electrophoresis assays at doses > 20 mg/l. Furthermore, an increase of nuclear aberrations that reflect DNA damage was observed. The frequencies of micronuclei and nuclear buds were elevated after 20-min exposure to 10-20 mg/l, while nucleoplasmatic bridges were only enhanced by R at the highest dose (20 mg/l). R was under all conditions more active than its active principle (G). Comparisons with results of earlier studies with lymphocytes and cells from internal organs indicate that epithelial cells are more susceptible to the cytotoxic and DNA-damaging properties of the herbicide and its formulation. Since we found genotoxic effects after short exposure to concentrations that correspond to a 450-fold dilution of spraying used in agriculture, our findings indicate that inhalation may cause DNA damage in exposed individuals: http://www.ncbi.nlm.nih.gov/pubmed/22331240

"Since we found genotoxic effects after short exposure to concentrations that correspond to a 450-fold dilution of spraying used in agriculture, our findings indicate that inhalation may cause DNA damage in exposed individuals"

Genotoxicity of AMPA, the environmental metabolite of glyphosate, assessed by the Comet assay and cytogenetic tests.

by Mañas F1, Peralta L, Raviolo J, García Ovando H, Weyers A, Ugnia L, Gonzalez Cid M, Larripa I, Gorla N.

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Abstract

Formulations containing glyphosate are the most widely used herbicides in the world. AMPA is the major environmental breakdown product of glyphosate. The purpose of this study is to evaluate the in vitro genotoxicity of AMPA using the Comet assay in Hep-2 cells after 4h of incubation and the chromosome aberration (CA) test in human lymphocytes after 48h of exposition. Potential in vivo genotoxicity was evaluated through the micronucleus test in mice. In the Comet assay, the level of DNA damage in exposed cells at 2.5-7.5mM showed a significant increase compared with the control group. In human lymphocytes we found statistically significant clastogenic effect AMPA at 1.8mM compared with the control group. In vivo, the micronucleus test rendered significant statistical increases at 200-400mg/kg. AMPA was genotoxic in the three performed tests. Very scarce data are available about AMPA potential genotoxicity.

"AMPA is the major environmental breakdown product of glyphosate. AMPA was genotoxic in the three performed tests. Very scarce data are available about AMPA potential genotoxicity."

Glyphosate: a non-toxic pesticide?

by Pieniazek D1, Bukowska B, Duda W.

Author information

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Abstract

Glyphosate is currently the most commonly applied herbicide and its use is still growing. Nowadays, over 50 commercial preparations containing this compound are used, and these formulations are much more toxic than their active compound, glyphosate, owing to the presence of many surfactants and carrier compounds. Toxicological investigations provide evidence that glyphosate is an extremely "safe" herbicide for animals. This is why its use in agriculture is universal. In June 1991, the Environmental Protection Agency (EPA) categorized this compound into class E (according to EPA there are five categories of carcinogenicity), which means that it is probably not carcinogenic to humans. Unfortunately, the study carried out by Swedish oncologists in 2001 showed that glyphosate may induce cancer of the lymphatic system. The results of the Swedish study have changed our opinion about "safety" of this herbicide. Investigations concerning both its accumulation and toxic effect in animals and plants are now under way in many laboratories: http://www.ncbi.nlm.nih.gov/pubmed/15055003

"Unfortunately, the study carried out by Swedish oncologists in 2001 showed that glyphosate may induce cancer of the lymphatic system. The results of the Swedish study have changed our opinion about the "safety" of this herbicide."

Glyphosate As An Acetylcholinesterase Inhibitor in Cnesterodon Decemmaculatus.

by Menéndez-Helman RJ1, Ferreyroa GV, dos Santos Afonso M, Salibián A.

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Abstract

The toxic effect of sublethal concentrations (1, 17.5 and 35 mg L(-1)) of pure glyphosate was evaluated on acetylcholinesterase (AChE) activity in the fish species, Cnesterodon decemmaculatus. Acute bioassays (96 h) under laboratory conditions were conducted and homogenates for each specimen corresponding to the anterior, middle and posterior body sections were performed. Fish survival was 100%, even at the highest concentration tested (35 mg L(-1)), in accordance with the low lethal toxicity reported for glyphosate. However, a significant inhibitory effect on AChE activity was recorded even for the lowest herbicide concentration tested (1 mg L(-1)), in the homogenates corresponding to the anterior body section. The inhibition ranged from 23 to 36%. The analytical determination of glyphosate in assay media by ion chromatography, was used to verify its stability. These results indicate that AChE-a neurotoxicity biomarker-in C. decemmaculatus may be affected by exposure to environmentally relevant concentrations of glyphosate: http://www.ncbi.nlm.nih.gov/pubmed/22002176

These results indicate that the AChE-a neurotoxicity biomarker in C. decemmaculatus may be affected by exposure to environmentally relevant concentrations of glyphosate

The influence of glyphosate on the microbiota and production of botulinum neurotoxin during ruminal fermentation

by Ackermann W1, Coenen M, Schrödl W, Shehata AA, Krüger M.

Author information

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Abstract

The aim of the present study is to investigate the impact of glyphosate on the microbiota and on the botulinum neurotoxin (BoNT) expression during in vitro ruminal fermentation. This study was conducted using two DAISY(II)-incubators with four ventilated incubation vessels filled with rumen fluid of a 4-year-old non-lactating Holstein-Friesian cow. Two hundred milliliter rumen fluid and 800 ml buffer solution were used with six filter bags containing 500 mg concentrated feed or crude fiber-enriched diet. Final concentrations of 0, 1, 10, and 100 µg/ml of glyphosate in the diluted rumen fluids were added and incubated under CO2-aerated conditions for 48 h. The protozoal population was analyzed microscopically and the ruminal flora was characterized using the fluorescence in situ hybridization technique. Clostridium botulinum and BoNT were quantified using most probable number and ELISA, respectively. Results showed that glyphosate had an inhibitory effect on select groups of the ruminal microbiota, but increased the population of pathogenic species. The BoNT was produced during incubation when inoculum was treated with high doses of glyphosate. In conclusion, glyphosate causes dysbiosis which favors the production of BoNT in the rumen. The global regulations restrictions for the use of glyphosate should be re-evaluated: http://www.ncbi.nlm.nih.gov/pubmed/25407376

In conclusion, glyphosate causes dysbiosis which favors the production of BoNT in the rumen. The global regulations restrictions for the use of glyphosate should be re-evaluated

Direct and indirect effects of the glyphosate formulation Glifosato Atanor® on freshwater microbial communities

by Vera MS1, Di Fiori E, Lagomarsino L, Sinistro R, Escaray R, Iummato MM, Juárez A, Ríos de Molina Mdel C, Tell G, Pizarro H.

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Abstract

Glyphosate-based formulations are among the most widely used herbicides in the world. The effect of the formulation Glifosato Atanor(®) on freshwater microbial communities (phytoplankton, bacterioplankton, periphyton and zooplankton) was assessed through a manipulative experiment using six small outdoor microcosms of small volume. Three of the microcosms were added with 3.5 mg l(-1) of glyphosate whereas the other three were left as controls without the herbicide. The treated microcosms showed a significant increase in total phosphorus, not fully explained by the glyphosate present in the Glifosato Atanor(®). Therefore, part of the phosphorus should have come from the surfactants of the formulation. The results showed significant direct and indirect effects of Glifosato Atanor(®) on the microbial communities. A single application of the herbicide caused a fast increase both in the abundance of bacterioplankton and planktonic picocyanobacteria and in chlorophyll a concentration in the water column. Although metabolic alterations related to oxidative stress were induced in the periphyton community, the herbicide favored its development, with a large contribution of filamentous algae typical of nutrient-rich systems, with shallow and calm waters. An indirect effect of the herbicide on the zooplankton was observed due to the increase in the abundance of the rotifer Lecane spp. as a consequence of the improved food availability given by picocyanobacteria and bacteria. The formulation affected directly a fraction of copepods as a target. It was concluded that the Glifosato Atanor(®) accelerates the deterioration of the water quality, especially when considering small-volume water systems: http://www.ncbi.nlm.nih.gov/pubmed/22539117

It was concluded that the
Glifosato Atanor® accelerates the
deterioration of the water quality,
especially when considering
small-volume water systems

Effect of pesticides on cell survival in liver and brain rat tissues

by Astiz M1, de Alaniz MJ, Marra CA.

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Abstract

Pesticides are the main environmental factor associated with the etiology of human neurodegenerative disorders such as Parkinson's disease. Our laboratory has previously demonstrated that the treatment of rats with low doses of dimethoate, zineb or glyphosate alone or in combination induces oxidative stress (OS) in liver and brain. The aim of the present work was to investigate if the pesticide-induced OS was able to affect brain and liver cell survival. The treatment of Wistar rats with the pesticides (i.p. 1/250 LD50, three times a week for 5 weeks) caused loss of mitochondrial transmembrane potential and cardiolipin content, especially in substantia nigra (SN), with a concomitant increase of fatty acid peroxidation. The activation of calpain apoptotic cascade (instead of the caspase-dependent pathway) would be responsible for the DNA fragmentation pattern observed. Thus, these results may contribute to understand the effect(s) of chronic and simultaneous exposure to pesticides on cell survival: http://www.ncbi.nlm.nih.gov/pubmed/19493570

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Thus, these results may contribute to understand
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exposure to pesticides on cell survival.

Glyphosate induced cell death through apoptotic and autophagic mechanisms

by Gui YX1, Fan XN, Wang HM, Wang G, Chen SD.

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Abstract

Herbicides have been recognized as the main environmental factor associated with human neurodegenerative disorders such as Parkinson's disease (PD). Previous studies indicated that the exposure to glyphosate, a widely used herbicide, is possibly linked to Parkinsonism, however the underlying mechanism remains unclear. We investigated the neurotoxic effects of glyphosate in differentiated PC12 cells and discovered that it inhibited viability of differentiated PC12 cells in dose-and time-dependent manners. Furthermore, the results showed that glyphosate induced cell death via autophagy pathways in addition to activating apoptotic pathways. Interestingly, deactivation of Beclin-1 gene attenuated both apoptosis and autophagy in glyphosate treated differentiated PC12 cells, suggesting that Beclin-1 gene is involved in the crosstalk between the two mechanisms: http://www.ncbi.nlm.nih.gov/pubmed/22504123

Herbicides have been recognized as the main environmental factor associated with human neurodegenerative disorders such as Parkinson's disease. Furthermore, the results showed that glyphosate induced cell death via autophagy pathways in addition to activating apoptotic pathways of cellular death.

Parkinsonism after glycine-derivate exposure

by Barbosa ER1, Leiros da Costa MD, Bacheschi LA, Scaff M, Leite CC.

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Abstract

This 54-year-old man accidentally sprayed himself with the chemical agent glyphosate, a herbicide derived from the amino acid glycine. He developed disseminated skin lesions 6 hours after the accident. One month later, he developed a symmetrical parkinsonian syndrome. Two years after the initial exposure to glyphosate, magnetic resonance imaging revealed hyperintense signal in the globus pallidus and substantia nigra, bilaterally, on T2-weighted images. Levodopa/benserazide 500/125 mg daily provided satisfactory clinical outcome: http://www.ncbi.nlm.nih.gov/pubmed/11391760

Parkinson's
by Jeff Prager

My love, Ann, has had Parkinsons for 2 decades and she recently had extraordinarily successful brain surgery. I don't have to tell you that I've probably read more current Parkinsons studies than our doctors.

This man discussed above was contaminated at an unknown level and we don't even know with how much glyphosate. Yet within 6 hours he exhibited disseminated skin lesions (pictured) and within 30 days he developed the initial and quite significant symptoms of Parkinson's syndrome. Two years later he required the standard dose of the primary Parkinson's anti-tremor medication—Levodopa 500/125—likely taken every 3-4 hours and costing a fortune, here in the USA at least. And he'll take these drugs for life and the number of different drugs he'll be prescribed will increase with the passage of time as the disease progresses. Until he receives the final Parkinson's gift, Parkinson's related dementia. He'll still have to take 8 different meds every 2.5 to 3 hours and they won't work very well any longer but his dementia will likely prevent him from knowing—anything at all. Next will come incontinence, adult diapers and strangers cleaning your private parts. Glyphosate causes Parkinson's, and rapidly, and we allow its manufacture."

Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize

by Séralini GE1, Clair E, Mesnage R, Gress S, Defarge N, Malatesta M, Hennequin D, de Vendômois JS

Author information

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Abstract

The health effects of a Roundup-tolerant genetically modified maize (from 11% in the diet), cultivated with or without Roundup, and Roundup alone (from 0.1 ppb in water), were studied 2 years in rats. In females, all treated groups died 2-3 times more than controls, and more rapidly. This difference was visible in 3 male groups fed GMOs. All results were hormone and sex dependent, and the pathological profiles were comparable. Females developed large mammary tumors almost always more often than and before controls, the pituitary was the second most disabled organ; the sex hormonal balance was modified by GMO and Roundup treatments. In treated males, liver congestions and necrosis were 2.5-5.5 times higher. This pathology was confirmed by optic and transmission electron microscopy. Marked and severe kidney nephropathies were also generally 1.3-2.3 greater. Males presented 4 times more large palpable tumors than controls which occurred up to 600 days earlier. Biochemistry data confirmed very significant kidney chronic deficiencies; for all treatments and both sexes, 76% of the altered parameters were kidney related. These results can be explained by the non linear endocrine-disrupting effects of Roundup, but also by the overexpression of the transgene in the GMO and its metabolic consequences: http://www.ncbi.nlm.nih.gov/pubmed/22999595

The results of this study;
unexpected early deaths, large
female mammary tumors, disabled pituitary glands, liver necrosis, severe kidney
nephropathies and chronic kidney
deficiencies are all explained
by RoundupTM poisoning

Pathological and toxicological findings in glyphosate-surfactant herbicide fatality: a case report

by Sribanditmongkol P1, Jutavijittum P, Pongraveevongsa P, Wunnapuk K, Durongkadech P.

Author information

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Abstract

Glyphosate herbicide is promoted by the manufacturer as having no risks to human health, with acute toxicity being very low in normal use. In Thailand, however, poisoning from glyphosate agricultural herbicides has been increasing. A case of rapid lethal intoxication from glyphosate-surfactant herbicide involved a 37-year-old woman, who deliberately ingested approximately 500 mL of concentrated Roundup formulation (41% glyphosate as the isopropylamine salt and 15% polyoxyethylene amine; Mosanto Company). The postmortem examination revealed that the stomach contained 550 mL of yellow fluid. The gastric mucosa of anterior fundus revealed hemorrhage and the small intestines had marked dilatation and thin walls. We used the high-performance liquid chromatography method for determination of serum and gastric content levels of glyphosate. The glyphosate levels of serum and gastric content were 3.05 and 59.72 mg/mL, respectively. Toxic effects of polyoxyethylene amine and Roundup were caused by their ability to erode tissues including mucous membranes and linings of the gastrointestinal and respiratory tracts. A mild degree of pulmonary congestion and edema was observed in both lungs. We proposed that the characteristic picture of microvesicular steatosis of the hepatocytes, seen predominantly in centrilobular zones of the liver, resembled drug-induced hepatic toxicity or secondary hypoxic stress: http://www.ncbi.nlm.nih.gov/pubmed/22835958

Suicide by Roundup:
a popular pass-time for uneducated farmers
that are coerced into using this failing, degrading
and earth poisoning technology.

In this suicide by glyphosate study the deadly
toxic effects of polyoxyethylene amine and Roundup were
caused by their ability to erode tissues
including mucous membranes and linings of the
gastrointestinal and respiratory tracts.

Predicting acute complicated glyphosate intoxication in the emergency department

by Moon JM1, Chun BJ.

Author information

1Department of Emergency Medicine, Chonnam National University Hospital, Gwangju, Republic of Korea.

Abstract

BACKGROUND:

Glyphosate herbicide intoxication results in a range of mortality and morbidity, depending on patients' factors. Predicting which patient will need intensive medical treatment might help reduce mortality by providing prompt treatment, as well as triage those patients not likely to develop complications. Thus, we sought to identify independent factors that could predict which patient will develop subsequent medical complications.

METHODS:

Seventy-six patients presenting with acute glyphosate herbicide ingestion at Chonnam National University Hospital were enrolled in this retrospective study. To identify the predictive factors for complications, objective variables easily assessed at presentation including previously reported predictive factors for mortality, such as age, vital signs, X-ray abnormalities, and laboratory findings, were analyzed by univariate and multivariate stepwise logistic regression analyses.

RESULTS:

Of the 76 patients, 32 (42.1%) had medical complications and 2 (2.6%) died. Metabolic acidosis was the most common medical complication. Whereas metabolic acidosis, respiratory failure, hypotension, acute kidney injury, hyperkalemia, and seizures developed within 24 h, acute pancreatitis occurred a few days after the ingestion. The univariate analysis showed that an advanced age, amount ingested >100 mL, X-ray abnormalities, elevated amylase, alanine aminotransferase (ALT), and blood nitrogen urea were significant factors. However, the multivariate analysis showed that advanced age, elevated ALT, and X-ray abnormalities were independent factors associated with serious complications and the need for intensive medical treatment.

CONCLUSIONS:

The results of this study showed that age > 50 years, X-ray abnormalities, and ALT > 40 U/L were significant predictive factors for complications in patients with glyphosate surfactant herbicide poisoning; patients with these findings might require admission to the intensive care unit: http://www.ncbi.nlm.nih.gov/pubmed/20849329

76 People Attempt Suicide By Glyphosate

A review: oxidative stress in fish induced by pesticides.

by Slaninova A1, Smutna M, Modra H, Svobodova Z.

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Abstract

The knowledge in oxidative stress in fish has a great importance for environmental and aquatic toxicology. Because oxidative stress is evoked by many chemicals including some pesticides, pro-oxidant factors' action in fish organism can be used to assess specific area pollution or world sea pollution. Hepatotoxic effect of DDT may be related with lipid peroxidation. Releasing of reactive oxygen species (ROS) after HCB exposure can be realized via two ways: via the uncoupling of the electron transport chain from monooxygenase activity and via metabolism of HCB major metabolite pentachlorophenol. Chlorothalonil disrupts mitochondrial metabolism due to the impairment of NADPH oxidase function. Activation of spleen macrophages and a decrease of catalase (CAT) activity have been observed after endosulfan exposure. Excessive release of superoxide radicals after etoxazole exposure can cause a decrease of CAT activity and increase phagocytic activity of splenocytes. Anticholinergic activity of organophosphates leads to the accumulation of ROS and resulting lipid peroxidation. Carbaryl induces changes in the content of glutathione and antioxidant enzymes activities. The antioxidant enzymes changes have been observed after actuation of pesticides deltamethrin and cypermethrin. Bipyridyl herbicides are able to form redox cycles and thereby cause oxidative stress. Low concentrations of simazine do not cause oxidative stress in carps during sub-chronic tests while sublethal concentrations of atrazin can induce oxidative stress in bluegill sunfish. Butachlor causes increased activity of superoxide dismutase -catalase system in the kidney. Rotenon can inhibit the electron transport in mitochondria and thereby increase ROS production. Dichloroaniline, the metabolite of diuron, has oxidative effects. Oxidative damage from fenpyroximate actuation is related to the disruption of mitochondrial redox respiratory chain. Low concentration of glyphosate can cause mild oxidative stress: http://www.ncbi.nlm.nih.gov/pubmed/20027135

Low concentration of glyphosate can cause mild oxidative stress

Glyphosate formulations induce apoptosis and necrosis in human umbilical, embryonic, and placental cells

by Benachour N1, Séralini GE

Author information

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Abstract

We have evaluated the toxicity of four glyphosate (G)-based herbicides in Roundup formulations, from 10(5) times dilutions, on three different human cell types. This dilution level is far below agricultural recommendations and corresponds to low levels of residues in food or feed. The formulations have been compared to G alone and with its main metabolite AMPA or with one known adjuvant of R formulations, POEA. HUVEC primary neonate umbilical cord vein cells have been tested with 293 embryonic kidney and JEG3 placental cell lines. All R formulations cause total cell death within 24 h, through an inhibition of the mitochondrial succinate dehydrogenase activity, and necrosis, by release of cytosolic adenylate kinase measuring membrane damage. They also induce apoptosis via activation of enzymatic caspases 3/7 activity. This is confirmed by characteristic DNA fragmentation, nuclear shrinkage (pyknosis), and nuclear fragmentation (karyorrhexis), which is demonstrated by DAPI in apoptotic round cells. G provokes only apoptosis, and HUVEC are 100 times more sensitive overall at this level. The deleterious effects are not proportional to G concentrations but rather depend on the nature of the adjuvants. AMPA and POEA separately and synergistically damage cell membranes like R but at different concentrations. Their mixtures are generally even more harmful with G. In conclusion, the R adjuvants like POEA change human cell permeability and amplify toxicity induced already by G, through apoptosis and necrosis. The real threshold of G toxicity must take into account the presence of adjuvants but also G metabolism and time-amplified effects or bioaccumulation. This should be discussed when analyzing the in vivo toxic actions of R. This work clearly confirms that the adjuvants in Roundup formulations are not inert. Moreover, the proprietary mixtures available on the market could cause cell damage and even death around residual levels to be expected, especially in food and feed derived from R formulation-treated crops: http://www.ncbi.nlm.nih.gov/pubmed/19105591

This work clearly confirms that the adjuvants in Roundup formulations are not inert. Moreover, the proprietary mixtures available on the market could cause cell damage and even death around residual levels to be expected, especially in food derived from Roundup formulation-treated crops

Time- and dose-dependent effects of roundup on human embryonic and placental cells

by Benachour N1, Sipahutar H, Moslemi S, Gasnier C, Travert C, Séralini GE.

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Abstract

Roundup is the major herbicide used worldwide, in particular on genetically modified plants that have been designed to tolerate it. We have tested the toxicity and endocrine disruption potential of Roundup (Bioforce on human embryonic 293 and placental-derived JEG3 cells, but also on normal human placenta and equine testis. The cell lines have proven to be suitable to estimate hormonal activity and toxicity of pollutants. The median lethal dose (LD(50)) of Roundup with embryonic cells is 0.3% within 1 h in serum-free medium, and it decreases to reach 0.06% (containing among other compounds 1.27 mM glyphosate) after 72 h in the presence of serum. In these conditions, the embryonic cells appear to be 2-4 times more sensitive than the placental ones. In all instances, Roundup (generally used in agriculture at 1-2%, i.e., with 21-42 mM glyphosate) is more efficient than its active ingredient, glyphosate, suggesting a synergistic effect provoked by the adjuvants present in Roundup. We demonstrated that serum-free cultures, even on a short-term basis (1 h), reveal the xenobiotic impacts that are visible 1-2 days later in serum. We also document at lower non-overtly toxic doses, from 0.01% (with 210 microM glyphosate) in 24 h, that Roundup is an aromatase disruptor. The direct inhibition is temperature-dependent and is confirmed in different tissues and species (cell lines from placenta or embryonic kidney, equine testicular, or human fresh placental extracts). Furthermore, glyphosate acts directly as a partial inactivator on microsomal aromatase, independently of its acidity, and in a dose-dependent manner. The cytotoxic, and potentially endocrine-disrupting effects of Roundup are thus amplified with time. Taken together, these data suggest that Roundup exposure may affect human reproduction and fetal development in case of contamination. Chemical mixtures in formulations appear to be underestimated regarding their toxic or hormonal impact: http://www.ncbi.nlm.nih.gov/pubmed/17486286

The cytotoxic,
and potentially endocrine-disrupting
effects of Roundup are thus amplified with time.

Taken together, these data suggest that Roundup exposure may affect human reproduction and fetal development in case of even low dose contamination

Acute poisoning with a glyphosate-surfactant herbicide ('Roundup'): a review of 93 cases

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Abstract

Between 1 January 1980, and 30 September 1989, 93 cases of exposure to herbicides containing glyphosphate and surfactant ('Roundup') were treated at Changhua Christian Hospital. The average amount of the 41% solution of glyphosate herbicide ingested by non-survivors was 184 +/- 70 ml (range 85-200 ml), but much larger amounts (500 ml) were reported to have been ingested by some patients and only resulted in mild to moderate symptomatology. Accidental exposure was asymptomatic after dermal contact with spray (six cases), while mild oral discomfort occurred after accidental ingestion (13 cases). Intentional ingestion (80 cases) resulted in erosion of the gastrointestinal tract (66%), seen as sore throat (43%), dysphagia (31%), and gastrointestinal haemorrhage (8%). Other organs were affected less often (non-specific leucocytosis 65%, lung 23%, liver 19%, cardiovascular 18%, kidney 14%, and CNS 12%). There were seven deaths, all of which occurred within hours of ingestion, two before the patient arrived at the hospital. Deaths following ingestion of 'Roundup' alone were due to a syndrome that involved hypotension, unresponsive to intravenous fluids or vasopressor drugs, and sometimes pulmonary oedema, in the presence of normal central venous pressure: http://www.ncbi.nlm.nih.gov/pubmed/1673618

80 Glyphosate Suicide Attempts
Seven Succeed

Mechanisms underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: involvement of glutamate excitotoxicity

by Cattani D1, de Liz Oliveira Cavalli VL1, Heinz Rieg CE1, Domingues JT1, Dal-Cim T1, Tasca CI1, Mena Barreto Silva FR1, Zamoner A2.

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Abstract

Previous studies demonstrate that glyphosate exposure is associated with oxidative damage and neurotoxicity. Therefore, the mechanism of glyphosate-induced neurotoxic effects needs to be determined. The aim of this study was to investigate whether Roundup(®) (a glyphosate-based herbicide) leads to neurotoxicity in hippocampus of immature rats following acute (30min) and chronic (pregnancy and lactation) pesticide exposure. Maternal exposure to pesticide was undertaken by treating dams orally with 1% Roundup(®) (0.38% glyphosate) during pregnancy and lactation (till 15-day-old). Hippocampal slices from 15 day old rats were acutely exposed to Roundup(®) (0.00005-0.1%) during 30min and experiments were carried out to determine whether glyphosate affects (45)Ca(2+) influx and cell viability. Moreover, we investigated the pesticide effects on oxidative stress parameters, (14)C-□-methyl-amino-isobutyric acid ((14)C-MeAIB) accumulation, as well as glutamate uptake, release and metabolism. Results showed that acute exposure to Roundup(®) (30min) increases (45)Ca(2+) influx by activating NMDA receptors and voltage-dependent Ca(2+) channels, leading to oxidative stress and neural cell death. The mechanisms underlying Roundup(®)-induced neurotoxicity also involve the activation of CaMKII and ERK. Moreover, acute exposure to Roundup(®) increased (3)H-glutamate released into the synaptic cleft, decreased GSH content and increased the lipoperoxidation, characterizing excitotoxicity and oxidative damage. We also observed that both acute and chronic exposure to Roundup(®) decreased (3)H-glutamate uptake and metabolism, while induced (45)Ca(2+) uptake and (14)C-MeAIB accumulation in immature rat hippocampus. Taken together, these results demonstrated that Roundup(®) might lead to excessive extracellular glutamate levels and consequently to glutamate excitotoxicity and oxidative stress in rat hippocampus: http://www.ncbi.nlm.nih.gov/pubmed/24636977

Previous studies demonstrate
that glyphosate exposure is associated with
oxidative damage and neurotoxicity.

Acute toxicity of a commercial glyphosate formulation on European sea bass juveniles (Dicentrarchus labrax L.):

Gene expressions of heme oxygenase-1 (ho-1), acetylcholinesterase (AChE) and aromatases (cyp19a and cyp19b)

by Prevot-D'Alvise N1, Richard S2, Coupé S2, Bunet R2, Grillasca JP2.

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Abstract

Acute toxicity of Roundup, a commercial glyphosate--based herbicide, was evaluated in a teleost marine fish, the European sea bass, after 96 h of exposure. The LC50 96-h value of Roundup was 529 mg/L. Juveniles (Dicentrarchus labrax L.) were exposed to a sublethal concentration (35% of the LC50, i.e. 193 mg/L) of Roundup for 96-h. The study of heme oxygenase-1 (ho-1) gene expression was performed in four tissues (liver, gills, brain and gonads) and highlighted the disruption of antioxidant defence system. Results showed that ho-1 mRNA levels in liver and gills significantly decreased ($p<0.001$ and $p<0.01$ respectively) in fish exposed to 193 mg/L of Roundup, whereas in brain and gonads, ho-1 mRNA level was not altered. The analysis of acetylcholinesterase expression was used to evaluate the overall neurotoxicity of the herbicide and aromatase genes to assess the alteration of the endocrine system. Results showed that AChE and cyp19b gene transcriptions significantly increased ($p<0.01$) in brain of sea bass, whereas aromatase gene expression (cyp19a) in gonads was not significantly altered. Our results showed complex tissue-specific transcriptional responses after 96 h of exposure to a sublethal concentration. All these disruptions confirmed the deleterious effects of this glyphosate-based herbicide in a marine species: http://www.ncbi.nlm.nih.gov/pubmed/24461331

Our results showed complex tissue-specific transcriptional responses after 96 hours of exposure to a sublethal concentration. All these disruptions confirmed the deleterious effects of this glyphosate-based herbicide in a marine species, the European Sea Bass

The impact of Eskoba, a glyphosate formulation, on the freshwater plankton community

by Reno U, Gutierrez MF, Regaldo L, Gagneten AM.

Abstract

This study analyzed the acute effects of a glyphosate-based herbicide (Eskoba) on the microalgae Chlorella vulgaris, the cladoceran Simocephalus vetulus, and the copepod Notodiaptomus conifer, and evaluated the recovery ability of the surviving micro-crustaceans. Survival, age of first reproduction, and fecundity were used as endpoints for S. vetulus, while survival and time to reach the adult stage were used as endpoints for N. conifer. The registered order of sensitivity was S. vetulus (48-hour effective concentration [EC50]: 21 mg/L) > C. vulgaris (72-hour EC50: 58.59 mg/ L) > N. conifer (48-hour EC50: 95 mg/L). Despite the growth of C. vulgaris stimulated after 24 hours of exposure to the commercial formulation of glyphosate Eskoba, it was inhibited after 48 hours by all the concentrations tested. In postexposure experiments, microcrustaceans reduced their life expectancy, S. vetulus decreased its fertility, and N. conifer inhibited its sexual maturity. In summary, it was demonstrated that these species lost their recovery ability: http://www.ncbi.nlm.nih.gov/pubmed/25654931

In summary,
it was demonstrated that these algal species
lost their ability to recover after exposure to glyphosate

Global transcriptomic profiling demonstrates induction of oxidative stress and of compensatory cellular stress responses in brown trout exposed to glyphosate and Roundup

by Uren Webster TM, Santos EM.

Abstract

Glyphosate, the active ingredient in Roundup formulations, is the most widely used herbicide worldwide, and as a result contaminates surface waters and has been detected in food residues, drinking water and human urine, raising concerns for potential environmental and human health impacts. Research has shown that glyphosate and Roundup can induce a broad range of biological effects in exposed organisms, particularly via generation of oxidative stress. However, there has been no comprehensive investigation of the global molecular mechanisms of toxicity of glyphosate and Roundup for any species. We aimed to characterise and compare the global mechanisms of toxicity of glyphosate and Roundup in the liver of brown trout (Salmo trutta), an ecologically and economically important vertebrate species, using RNA-seq on an Illumina HiSeq 2500 platform. To do this, we exposed juvenile female brown trout to 0, 0.01, 0.5 and 10 mg/L of glyphosate and Roundup (glyphosate acid equivalent) for 14 days, and sequenced 6 replicate liver samples from each treatment.

Results

We assembled the brown trout transcriptome using an optimised de novo approach, and subsequent differential expression analysis identified a total of 1020 differentially-regulated transcripts across all treatments. These included transcripts encoding components of the antioxidant system, a number of stress-response proteins and pro-apoptotic signalling molecules. Functional analysis also revealed over-representation of pathways involved in regulating of cell-proliferation and turnover, and up-regulation of energy metabolism and other metabolic processes.

Conclusions

These transcriptional changes are consistent with generation of oxidative stress and the widespread induction of compensatory cellular stress response pathways. The mechanisms of toxicity identified were similar across both glyphosate and Roundup treatments, including for environmentally relevant concentrations. The significant alterations in transcript expression observed at the lowest concentrations tested raises concerns for the potential toxicity of this herbicide to fish populations inhabiting contaminated rivers: http://www.ncbi.nlm.nih.gov/pubmed/25636363

The significant alterations in transcript expression observed at the lowest concentrations tested raises concerns for the potential toxicity of this herbicide to fish populations inhabiting contaminated rivers

The herbicide glyphosate causes behavioral changes and alterations in dopaminergic markers in male Sprague-Dawley rat

by Hernández-Plata I1, Giordano M1, Díaz-Muñoz M2, Rodríguez VM3.

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Abstract

Glyphosate (Glyph) is the active ingredient of several herbicide formulations. Reports of Glyph exposure in humans and animal models suggest that it may be neurotoxic. To evaluate the effects of Glyph on the nervous system, male Sprague-Dawley rats were given six intraperitoneal injections of 50, 100, or 150mg Glyph/kg BW over 2 weeks (three injections/week). We assessed dopaminergic markers and their association with locomotor activity. Repeated exposure to Glyph caused hypoactivity immediately after each injection, and it was also apparent 2 days after the last injection in rats exposed to the highest dose. Glyph did not decrease monoamines, tyrosine hydroxylase (TH), or mesencephalic TH+ cells when measured 2 or 16 days after the last Glyph injection. In contrast, Glyph decreased specific binding to D1 dopamine (DA) receptors in the nucleus accumbens (NAcc) when measured 2 days after the last Glyph injection. Microdialysis experiments showed that a systemic injection of 150mg Glyph/kg BW decreased basal extracellular DA levels and high-potassium-induced DA release in striatum. Glyph did not affect the extracellular concentrations of 3,4-dihydroxyphenylacetic acid or homovanillic acid. These results indicate that repeated Glyph exposure results in hypoactivity accompanied by decreases in specific binding to D1-DA receptors in the NAcc, and that acute exposure to Glyph has evident effects on striatal DA levels. Additional experiments are necessary in order to unveil the specific targets of Glyph on dopaminergic system, and whether Glyph could be affecting other neurotransmitter systems involved in motor control: http://www.ncbi.nlm.nih.gov/pubmed/25522657

The herbicide glyphosate causes behavioral changes and neurological disorders

Using a toxicity test with Ruppia maritima (Linnaeus) to assess the effects of Roundup

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Abstract

Glyphosate, the active ingredient in Monsanto's broad-spectrum herbicide Roundup, consists of one of the most used pesticides worldwide, but its effects on the marine flora are still not well understood. Were examined Roundup toxic effects on Ruppia maritima specimens collected from Jansen Lagoon (São Luís, MA, Brazil) and acclimatized under laboratory conditions. The numbers of new and dead leaves, the root and leaf length, the chlorophyll a content, and the weight of R. maritima branches were determined before and after exposure to different Roundup concentrations for seven days. High concentrations caused a significant lethal effect. In addition, significant changes were observed in the wet and dry weights, the number and length of the leaves, and the chlorophyll a content. Leaf elongation was observed in the branches exposed to low concentrations, and this change was likely activated as a compensatory mechanism. The results indicate that high concentrations of this herbicide may compromise estuarine flora: http://www.ncbi.nlm.nih.gov/pubmed/25455815

Monsanto's broad-spectrum herbicide Roundup, consists of one of the most used pesticides worldwide, but its effects on the marine flora are still not well understood. The results of this study indicate that high concentrations of this herbicide may compromise estuarine flora

Progression of DNA damage induced by a glyphosate-based herbicide in fish (Anguilla anguilla) upon exposure and post-exposure periods: insights into the mechanisms of genotoxicity and DNA repair

by Marques A1, Guilherme S2, Gaivão I3, Santos MA2, Pacheco M2.

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Abstract

Roundup® is a glyphosate-based herbicide widely used with both agricultural and non-agricultural purposes, which has been demonstrated to represent a risk to non-target aquatic organisms, namely fish. Among the described effects to fish, genotoxicity has been pointed out as one of the most hazardous. However, the genotoxic mechanisms of Roundup® as well as the involvement of the oxidative DNA damage repair system are not entirely understood. Hence, this work aimed to improve the knowledge on the progression of DNA damage upon short-term exposure (3 days) and post-exposure (1-14 days) periods in association with DNA repair processes in Anguilla anguilla exposed to Roundup® (58 and 116 µg L(-1)). DNA damage in hepatic cells was evaluated by the comet assay improved with the DNA-lesion specific endonucleases FPG and EndoIII. In order to evaluate the oxidative DNA damage repair ability, an in vitro base excision repair (BER) assay was performed, testing hepatic subcellular extracts. Besides the confirmation of the genotoxic potential of this herbicide, oxidative damage was implicit as an important mechanism of genetic damage, which showed to be transient, since DNA integrity returned to the control levels on the first day after cessation of exposure. An increased capacity to repair oxidative DNA damage emerging in the post-exposure period revealed to be a crucial pathway for the A. anguilla recovery; nevertheless, DNA repair machinery showed to be susceptible to inhibitory actions during the exposure period, disclosing another facet of the risk associated with the tested agrochemical: http://www.ncbi.nlm.nih.gov/pubmed/25110831

Among the described effects to fish, genotoxicity has been pointed out as one of the most hazardous

Glyphosate formulations induce apoptosis and necrosis in human umbilical, embryonic, and placental cells

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Abstract

We have evaluated the toxicity of four glyphosate (G)-based herbicides in Roundup formulations, from 10(5) times dilutions, on three different human cell types. This dilution level is far below agricultural recommendations and corresponds to low levels of residues in food or feed. The formulations have been compared to G alone and with its main metabolite AMPA or with one known adjuvant of R formulations, POEA. HUVEC primary neonate umbilical cord vein cells have been tested with 293 embryonic kidney and JEG3 placental cell lines. All R formulations cause total cell death within 24 h, through an inhibition of the mitochondrial succinate dehydrogenase activity, and necrosis, by release of cytosolic adenylate kinase measuring membrane damage. They also induce apoptosis via activation of enzymatic caspases 3/7 activity. This is confirmed by characteristic DNA fragmentation, nuclear shrinkage (pyknosis), and nuclear fragmentation (karyorrhexis), which is demonstrated by DAPI in apoptotic round cells. G provokes only apoptosis, and HUVEC are 100 times more sensitive overall at this level. The deleterious effects are not proportional to G concentrations but rather depend on the nature of the adjuvants. AMPA and POEA separately and synergistically damage cell membranes like R but at different concentrations. Their mixtures are generally even more harmful with G. In conclusion, the R adjuvants like POEA change human cell permeability and amplify toxicity induced already by G, through apoptosis and necrosis. The real threshold of G toxicity must take into account the presence of adjuvants but also G metabolism and time-amplified effects or bioaccumulation. This should be discussed when analyzing the in vivo toxic actions of R. This work clearly confirms that the adjuvants in Roundup formulations are not inert. Moreover, the proprietary mixtures available on the market could cause cell damage and even death around residual levels to be expected, especially in food and feed derived from R formulation-treated crops: http://www.ncbi.nlm.nih.gov/pubmed/19105591

We have evaluated the toxicity of four glyphosate (G)-based herbicides in Roundup formulations, from 10(5) times dilutions, on three different human cell types. This dilution level is far below agricultural recommendations and corresponds to low levels of residues in food or feed. This work clearly confirms that the adjuvants in Roundup formulations are not inert. Moreover, the proprietary mixtures available on the market could cause cell damage and even death around residual levels to be expected, especially in food and feed derived from R formulation-treated crops

Glyphosate-Based Herbicides Produce Teratogenic Effects on Vertebrates by Impairing Retinoic Acid Signaling

Publication Date (Web): August 9, 2010

Abstract

The broad spectrum herbicide glyphosate is widely used in agriculture worldwide. There has been ongoing controversy regarding the possible adverse effects of glyphosate on the environment and on human health. Reports of neural defects and craniofacial malformations from regions where glyphosate-based herbicides (GBH) are used led us to undertake an embryological approach to explore the effects of low doses of glyphosate in development. Xenopus laevis embryos were incubated with 1/5000 dilutions of a commercial GBH. The treated embryos were highly abnormal with marked alterations in cephalic and neural crest development and shortening of the anterior□posterior (A-P) axis. Alterations on neural crest markers were later correlated with deformities in the cranial cartilages at tadpole stages. Embryos injected with pure glyphosate showed very similar phenotypes. Moreover, GBH produced similar effects in chicken embryos, showing a gradual loss of rhombomere domains, reduction of the optic vesicles, and microcephaly. This suggests that glyphosate itself was responsible for the phenotypes observed, rather than a surfactant or other component of the commercial formulation. A reporter gene assay revealed that GBH treatment increased endogenous retinoic acid (RA) activity in Xenopus embryos and cotreatment with a RA antagonist rescued the teratogenic effects of the GBH. Therefore, we conclude that the phenotypes produced by GBH are mainly a consequence of the increase of endogenous retinoid activity. This is consistent with the decrease of Sonic hedgehog (Shh) signaling from the embryonic dorsal midline, with the inhibition of otx2 expression and with the disruption of cephalic neural crest development. The direct effect of glyphosate on early mechanisms of morphogenesis in vertebrate embryos opens concerns about the clinical findings from human offspring in populations exposed to GBH in agricultural fields: http://pubs.acs.org/doi/citedby/10.1021/tx1001749

The direct effect of glyphosate on early mechanisms of morphogenesis in vertebrate embryos opens concerns about the clinical findings from human offspring in populations exposed to GBH in agricultural fields. Xenopus laevis embryos were incubated with 1/5000 dilutions of a commercial GBH. The treated embryos were highly abnormal with marked alterations in cephalic and neural crest development and shortening of the anterior-posterior (A-P) axis.

Detection of Glyphosate Residues in Animals and Humans

Environmental & Analytical Toxicology

by Monika Krüger1, Philipp Schledorn1, Wieland Schrödl1, Hans-Wolfgang Hoppe2, Walburga Lutz3 and Awad A. Shehata1,4*

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Abstract

In the present study glyphosate residues were tested in urine and different organs of dairy cows as well as in urine of hares, rabbits and humans using ELISA and Gas Chromatography-Mass Spectroscopy (GC-MS). The correlation coefficients between ELISA and GC-MS were 0.96, 0.87, 0.97and 0.96 for cattle, human, and rabbit urine and organs, respectively. The recovery rate of glyphosate in spiked meat using ELISA was 91%. Glyphosate excretion in German dairy cows was significantly lower than Danish cows. Cows kept in genetically modified free area had significantly lower glyphosate concentrations in urine than conventional husbandry cows. Also glyphosate was detected in different organs of slaughtered cows as intestine, liver, muscles, spleen and kidney. Fattening rabbits showed significantly higher glyphosate residues in urine than hares. Moreover, glyphosate was significantly higher in urine of humans with conventional feeding. Furthermore, chronically ill humans showed significantly higher glyphosate residues in urine than healthy population. The presence of glyphosate residues in both humans and animals could haul the entire population towards numerous health hazards, studying the impact of glyphosate residues on health is warranted and the global regulations for the use of glyphosate may have to be re-evaluated.

Conclusions

Glyphosate residue could reach humans and animals through feed and excreted in urine. Presence of glyphosate in urine and its accumulation in animal tissues is alarming even at low concentrations. Unknown impacts of glyphosate on human and animal health warrants further investigations of glyphosate residues in vertebrates and other non-target organisms. Chronically ill humans had significantly higher glyphosate residues in urine than healthy humans.

Chronically ill humans
had significantly higher glyphosate residues in urine
than healthy humans

Aluminum and Glyphosate Can Synergistically Induce Pineal Gland Pathology: Connection to Gut Dysbiosis and Neurological Disease

by Stephanie Seneff1*, Nancy Swanson2, Chen Li1

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Abstract

Many neurological diseases, including autism, depression, dementia, anxiety disorder and Parkinson's disease, are associated with abnormal sleep patterns, which are directly linked to pineal gland dysfunction. The pineal gland is highly susceptible to environmental toxicants. Two pervasive substances in modern industrialized nations are aluminum and glyphosate, the active ingredient in the herbicide, Roundup®. In this paper, we show how these two toxicants work synergistically to induce neurological damage. Glyphosate disrupts gut bacteria, leading to an overgrowth of Clostridium difficile. Its toxic product, p-cresol, is linked to autism in both human and mouse models. p-Cresol enhances uptake of aluminum via transferrin. Anemia, a result of both aluminum disruption of heme and impaired heme synthesis by glyphosate, leads to hypoxia, which induces increased pineal gland transferrin synthesis. Premature birth is associated with hypoxic stress and with substantial increased risk to the subsequent development of autism, linking hypoxia to autism. Glyphosate chelates aluminum, allowing ingested aluminum to bypass the gut barrier. This leads to anemia-induced hypoxia, promoting neurotoxicity and damaging the pineal gland. Both glyphosate and aluminum disrupt cytochrome P450 enzymes, which are involved in melatonin metabolism. Furthermore, melatonin is derived from tryptophan, whose synthesis in plants and microbes is blocked by glyphosate. We also demonstrate a plausible role for vitamin D3 dysbiosis in impaired gut function and impaired serotonin synthesis. This paper proposes that impaired sulfate supply to the brain mediates the damage induced by the synergistic action of aluminum and glyphosate on the pineal gland and related midbrain nuclei.

Many neurological diseases, including autism, depression, dementia,
anxiety disorder and Parkinson's disease, are associated with
abnormal sleep patterns, which are directly linked to pineal gland
dysfunction. The pineal gland is highly susceptible to environmental
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are aluminum and glyphosate, the active ingredient in the herbicide,
Roundup®. In this paper, we show how these two toxicants
work synergistically to induce neurological damage

Hypothetical link between infertility and genetically modified food

by Gao M, Li B, Yuan W, Zhao L, Zhang X1.

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Abstract

It is speculated that genetically modified food (GMF)/genetically modified organism (GMO) is responsible for infertility development. The risk linked with a wide use of GMFs/GMOs offers the basic elements for social criticism. However, to date, it has not been justified whether the bad effects are directly resulted from products of genetic modifications or trans-genesis process. Extensive experience with the risk assessment of whole foods has been applied recently on the safety and nutritional testing of GMFs/GMOs. Investigations have tested the safety of GMFs including sub-acute, chronic, reproductive, multi-generation and carcinogenicity studies. We extrapolated the potential risks associated with GMFs/GMOs on reproduction, and analyzed the multi-aspect linked between infertility and GMFs/GMOs. It could be conjectured that GMFs/GMOs could be potential hazard on reproduction, linking to the development of infertility through influencing the endocrine metabolism, endometriosis. However, little evidence shows the impaction on embryo or reproductive related tumor due to the limited literatures, and needs further research. The article presents some related patents on GMFs/GMOs, and some methods for tracking GMOs: http://www.ncbi.nlm.nih.gov/pubmed/25342149

It is speculated that genetically modified food (GMF)/genetically modified organism (GMO) is responsible for infertility development

Expert opinion vs. empirical evidence: the precautionary principle applied to GM crops.

by Herman RA1, Raybould A2.

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Abstract

Expert opinion is often sought by government regulatory agencies when there is insufficient empirical evidence to judge the safety implications of a course of action. However, it can be reckless to continue following expert opinion when a preponderance of evidence is amassed that conflicts with this opinion. Factual evidence should always trump opinion in prioritizing the information that is used to guide regulatory policy. Evidence-based medicine has seen a dramatic upturn in recent years spurred by examples where evidence indicated that certain treatments recommended by expert opinions increased death rates. We suggest that scientific evidence should also take priority over expert opinion in the regulation of genetically modified crops (GM). Examples of regulatory data requirements that are not justified based on the mass of evidence are described, and it is suggested that expertise in risk assessment should guide evidence-based regulation of GM crops.

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Debate on GMOs health risks after statistical findings in regulatory tests

by de Vendômois JS1, Cellier D, Vélot C, Clair E, Mesnage R, Séralini GE.

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Abstract

We summarize the major points of international debate on health risk studies for the main commercialized edible GMOs. These GMOs are soy, maize and oilseed rape designed to contain new pesticide residues since they have been modified to be herbicide-tolerant (mostly to Roundup) or to produce mutated Bt toxins. The debated alimentary chronic risks may come from unpredictable insertional mutagenesis effects, metabolic effects, or from the new pesticide residues. The most detailed regulatory tests on the GMOs are three-month long feeding trials of laboratory rats, which are biochemically assessed. The tests are not compulsory, and are not independently conducted. The test data and the corresponding results are kept in secret by the companies. Our previous analyses of regulatory raw data at these levels, taking the representative examples of three GM maize NK 603, MON 810, and MON 863 led us to conclude that hepatorenal toxicities were possible, and that longer testing was necessary. Our study was criticized by the company developing the GMOs in question and the regulatory bodies, mainly on the divergent biological interpretations of statistically significant biochemical and physiological effects. We present the scientific reasons for the crucially different biological interpretations and also highlight the shortcomings in the experimental protocols designed by the company. The debate implies an enormous responsibility towards public health and is essential due to nonexistent traceability or epidemiological studies in the GMO-producing countries: http://www.ncbi.nlm.nih.gov/pubmed/20941377

The most detailed regulatory tests on the GMOs are three-month long feeding trials of laboratory rats, which are biochemically assessed. The tests are not compulsory, and are not independently conducted. The test data and the corresponding results are kept in secret by the companies.

Transgenic soybean pollen (Glycine max L.) in honey from the Yucatán peninsula, Mexico

by Villanueva-Gutiérrez R1, Echazarreta-González C2, Roubik DW3, Moguel-Ordóñez YB4.

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Abstract

Using precise pollen species determination by conventional microscopic methods, accompanied by molecular genetic markers, we found bees collect GMO (genetically modified) soybean pollen and incorporate it in Yucatan honey. Honey comb samples from Las Flores, Campeche, Mexico, often contained soybean pollen. Pollen in honey was analyzed in nine samples; six contained substantial soy pollen and two tested positive for soybean GMO. Our analyses confirm field observations that honey bees, Apis mellifera, gather soybean pollen and nectar. The resultant risk for honey production in the Yucatán Peninsula and Mexico is evident in wholesale price reduction of 12% when GMO products are detected and honey consignments are rejected. Although this affects only 1% of current export honey (2011-2013) GMO soybean is an unacknowledged threat to apiculture and its economics in one of the world's foremost honey producing areas: http://www.ncbi.nlm.nih.gov/pubmed/24503936

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Mutagenicity testing of nine herbicides and pesticides currently used in agriculture

by Kale PG1, Petty BT Jr, Walker S, Ford JB, Dehkordi N, Tarasia S, Tasie BO, Kale R, Sohni YR.

Author information

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Abstract

Nine herbicides and pesticides were tested for their mutagenicity using the Drosophila sex-linked recessive lethal mutation assay. These are Ambush, Treflan, Blazer, Roundup, 2,4-D Amine, Crossbow, Galecron, Pramitol, and Pondmaster. All of these are in wide use at present. Unlike adult feeding and injection assays, the larvae were allowed to grow in medium with the test chemical, thereby providing long and chronic exposure to the sensitive and dividing diploid cells, i.e., mitotically active spermatogonia and sensitive spermatocytes. All chemicals induced significant numbers of mutations in at least one of the cell types tested. Some of these compounds were found to be negative in earlier studies. An explanation for the difference in results is provided. It is probable that different germ cell stages and treatment regimens are suitable for different types of chemicals. larval treatment may still be valuable and can complement adult treatment in environmental mutagen testing: http://www.ncbi.nlm.nih.gov/pubmed/7698107

All chemicals induced significant numbers of mutations in at least one of the cell types tested

Glyphosate in northern ecosystems

by Helander M1, Saloniemi I, Saikkonen K.

Author information

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Abstract

Glyphosate is the main nonselective, systemic herbicide used against a wide range of weeds. Its worldwide use has expanded because of extensive use of certain agricultural practices such as no-till cropping, and widespread application of glyphosate-resistant genetically modified crops. Glyphosate has a reputation of being nontoxic to animals and rapidly inactivated in soils. However, recent evidence has cast doubts on its safety. Glyphosate may be retained and transported in soils, and there may be cascading effects on nontarget organisms. These processes may be especially detrimental in northern ecosystems because they are characterized by long biologically inactive winters and short growing seasons. In this opinion article, we discuss the potential ecological, environmental and agricultural risks of intensive glyphosate use in boreal regions.

Glyphosate has a reputation of being nontoxic to animals and rapidly inactivated in soils. However, recent evidence has cast doubts on its safety. Glyphosate may be retained and transported in soils, and there may be cascading effects on nontarget organisms.

Effects of glyphosate and its formulation, roundup, on reproduction in zebrafish (Danio rerio).

by Uren Webster TM1, Laing LV, Florance H, Santos EM.

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Abstract

Roundup and its active ingredient glyphosate are among the most widely used herbicides worldwide and may contaminate surface waters. Research suggests both Roundup and glyphosate induce oxidative stress in fish and may also cause reproductive toxicity in mammalian systems. We aimed to investigate the reproductive effects of Roundup and glyphosate in fish and the potential associated mechanisms of toxicity. To do this, we conducted a 21-day exposure of breeding zebrafish (Danio rerio) to 0.01, 0.5, and 10 mg/L (glyphosate acid equivalent) Roundup and 10 mg/L glyphosate. 10 mg/L glyphosate reduced egg production but not fertilization rate in breeding colonies. Both 10 mg/L Roundup and glyphosate increased early stage embryo mortalities and premature hatching. However, exposure during embryogenesis alone did not increase embryo mortality, suggesting that this effect was caused primarily by exposure during gametogenesis. Transcript profiling of the gonads revealed 10 mg/L Roundup and glyphosate induced changes in the expression of cyp19a1 and esr1 in the ovary and hsd3b2, cat, and sod1 in the testis. Our results demonstrate that these chemicals cause reproductive toxicity in zebrafish, although only at high concentrations unlikely to occur in the environment, and likely mechanisms of toxicity include disruption of the steroidogenic biosynthesis pathway and oxidative stress: http://www.ncbi.nlm.nih.gov/pubmed/24364672

Our results demonstrate that these chemicals cause reproductive toxicity in zebrafish, although only at high concentrations unlikely to occur in the environment, and likely mechanisms of toxicity include disruption of the steroidogenic biosynthesis pathway and oxidative stress

The endocrine disrupter effect of atrazine and glyphosate on Biomphalaria alexandrina snails

by Omran NE1, Salama WM.

Author information

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Abstract

Atrazine (AZ) and glyphosate (GL) are herbicides that are widely applied to cereal crops in Egypt. The present study was designed to investigate the response of the snail Biomphalaria alexandrina (Mollusca: Gastropoda) as a bioindicator for endocrine disrupters in terms of steroid levels (testosterone (T) and 17-estradiol (E)), alteration of microsomal CYP4501B1-like immunoreactivity, total protein (TP) level, and gonadal structure after exposure to sublethal concentrations of AZ or GL for 3 weeks. In order to study the ability of the snails' recuperation, the exposed snails were subjected to a recovery period for 2 weeks. The results showed that the level of T, E, and TP contents were significantly decreased ($p \leq 0.05$) in both AZ- and GL-exposed groups compared with control (unexposed) group. The level of microsomal CYP4501B1-like immunoreactivity increased significantly ($p \leq 0.05$) in GL- and AZ-exposed snails and reach nearly a 50% increase in AZ-exposed group. Histological investigation of the ovotestis showed that AZ and GL caused degenerative changes including azoospermia and oocytes deformation. Interestingly, all the recovered groups did not return back to their normal state. It can be concluded that both herbicides are endocrine disrupters and cause cellular toxicity indicated by the decrease of protein content and the increase in CYP4501B1-like immunoreactivity. This toxicity is irreversible and the snail is not able to recover its normal state. The fluctuation of CYP4501B1 suggests that this vertebrate-like enzyme may be functional also in the snail and may be used as a biomarker for insecticide toxicity: http://www.ncbi.nlm.nih.gov/pubmed/24215068

It can be concluded that both herbicides are endocrine disrupters and cause cellular toxicity indicated by the decrease of protein content and the increase in CYP4501B1-like immunoreactivity. This toxicity is irreversible and the snail is not able to recover its normal state.

Roundup® disrupts male reproductive functions by triggering calcium-mediated cell death in rat testis and Sertoli cells

by de Liz Oliveira Cavalli VL1, Cattani D, Heinz Rieg CE, Pierozan P, Zanatta L, Benedetti Parisotto E, Wilhelm Filho D, Mena Barreto Silva FR, Pessoa-Pureur R, Zamoner A.

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Abstract

Glyphosate is the primary active constituent of the commercial pesticide Roundup. The present results show that acute Roundup exposure at low doses (36 ppm, 0.036 g/L) for 30 min induces oxidative stress and activates multiple stress-response pathways leading to Sertoli cell death in prepubertal rat testis. The pesticide increased intracellular Ca(2+) concentration by opening L-type voltage-dependent Ca(2+) channels as well as endoplasmic reticulum IP3 and ryanodine receptors, leading to Ca(2+) overload within the cells, which set off oxidative stress and necrotic cell death. Similarly, 30 min incubation of testis with glyphosate alone (36 ppm) also increased (45)Ca(2+) uptake. These events were prevented by the antioxidants Trolox and ascorbic acid. Activated protein kinase C, phosphatidylinositol 3-kinase, and the mitogen-activated protein kinases such as ERK1/2 and p38MAPK play a role in eliciting Ca(2+) influx and cell death. Roundup decreased the levels of reduced glutathione (GSH) and increased the amounts of thiobarbituric acid-reactive species (TBARS) and protein carbonyls. Also, exposure to glyphosate-Roundup stimulated the activity of glutathione peroxidase, glutathione reductase, glutathione S-transferase, □-glutamyltransferase, catalase, superoxide dismutase, and glucose-6-phosphate dehydrogenase, supporting downregulated GSH levels. Glyphosate has been described as an endocrine disruptor affecting the male reproductive system; however, the molecular basis of its toxicity remains to be clarified. We propose that Roundup toxicity, implicated in Ca(2+) overload, cell signaling misregulation, stress response of the endoplasmic reticulum, and/or depleted antioxidant defenses, could contribute to Sertoli cell disruption in spermatogenesis that could have an impact on male fertility.

Glyphosate has been described as an endocrine disruptor affecting the male reproductive system; however, the molecular basis of its toxicity remains to be clarified. We propose that Roundup toxicity, implicated in Ca(2+) overload, cell signaling misregulation, stress response of the endoplasmic reticulum, and/or depleted antioxidant defenses, could contribute to Sertoli cell disruption in spermatogenesis that could have an impact on male fertility.

Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity

by Mesnage R1, Bernay B, Séralini GE

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14032 Caen, Cedex, France; CRIIGEN, 40 rue de Monceau, 75008 Paris, France.

Abstract

Pesticides are always used in formulations as mixtures of an active principle with adjuvants. Glyphosate, the active ingredient of the major pesticide in the world, is an herbicide supposed to be specific on plant metabolism. Its adjuvants are generally considered as inert diluents. Since side effects for all these compounds have been claimed, we studied potential active principles for toxicity on human cells for 9 glyphosate-based formulations. For this we detailed their compositions and toxicities, and as controls we used a major adjuvant (the polyethoxylated tallowamine POE-15), glyphosate alone, and a total formulation without glyphosate. This was performed after 24h exposures on hepatic (HepG2), embryonic (HEK293) and placental (JEG3) cell lines. We measured mitochondrial activities, membrane degradations, and caspases 3/7 activities. The compositions in adjuvants were analyzed by mass spectrometry. Here we demonstrate that all formulations are more toxic than glyphosate, and we separated experimentally three groups of formulations differentially toxic according to their concentrations in ethoxylated adjuvants. Among them, POE-15 clearly appears to be the most toxic principle against human cells, even if others are not excluded. It begins to be active with negative dose-dependent effects on cellular respiration and membrane integrity between 1 and 3ppm, at environmental/occupational doses. We demonstrate in addition that POE-15 induces necrosis when its first micellization process occurs, by contrast to glyphosate which is known to promote endocrine disrupting effects after entering cells. Altogether, these results challenge the establishment of guidance values such as the acceptable daily intake of glyphosate, when these are mostly based on a long term in vivo test of glyphosate alone. Since pesticides are always used with adjuvants that could change their toxicity, the necessity to assess their whole formulations as mixtures becomes obvious. This challenges the concept of active principle of pesticides for non-target species.

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A glyphosate-based herbicide induces necrosis and apoptosis in mature rat testicular cells in vitro and testosterone decrease at lower levels

by Clair E1, Mesnage R, Travert C, Séralini GÉ.

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1Université de Caen Basse-Normandie, EA2608, Institute of Biology, Esplanade de la Paix, 14032 Caen Cedex, France.

Abstract

The major herbicide used worldwide, Roundup, is a glyphosate-based pesticide with adjuvants. Glyphosate, its active ingredient in plants and its main metabolite (AMPA) are among the first contaminants of surface waters. Roundup is being used increasingly in particular on genetically modified plants grown for food and feed that contain its residues. Here we tested glyphosate and its formulation on mature rat fresh testicular cells from 1 to 10000ppm, thus from the range in some human urine and in environment to agricultural levels. We show that from 1 to 48h of Roundup exposure Leydig cells are damaged. Within 24-48h this formulation is also toxic on the other cells, mainly by necrosis, by contrast to glyphosate alone which is essentially toxic on Sertoli cells. Later, it also induces apoptosis at higher doses in germ cells and in Sertoli/germ cells co-cultures. At lower non toxic concentrations of Roundup and glyphosate (1ppm), the main endocrine disruption is a testosterone decrease by 35%. The pesticide has thus an endocrine impact at very low environmental doses, but only a high contamination appears to provoke an acute rat testicular toxicity. This does not anticipate the chronic toxicity which is insufficiently tested, and only with glyphosate in regulatory tests.

We show that from 1 to 48 hours of Roundup exposure Leydig cells are damaged. Within 24-48 hours this formulation is also toxic on other cells, mainly by necrosis, by contrast to glyphosate alone which is essentially toxic on Sertoli cells. Later, it also induces apoptosis at higher doses in germ cells and in Sertoli/germ cells co-cultures. At lower non toxic concentrations of Roundup and glyphosate (1ppm), the main endocrine disruption is a testosterone decrease by 35%

Glyphosate impairs male offspring reproductive development by disrupting gonadotropin expression

by Romano MA1, Romano RM, Santos LD, Wisniewski P, Campos DA, de Souza PB, Viau P, Bernardi MM, Nunes MT, de Oliveira CA.

Author information

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Abstract

Sexual differentiation in the brain takes place from late gestation to the early postnatal days. This is dependent on the conversion of circulating testosterone into estradiol by the enzyme aromatase. The glyphosate was shown to alter aromatase activity and decrease serum testosterone concentrations. Thus, the aim of this study was to investigate the effect of gestational maternal glyphosate exposure (50 mg/kg, NOAEL for reproductive toxicity) on the reproductive development of male offspring. Sixty-day-old male rat offspring were evaluated for sexual behavior and partner preference; serum testosterone concentrations, estradiol, FSH and LH; the mRNA and protein content of LH and FSH; sperm production and the morphology of the seminiferous epithelium; and the weight of the testes, epididymis and seminal vesicles. The growth, the weight and age at puberty of the animals were also recorded to evaluate the effect of the treatment. The most important findings were increases in sexual partner preference scores and the latency time to the first mount; testosterone and estradiol serum concentrations; the mRNA expression and protein content in the pituitary gland and the serum concentration of LH; sperm production and reserves; and the height of the germinal epithelium of seminiferous tubules. We also observed an early onset of puberty but no effect on the body growth in these animals. These results suggest that maternal exposure to glyphosate disturbed the masculinization process and promoted behavioral changes and histological and endocrine problems in reproductive parameters. These changes associated with the hypersecretion of androgens increased gonadal activity and sperm production.

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Hypothetical link between endometriosis and xenobiotics-associated genetically modified food

by Aris A1, Paris K.

Abstract

Endometriosis is an oestrogen-dependent inflammatory disease affecting 10 % of reproductive-aged women. Often accompanied by chronic pelvic pain and infertility, endometriosis rigorously interferes with women's quality of life. Although the pathophysiology of endometriosis remains unclear, a growing body of evidence points to the implication of environmental toxicants. Over the last decade, an increase in the incidence of endometriosis has been reported and coincides with the introduction of genetically modified foods in our diet. Even though assessments of genetically modified food risk have not indicated any hazard on human health, xenobiotics-associated genetically modified food, such as pesticides residues and xenoproteins, could be harmful in the long-term. The "low-dose hypothesis", accumulation and biotransformation of pesticides-associated genetically modified food and the multiplied toxicity of pesticides-formulation adjuvants support this hypothesis. This review summarizes toxic effects (in vitro and on animal models) of some xenobiotics-associated genetically modified food, such as glyphosate and Cry1Ab protein, and extrapolates on their potential role in the pathophysiology of endometriosis. Their roles as immune toxicants, pro-oxidants, endocrine disruptors and epigenetic modulators are discussed: http://www.ncbi.nlm.nih.gov/pubmed/21111655

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Prepubertal exposure to commercial formulation of the herbicide glyphosate alters testosterone levels and testicular morphology

by Romano RM1, Romano MA, Bernardi MM, Furtado PV, Oliveira CA.

Abstract

Glyphosate is a herbicide widely used to kill weeds both in agricultural and non-agricultural landscapes. Its reproductive toxicity is related to the inhibition of a StAR protein and an aromatase enzyme, which causes an in vitro reduction in testosterone and estradiol synthesis. Studies in vivo about this herbicide effects in prepubertal Wistar rats reproductive development were not performed at this moment. Evaluations included the progression of puberty, body development, the hormonal production of testosterone, estradiol and corticosterone, and the morphology of the testis. Results showed that the herbicide (1) significantly changed the progression of puberty in a dose-dependent manner; (2) reduced the testosterone production, in semineferous tubules' morphology, decreased significantly the epithelium height ($P < 0.001$; control = 85.8 +/- 2.8 microm; 5 mg/kg = 71.9 +/- 5.3 microm; 50 mg/kg = 69.1 +/- 1.7 microm; 250 mg/kg = 65.2 +/- 1.3 microm) and increased the luminal diameter ($P < 0.01$; control = 94.0 +/- 5.7 microm; 5 mg/kg = 116.6 +/- 6.6 microm; 50 mg/kg = 114.3 +/- 3.1 microm; 250 mg/kg = 130.3 +/- 4.8 microm); (4) no difference in tubular diameter was observed; and (5) relative to the controls, no differences in serum corticosterone or estradiol levels were detected, but the concentrations of testosterone serum were lower in all treated groups ($P < 0.001$; control = 154.5 +/- 12.9 ng/dL; 5 mg/kg = 108.6 +/- 19.6 ng/dL; 50 mg/dL = 84.5 +/- 12.2 ng/dL; 250 mg/kg = 76.9 +/- 14.2 ng/dL). These results suggest that commercial formulation of glyphosate is a potent endocrine disruptor in vivo, causing disturbances in the reproductive development of rats when the exposure was performed during the puberty period: http://www.ncbi.nlm.nih.gov/pubmed/20012598

These results suggest that commercial formulation of glyphosate is a potent endocrine disruptor in vivo, causing disturbances in the reproductive development of rats when the exposure was performed during the puberty period

Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines

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Abstract

Glyphosate-based herbicides are the most widely used across the world; they are commercialized in different formulations. Their residues are frequent pollutants in the environment. In addition, these herbicides are spread on most eaten transgenic plants, modified to tolerate high levels of these compounds in their cells. Up to 400 ppm of their residues are accepted in some feed. We exposed human liver HepG2 cells, a well-known model to study xenobiotic toxicity, to four different formulations and to glyphosate, which is usually tested alone in chronic in vivo regulatory studies. We measured cytotoxicity with three assays (Alamar Blue, MTT, ToxiLight), plus genotoxicity (comet assay), anti-estrogenic (on ERalpha, ERbeta) and anti-androgenic effects (on AR) using gene reporter tests. We also checked androgen to estrogen conversion by aromatase activity and mRNA. All parameters were disrupted at sub-agricultural doses with all formulations within 24h. These effects were more dependent on the formulation than on the glyphosate concentration. First, we observed a human cell endocrine disruption from 0.5 ppm on the androgen receptor in MDA-MB453-kb2 cells for the most active formulation (R400), then from 2 ppm the transcriptional activities on both estrogen receptors were also inhibited on HepG2. Aromatase transcription and activity were disrupted from 10 ppm. Cytotoxic effects started at 10 ppm with Alamar Blue assay (the most sensitive), and DNA damages at 5 ppm. A real cell impact of glyphosate-based herbicides residues in food, feed or in the environment has thus to be considered, and their classifications as carcinogens/mutagens/reprotoxics is discussed.

Cytotoxic effects started at 10 ppm with Alamar Blue assay (the most sensitive), and DNA damages at 5 ppm. A real cell impact of glyphosate-based herbicides residues in food, feed or in the environment has thus to be considered, and their classifications as carcinogens/mutagens/reprotoxics is discussed.

Differential effects of glyphosate and roundup on human placental cells and aromatase

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Abstract

Roundup is a glyphosate-based herbicide used worldwide, including on most genetically modified plants that have been designed to tolerate it. Its residues may thus enter the food chain, and glyphosate is found as a contaminant in rivers. Some agricultural workers using glyphosate have pregnancy problems, but its mechanism of action in mammals is questioned. Here we show that glyphosate is toxic to human placental JEG3 cells within 18 hr with concentrations lower than those found with agricultural use, and this effect increases with concentration and time or in the presence of Roundup adjuvants. Surprisingly, Roundup is always more toxic than its active ingredient. We tested the effects of glyphosate and Roundup at lower nontoxic concentrations on aromatase, the enzyme responsible for estrogen synthesis. The glyphosate-based herbicide disrupts aromatase activity and mRNA levels and interacts with the active site of the purified enzyme, but the effects of glyphosate are facilitated by the Roundup formulation in microsomes or in cell culture. We conclude that endocrine and toxic effects of Roundup, not just glyphosate, can be observed in mammals. We suggest that the presence of Roundup adjuvants enhances glyphosate bioavailability and/or bioaccumulation.

Here we show that glyphosate is toxic to human placental JEG3 cells within 18 hours with concentrations lower than those found with agricultural use, and this effect increases with concentration and time or in the presence of Roundup adjuvants. Surprisingly, Roundup is always more toxic than its active ingredient. We conclude that endocrine and toxic effects of Roundup, not just glyphosate, can be observed in mammals. We suggest that the presence of Roundup adjuvants enhances glyphosate bioavailability and/or bioaccumulation.

The teratogenic potential of the herbicide glyphosate-Roundup in Wistar rats

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Abstract

The aim of this study was to assess the teratogenicity of the herbicide glyphosate-Roundup (as commercialized in Brazil) to Wistar rats. Dams were treated orally with water or 500, 750 or 1000 mg/kg glyphosate from day 6 to 15 of pregnancy. Cesarean sections were performed on day 21 of pregnancy, and number of corpora lutea, implantation sites, living and dead fetuses, and resorptions were recorded. Weight and gender of the fetuses were determined, and fetuses were examined for external malformations and skeletal alterations. The organs of the dams were removed and weighed. Results showed a 50%, mortality rate for dams treated with 1000 mg/kg glyphosate. Skeletal alterations were observed in 15.4, 33.1, 42.0 and 57.3% of fetuses from the control, 500, 750 and 1000 mg/kg glyphosate groups, respectively. We may conclude that glyphosate-Roundup is toxic to the dams and induces developmental retardation of the fetal skeleton.

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Exposure to glyphosate- and/or Mn/Zn-ethylene-bis-dithiocarbamate-containing pesticides leads to degeneration of aminobutyric acid and dopamine neurons in Caenorhabditis elegans

by Negga R1, Stuart JA, Machen ML, Salva J, Lizek AJ, Richardson SJ, Osborne AS, Mirallas O, McVey KA, Fitsanakis VA.

Abstract

Previous studies demonstrate a positive correlation between pesticide usage and Parkinson's disease (PD), which preferentially targets dopaminergic (DAergic) neurons. In order to examine the potential relationship between two common pesticides and specific neurodegeneration, we chronically (24 h) or acutely (30 min) exposed two Caenorhabditis elegans (C. elegans) strains to varying concentrations (LC(25), LC(50) or LC(75)) of TouchDown(®) (TD) as percent active ingredient (glyphosate), or Mancozeb(®) (MZ) as percent active ingredient (manganese/zinc ethylene-bis-dithiocarbamate). Furthermore, to more precisely model environmental exposure, worms were also exposed to TD for 30 min, followed by 30-min incubation with varying MZ concentrations. Previous data from out lab suggested general neuronal degeneration using the worm strain NW1229 (pan-neuronal//green fluorescent protein (GFP) construct). To determine whether distinct neuronal groups were preferentially affected, we specifically used EG1285 (GABAergic neurons//GFP construct) and BZ555 (DAergic neurons//GFP construct) worms to verify GABAergic and DAergic neurodegeneration, respectively. Results indicated a statistically significant decrease, when compared to controls (CN), in number of green pixels associated with GABAergic neurons in both chronic (*P < 0.05) and acute (*P < 0.05) treatment paradigms. Analysis of the BZ555 worms indicated a statistically significant decrease (*P < 0.05) in number of green pixels associated with DAergic neurons in both treatment paradigms (chronic and acute) when compared to CN. Taken together, our data suggest that exposure to TD and/or MZ promotes neurodegeneration in both GABAergic and DAergic neurons in the model organism C. elegant: http://www.ncbi.nlm.nih.gov/pubmed/21922334

Previous studies demonstrate a positive correlation between pesticide usage and Parkinson's disease. Taken together, our data suggest that exposure to TD and/or MZ promotes neurodegeneration in both GABAergic and DAergic neurons in the model organism C. elegant.

Scientific American Disinformation on GMOs

October 14, 2013
by Dr Mae-Wan Ho

America's most trusted science magazine is spreading disinformation on behalf of a failing and desperate industry, in utter disregard of scientific integrity and the overwhelming evidence of hazards to health and the environment.

by Dr Mae Wan Ho, Dr Eva Sirinathsinghji and Prof Peter Saunders.

Deceptively authoritative pronouncements not backed up by evidence, scientific or otherwise.

A recent editorial in Scientific American entitled "Labels for GMO Foods are a Bad idea" caught most people by surprise. In beguilingly authoritarian tone and without providing references for any of its confident-sounding assertions, it tells us that labelling GM Foods [1] "would only intensify the misconception that so-called Frankenfoods endanger people's health." If anything, the editorial itself is guilty of spreading disinformation regarding GMOs, which is very disappointing for a normally trustworthy and serious science magazine. We feel obliged to expose some of the major misconceptions in the editorial.

The piece begins with the tired old pronouncement used by industry to reassure the public since the early 1990s that humans have been "tinkering" with crop genomes since the beginning of time through the process of conventional breeding, implying that genetic modification is no different. In reality, there is no longer any doubt that genetic modification is distinct from conventional breeding and introduces new risks, as fully acknowledged in the Cartagena Protocol on Biosafety for regulating GMOs under the United Nations Convention on Biological Diversity [2], which was adopted by the international community on 29 January 2000 and entered into force on 11 September 2003.

The assertion that genetic engineering is more "precise" than natural plant reproduction flies in the face of abundant evidence documenting extensive mutations and scrambling (rearrangements) of the host genome as the result of genetic modification, with new transcripts and harmful proteins found in the rare cases that were subjected to further investigations [3].

Using American citizens as guinea pigs for the past 20 years is another common justification for GM food. The claim that they are eating it without evidence of harm is not based on science, as without GM labelling it is impossible to tell who has eaten GM food and who has not or in what amounts. The only way one could tell if GM food has any effect on the health of American citizens is to compare their health status before and after GM food was introduced.

Increase in GMOs parallels deterioration of health in the United States

Dr Nancy Swanson, retired scientist of the US Navy, used data from official sources — including the Centers for Disease Control, National Cancer Institute, National Kidney and Urologic Diseases Information Clearinghouse and US Renal Data System — to find out if the status of health of US citizens has changed since GM crops were introduced [4]. According to Swanson, the data revealed a "marked deterioration of health" with the introduction of GM crops. The incidence of diseases and adverse conditions that have gone up in parallel with the increase in GM crops and the use of glyphosate herbicide since 1994 (first year of commercialization of GM crops) include thyroid cancer, liver and bile duct cancer, obesity, high blood pressure, hospitalizations for acute kidney injury, diabetes, and end stage renal disease. As Swanson points out, correlation does not necessarily imply cause and effect, and there may be other factors, i.e., a long list of environmental endocrine disruptors and toxic substances including food additives and preservatives. "GMOs may be pushing us off the cliff." She said. "Certainly more research should be done to firmly establish causality."

Although the epidemiological findings do not establish cause and effect, there is now overwhelming evidence from laboratory studies on cells and animals documenting damages to practically every organ system from exposure to GMOs and/or glyphosate herbicides, confirming what farmers have been experiencing for years in the fields (see our comprehensive report [5] Ban GMOs Now).

GM crops do not increase yield

A common myth perpetrated by the pro-GM lobby is that GM crops increase yield, which is blatantly untrue. A recent study based on yield data from United Nations Food and Agriculture Organization showed that the US staple crop system has been failing since the adoption of GMOs and is being overtaken by predominantly non-GM Europe in all respects including yields, resilience, pesticide use, and genetic diversity [6, 7] (US Staple Crop System Failing from GM and Monoculture, SiS 59).

The Scientific American editors tell us that [1] "a seven-year study of Indian farmers show that those growing a genetically modified crop increased their yield per acre by 24 percent and boosted profits by 50 percent." This was a real surprise, as the failures of Bt cotton in India were

documented by many grassroots organisations and widely publicised as was its role in accelerating farm suicides (see ISIS review [8] Farmer Suicides and Bt Cotton Nightmare Unfolding in India, SiS 45). As recently as April 2013, the agriculture minister of Maharashtra (one of the main cotton states) openly admitted that Bt cotton was a failure [9]. He stressed the need for agriculture officials to be more proactive. Bt cotton spread has increased to 95 %. “Cotton yields in Vidarbha [in India’s cotton belt] remains an abysmal 177 kg per acre.” The agriculture minister said. “Even Pakistan was doing 400 kg average yield.” He noted that Bt cotton was benefiting seed companies more than farmers and wondered why agriculture scientists and officials failed to promote time-tested traditional varieties and indigenously developed hybrids.

So what is the Scientific American editors’ assertion based on?

Our investigation turned up a paper [10] published in top journal Science (which has long become the apparent mouthpiece of the GM industry). The main author Martin Qaim at University of Bonn in Germany is notorious for having previously co-authored a paper published in the same journal in 2003 claiming even greater (80 %) yield increases from Monsanto’s GM cotton [11]. That paper drew a storm of protest and derision, as Monsanto had provided the data, and the findings were completely at odds with reports coming from Indian farmers and grassroots organisations. Dr Devinder Sharma, a food policy expert, called the paper a “scientific fairytale” [12]. Bt cotton has been an unmitigated disaster for India in exacerbating farm suicides, with an ecological and agronomic nightmare still unfolding in plagues of secondary and novel pests, pest resistance, novel diseases, and soils so depleted in nutrients and essential microorganisms that they will no longer support the growth of any crop [8].

Beneficial GM crops that do not exist

In order to put a beneficent gloss over GM crops – now consisting of two major categories, Bt and glyphosate tolerant, both damaging to health and ecosystems and benefiting no one else but the companies [5] – the pro-GM lobby is conjuring crops supposedly good for health and the environment out of thin air.

The most publicised is the GM golden rice, engineered to make pro-Vitamin A, which the editors tell us [1] will curb vitamin A deficiency that “blinds as many as 500,000 children worldwide every year and kills half of them.” But “Greenpeace and other anti-GMO organizations have used misinformation and hysteria to delay the introduction of Golden Rice to the Philippines, India and China.”

The truth is that Golden Rice does not exist, at least not as a variety that is ready for commercialization. Golden Rice (GR1) was created as a public relations exercise nearly 14 years ago [13] (see ‘Golden Rice’ – an exercise in how not to do science, ISIS/TWN Report). It produced so little pro-vitamin A that you would have to eat buckets every day to get enough. Golden Rice staged a comeback as GR2 in 2008 with a special feature in Science [14], which revealed that Tufts University in Boston USA has been carrying out ‘clinical trials’ of Golden Rice on children. More than 30 senior scientists and academics signed an open letter (16 February 2009) condemning the work [15] (Scientists Protest Unethical Clinical Trials of GM Golden Rice) as being in breach of the Nuremberg Code of Ethics. Two of the studies involved children 6-10 years old. Furthermore, the Golden rice in the trials (GR2) was not one identifiable variety. Instead it was a collection of experimental transgenic events still in the laboratory [16] (The Golden Rice Scandal Unfolds, SiS 42), not characterized in terms of basic molecular genetics or biological and biochemical properties, not tested pre-clinically on animals, or subjected to any other safety assessment. The Tufts University scientist and the Chinese scientists involved in the trials have been reprimanded by Tufts University authorities and the Chinese government respectively since [17]. The editors tell us that for the past 20 years, Americans have been eating plants genetically modified to “tolerate drought” [1]. Actually, a GM crop claimed to be drought tolerant is commercially available for the first time in 2013 [18].

But it is the GM cassava that gets the prize for disinformation. The editors wrote [1] “An international team of researchers has engineered a variety of cassava – a staple food for 600 million people – with 30 times the usual amount of beta-carotene and four times as much iron, as well as higher levels of protein and zinc.” Our investigation failed to locate any such GM cassava, except as stated intentions, or at best in experimental varieties subjected to “contained” field trials [19], all created with the Agrobacterium vector system that’s especially hazardous for health and the environment (see [5]). The only GM cassava created by the Donald Danforth Plant Research Center in St. Louis Missouri and actually described in a paper published in 2011 was retracted in September 2012 because [20] “an institutional investigation revealed that significant amounts of data and supporting documentation that were claimed to be produced by the first author could not be found” and “the validity of the results could not be verified.”

Instead, great strides have already been made in improving cassava through conventional breeding, including three varieties of b-carotene rich cassava that are being widely released in Nigeria [21] (How Non-GM Cassava Can Help Feed the World, SiS 59).

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A Roundup of RoundupÆ Reveals Converging Pattern of Toxicity from Farm to Clinic to Laboratory Studies

We need to ban glyphosate from our own communities as most governments fail to protect citizens

by Dr Eva Sirinathsinghji

Institute Of Science In Society
Report of January 19, 2015

What Is Glyphosate?

Glyphosate, perhaps surprisingly for a chemical so ubiquitously associated with our food, was not first used as an agricultural chemical but instead first patented as a metal chelator in 1964 by Stauffer Chemical company (US 3160632 A) [1] and used as an industrial pipe cleaner. It was later patented by Monsanto as an herbicidal agent in 1974 (US3799758 A) [2] based on its ability to block the shikimate pathway involved in the production of aromatic amino acids in both plants and bacteria. It has become the most popular herbicide in the world especially since glyphosate tolerant genetically modified (GM) crops were commercialized in the mid-1990s, together with the assumption (perpetrated by Monsanto) that the herbicide is safe for health and the environment. In 2010, it was also patented by Monsanto as an antibiotic agent. Moreover, it is being increasingly used as a pre-harvest desiccant for drying seeds, a process that results in contamination of non-GM grains, one of the main exposure routes in the EU where GM crops are not commonly grown. Thus, an estimated 70 % of UK oil seed rape (canola) and 50-60 % of EU sunflowers are sprayed with glyphosate [3], resulting in products of major food brands in the UK testing positive for glyphosate residues in a 2014 analysis by GM Freeze, with glyphosate the most commonly detected of all chemicals [4].

The evidence of glyphosate toxicity to both human and animal health and the ecosystem has built up to such an extent that some governments are taking action. As mentioned earlier, both El Salvador and Sri Lanka have made steps towards banning the herbicide. The Netherlands successfully banned its sale to private individuals. Russia has recently decided to ban the import and cultivation of all GM crops due to health and environmental concerns, while a section of the Chinese army has reportedly banned its consumption. In Brazil a public prosecutor is also looking to suspend its use.

All of glyphosateís chemical properties already mentioned have implications for the health of both people and planet. Scientific research has additionally implicated glyphosate as an endocrine disruptor and a DNA mutagen; and it affects over 291 different enzymes in the body [5]. It is increasingly linked with a wide variety of illnesses, the sharp rises in illnesses occurring in parallel with glyphosate application across various GM cultivating regions of the world.

The most convincing evidence of glyphosate toxicity is the consistent pattern of diseases associated with glyphosate that has emerged from the farm to the clinic and from scientific studies to citizen testimonials.

Glyphosate Widespread In The Environment And In Our Bodies

Glyphosateís popularity is due in large measure to its concomitant use with the most widely planted type of GM crops, those tolerant to glyphosate-herbicides. Monsanto commercialised the first Roundup-ready crop in 1996 (Roundup being the commercial formulation containing ëadjuvantsí that make it much more toxic than the active ingredient glyphosate alone, see later). In countries such as Argentina where large swaths of the country have been dubbed soy deserts, GM soybean cultivation has resulted in an 858 % rise in glyphosate use (see [6] Devastating Impacts of Glyphosate Use with GMO Seeds in Argentina, to appear). Similarly, the US has seen even greater rises of 2 500 % from 1987 to 2007 [7].

This widespread and massive application of glyphosate herbicides has resulted in almost ubiquitous contamination of the environment. A 2014 study on US water systems across 38 states found glyphosate and its principle metabolite AMPA (aminomethylphosphonic acid) not only in rivers, lakes and streams, but also rain, soil and sediment, ditches and drains and groundwater (see [7]). Some 70 % of rain samples tested positive for glyphosate. Similarly in Europe, (in Catalonia, a large region of Spain) it was found that all 11 groundwater sites were positive for glyphosate despite it being a region free from glyphosate-tolerant crop cultivation; 41 % of samples were above detection limits [8]. The detection in groundwater goes against one of the claims on glyphosate safety that its propensity to bind to soil and sediment means it will not leach into our fresh water supplies. In Argentina, new data of rain sample measurements averaged an extreme 6.5 µg/L and reaching as high as 67 µg/L (67 ppb) across four regions from October 2012 to April 2014 [9]. These levels are far higher than those seen in US rain samples where the average and maximum concentrations were 0.11 µg/L and 2.5 µg/L respectively [7].

Tap water and rivers also test positive for glyphosate with UK samples coming up (30 parts per trillion (ppt) and 190 ppt respectively) at concentrations within range of those found to be toxic in lab studies (see [10] How Roundup Poisoned my Nature Reserve, SiS 64). Urban areas also get sprayed, prompting London citizens to organise banning campaigns of glyphosate spraying in public areas including child-friendly zones [11]. Even oceans are not spared from glyphosate poisoning, with run-offs into the sea persisting for up to 267 days in sea water obtained from the Great Barrier Reef and tested in the lab [12].

Due to the official ësafeí status of glyphosate, data on how much we are being exposed have been scarce, forcing citizen activists and civil society organizations to find out for themselves. Friends of the Earth Europe commissioned an analysis of 182 volunteers across 18 EU countries and found detectable levels in 44 % of urine samples [13] with concentrations ranging from 0.16 ug/L average in Switzerland, to 1.82ug/L in Latvia. Of the UK citizens tested, 7 out of 10 were positive. In the US, urine samples show concentrations 8 times those in Europe [13]. The analysis, commissioned by Moms Across America, also tested 10 motherís breast milk, which came up positive for glyphosate with levels ranging from 76 µg/L to 166 µg/L (76-166 ppb) (see [14]). These levels are 760 to 1600 times higher than the European Drinking Water Directive allows for individual pesticides, and raise obvious concerns as they fall within the range of concentrations at which developmental toxicity has been observed in animal studies (see below). This analysis is the only study on breast milk to date, as no government or public health body has found it necessary to carry out any study on bioaccumulation in internal organs and tissues or in breast milk fed to infants.

Recent independent scientific studies have backed up the work of activists and civil society organisations. Awad Shehata and colleagues in Germany looked at glyphosate levels in the urine of both chronically ill and healthy people, and found significantly higher levels in ill people in samples taken from 102 and 199 healthy and chronically ill people respectively [15]. Those who ate predominantly organic food had lower levels, along with livestock that were fed conventional versus genetically modified feed. The study also looked at levels in cow tissues as well as urine. Detection of glyphosate in the tissues contradicts one of the assumption-based arguments used by industry and regulators that due to glyphosateís high water solubility, it is rapidly excreted from the body and therefore risks of harm are negligible. In such a case, the levels of glyphosate in urine would be expected to be

much greater than levels found in the tissues. However, urine levels in cows averaged 27-42 µg/ml (27-42 parts per million (ppm)), while the level in tissues (intestine, liver, spleen, kidney and muscle) averaged between 14-20 µg/ml, which is within range of urine levels. Though they did not compare glyphosate levels in urine and internal organs of the same cow, the average levels across all cow samples dispute the assumptions taken by regulators that glyphosate does not remain in the body at levels that can cause harm.

In summary, glyphosate is almost ubiquitous in our environment and in people and livestock; it has even been discovered in hospital feeding tubes for child cancer patients in the US [16]. The impacts are described below.

A Birth Defect Epidemic In People And Animals

Argentina is one of the biggest cultivators of GM soybeans and the country has witnessed a sharp increase in serious illnesses since cultivation began. Concerned doctors and health practitioners founded the Network of Physicians of Crop Sprayed Towns and met in 2010. They presented data showing increased incidence of birth defects, spontaneous abortions, infertility, still births, cancers, Downís syndrome, mental disability, immune and endocrine disorders, as well as acute effects such as increased convulsions in epileptic patients at time of fumigation, respiratory and dermatological problems (see [6]) and [17] Pesticide Illnesses and GM Soybeans, SiS53) [18].

The Network, together with a large citizen movement, is pushing for a complete ban on aerial spraying of agrochemicals plus a ban of its use within a kilometre of residential areas. They documented a 2-5 times increase in birth defects in sprayed towns compared to before spraying began. Common defects include neural tube defects, which are replicated in laboratory studies on glyphosate (see later).

A 2013 report from the Centre of Congenital defects claims that nationally, the number of cases has not gone up, but a closer scrutiny gives a different picture. Data gathered during a 6 month period from the hospital Maternidad Provincial in CÛrdoba showed that despite recording a low level of birth defects of 36 out of a total of 2140 births (1.68 %), 22 of those came from mothers living in crop-sprayed towns, which accounts for 61 % of all the birth defects (see [6]).

The US has seen a surge in neural tube birth defects (anencephaly) in the Yakima River, Washington State. The source remains a mystery to officials who have ruled out common causes such as low folic acid and lifestyle choices. Rates have reached 8 cases per 10 000 births from 2010-2013 compared to a national average of 3 cases per 10 000 births. Glyphosate has emerged as a prime suspect as the state of Washington use herbicides, most often glyphosates, to kill noxious weeds in both land and water. An estimated 146 pesticides were applied in the area in the year 2000, and studies are now needed to confirm whether or not glyphosate, either alone or in combination with other chemicals is responsible for neural tube defects in the area [19].

Reproductive problems such as miscarriages and infertility have also risen in Argentina (see [20] Glyphosate/ Roundup & Human Male Infertility, SiS 62). Physicians of sprayed towns have recorded as many as 23 % of women suffering from miscarriage in the last 5 years [18].

The latest victims of Argentinaís chemical agricultural system, of which GM cultivation is an extreme example, could very well have been spared if the evidence of the teratogenic properties of glyphosate produced by industry since the 1980s had not been dismissed [21]. Monsantoís own toxicology tests submitted to the EU commission showed evidence of teratogenicity (see [22]EU Regulators and Monsanto Exposed for Hiding Glyphosate Toxicity, SiS51).

The submitted test reports describe rats and rabbits with skeletal abnormalities including the development of a 13th rib in offspring, as well as cardiac abnormalities. Scientific studies such as that of the late Professor AndrÈs Carrasco reporting neural tube birth defects in frog and chick embryos exposed to agricultural concentrations of glyphosate [23] have validated both Monsantoís findings and clinical observations (see also [24] Lab Study Establishes Glyphosate Link to Birth Defects, SiS48). Probing into the mechanisms underlying the defects, Carrasco discovered that glyphosate disrupted retinoic acid activity, a well-known regulator of developmental processes.

Epidemiological studies have linked increased incidence of birth defects (spina bifida, circulatory/respiratory anomalies, tracheo-esophogeal defects, gastrointestinal defects, urogenital defects, cleft lip, adactyly, clubfoot, musculoskeletal anomalies, Down's syndrome and other birth defects) and reproductive toxicity in those who live near agrochemical-sprayed fields [25-27] while other lab studies are accumulating evidence of birth defects and reproductive toxicity in a range of animals from rats to catfish [28-31].

Evidence from the farm follows the same pattern. Ib Borup Pedersen recently documented personal experiences on his pig farm, where removing GM soybean feed from the diet resulted in pronounced improvement in the health of his pigs, reducing medicine use by a third and increasing his profits (see [32] "Changing from GMO to Non-GMO Natural Soy, Experiences from Denmark, SiS 64). Profits were also increased due to his sows living longer and giving birth to more piglets. After researching glyphosate and GMOs Ib investigated further and collaborated with scientists in Germany who analysed 38 of his 1-day old deformed piglets, finding glyphosate in various organs of the pigs. Pigs suffered defects ranging from severe to mild, including spinal, cranial defects and others affecting limbs, gender, internal organs, tongue and more. Many appear to be neural tube defects as seen in the clinic and laboratory.

Cancer Rates Skyrocket In South American Regions Employing GM Cultivation

Neighbourhood resident organisations such as the association of Mothers of Ituzaingo, in collaboration with the Network of Sprayed Towns have been mapping cancer incidence in their towns for many years to draw attention to the epidemic they are facing. It is has reached the point where now, 30 % of all deaths in these regions are from cancers, affecting both adults and children. Cities such as Hernando have seen a 258 % rise in cases between 2001-2002 and 2010-2012 [6].

Rises in cancer rates can be explained by glyphosateís role in cancer-causing mechanisms including DNA damage and endocrine disruption. Endocrine disruption may well also underlie some of the reproductive and teratogenic effects of glyphosate described above. Lab studies show glyphosate damages DNA in lab animals as well as in people who were exposed to the chemical in Argentina [33-35]. It also disrupts cell cycle regulation that can lead to increased cell division and cancer development [36,37]. The glyphosate metabolite AMPA was also shown in a 2014 study to induce DNA damage in fish at concentration ranges previously documented in streams and surface water in N. America [38]. Glyphosateís carcinogenic potential has been documented since the 1980s (see [39] Glyphosate & Cancer, SiS 62)

Distinct from DNA damaging properties, glyphosate also mimics oestrogen at very low levels and promotes the growth of hormone-dependent breast cancer cell lines [40]. Actually glyphosate is an endocrine disruptor and alters the expression of multiple hormones including testosterone, leutinising hormone, follicle-stimulating hormone, and the aromatase enzyme complexes that convert testosterone to oestrogen [31, 42, 42].

Epidemiological studies corroborate lab studies and reports from local citizens in Argentina and the US [43-45]. The Ministry of Health of CÛrdoba in Argentina reported in June 2014 the doubling of cancer cases in high agrochemical use areas compared to the national average [46]. Consistently, a new meta-analysis found association between glyphosate and cancers following occupational exposure [47]. The study looked at all epidemiological papers on non-Hodgkin lymphoma (NHL) incidence that had been published in English since 1980 that reported agricultural, occupational exposure to specific pesticides. A total of 44 papers were analysed, covering 80 active ingredients and 21 pesticide chemicals, finding the strongest associations between pesticides and specific subtypes of NHL, including an association between glyphosate and B lymphoma. They also found that phenoxy herbicides, carbamate insecticides, organophosphorus insecticides and the active ingredient lindane, an organochlorine insecticide, were positively associated with NHL.

The most comprehensive GMO feeding study to date carried out by Gilles-Eric SÈralini and his team, looked at the effects glyphosate and glyphosate tolerant maize NK603 on rats during their life-time (2 years). It showed increased incidence of tumours (including cancers), other illnesses, as well as reduced life-span and altered hormone status [48]. The 2012 publication was aggressively attacked by industry and its supporters and unilaterally and illicitly retracted a year after publication following the appointment of an ex-Monsanto employee as an editor for the journal (see [49] Retracting SÈralini Study Violates Science and Ethics, SiS 61). It has subsequently been republished elsewhere [50] after massive public protest (see [51] Open Letter on Retraction and Pledge to Boycott, SiS 61).

Fatal Kidney Disease Epidemic Across Continents Foreseen By Lab Studies

Kidney disease has reached epidemic levels in regions that heavily use glyphosate such as farmers in Sri Lanka and sugar cane workers in Central America. Kidney problems have been highlighted by scientific studies, including SÈraliniís rat feeding study where kidney tumours were observed [50]. A meta-analysis of feeding studies conducted by SÈraliniís lab revealed kidney pathology in animals fed Roundup Ready soybeans, while in vitro studies have shown that glyphosate had cytotoxic effects on human embryonic kidney cell lines [52,53] (see [54] GM Feed Toxic, Meta-Analysis Confirms, SiS52, [55] Death by multiple poisoning ,glyphosate and Roundup, SiS 42).

In Sri Lanka, chronic kidney disease of unknown aetiology (CKDu) has afflicted the agricultural population in recent years. A study published in 2014 linked glyphosate-based herbicides to the epidemic. It appears that hard water in the agricultural regions leads to heavy metal toxicity in the kidneys via glyphosateís metal chelating activity, and is responsible for the 400 000 cases of the disease and 20 000 fatalities [56] (see [57] Sri Lanka Partially Bans Glyphosate for Deadly Kidney Disease Epidemic, SiS 62). The government temporarily banned glyphosate from hard water areas, but this decision was reversed due to a lack of agricultural workers to take over the manual weeding required without the application of glyphosate. Similar health problems are widely affecting communities in Central America with one in four sugar cane workers reporting kidney disease in some areas [58, 59]. This epidemic forced the El Salvador government to call for international help after the epidemic began overwhelming the health systems. The El Salvadorian government has since approved legislation to ban glyphosate herbicides, though this is yet to be enforced.

Digestive Disorders Widespread

Digestive illnesses plagued the pig farm in Denmark (mentioned earlier) while they were being fed GM soy. When GM produce and glyphosate were removed from their diet, the pigs no longer suffered chronic diarrhoea, which was so severe that 30 % of new born piglets were dying as a result (see [32]). Chronic botulism, caused by the Clostridium botulinum bacteria, has also been on the rise in livestock in Germany, the US, and UK since the 1990s [60]. The latest study shows that glyphosate results in dysbiosis of the cow gut, with a reduction of beneficial bacteria in the rumen of cows accompanied by a rise in C. botulinum microbes [61].

The digestive illnesses in livestock mirrors a growing health problem in the West, particularly in the US where food intolerances, allergies, celiac disease, bowel diseases, infections and other problems continue to become more common. Nancy Swanson and colleagues showed a clear correlation between spikes in both inflammatory bowel disease and intestinal infection with glyphosate in the US [62]. Deaths from intestinal infections have risen from less than 0.25 deaths per 100 000 in 1979 to over 80 deaths per 100 000 in 2010. Inflammatory bowel disease has risen from around 3 diagnosed cases per 100 000 in 1990 to almost 90 per 100 000 in 2010. Moms across Americaís testimonials reflect the evidence from the farm and science studies, with children who come off GM and glyphosate covered foods reducing the severity of allergy symptoms as well as other problems such as regular vomiting [63]. With glyphosateís antibiotic properties, it had already been previously shown to cause disruption of the gut bacteria in poultry, swine and cows [64-66].

Salmonella and Clostridium are highly resistant to glyphosate, whereas Enterococcus, Bifidobacteria, and Lactobacillus are especially susceptible. Perturbation in the balance of these microbial species is associated with digestive disorders such as celiac disease. Similarly, chronic botulism in cows is rectified in livestock by feeding fermented and pro-biotic foods along with charcoal and humic acids. These both bind to the toxins produced by the bacterial pathogen. This treatment also reduces the urinary content of glyphosate, suggesting its binding as an underlying mechanism in the recovery of the infection (see [66]).

Autistic people are well known to have disturbed intestinal function and dysbiosis of the gut. Autism rates are also spiking in parallel with glyphosate use in the US and glyphosateís antibiotic activity may well be an underlying mechanism behind this. Indeed, mothers have also documented much improved autism symptoms in their children upon giving them a glyphosate and GM-free diet.

Health Of Americans Rapidly Deteriorating

One argument for the safety of GM food and their associated pesticides is that the US has been consuming them for years without ill effect. However, in the absence of labelling GM foods, it is illegitimate to make such a claim. On the contrary, there has been a drastic deterioration of public health in the US since GM crops were introduced. A new publication by Swanson and colleagues plots the rise of 20 chronic diseases using available US government data, all correlating closely with increasing glyphosate application to corn and soy crops, especially over the past several years. The diseases included cancers, Parkinsonís, autism, obesity, diabetes, heart disease, digestive disease and kidney failure [62]. Correlation does not prove causation, but such strong association certainly cannot be dismissed, especially in combination with the plethora of other evidence from laboratory studies, and the experiences of doctors in their clinics and farmers in the fields. For a detailed analysis of the study please see [67] Marked Deterioration of Public Health Parallels Increase in GM Crops and Glyphosate Use, US Government Data Show (SiS 65).

Though heart disease had not been studied as extensively as cancers and birth defects in relation to glyphosate, the above study implicates its role in cardiac dysfunction. This is corroborated by the new finding that glyphosate formulations cause abnormal heart rhythms (arrhythmia) by interfering with the electrical activity of heart cells in rabbits [68].

A new study published in 2015 finds a correlation between glyphosate use and pineal gland pathology. The pineal gland is located in the brain and is known to regulate circadian rhythm through melatonin secretion. Glyphosate is hypothesised to disrupt melatonin metabolism, as well as induce pineal gland neuropathology through aluminium-induced hypoxia that results from the metal chelating properties of glyphosate. In this way, glyphosate use tightly correlates with the rises in sleep disorders as well as other disorders with symptoms of sleep dysfunction such as autism and dementia [69].

It is becoming clear that glyphosate has multiple toxicities that link it to many diseases through its metal chelating, antibiotic, endocrine disrupting, and genotoxic properties. Glyphosate also has the ability to block cytochrome P450 (CYP) enzyme activity, a class of enzymes involved in detoxifying xenobiotics amongst other things. Glyphosate therefore not only is a toxin in its own right, but enhances the toxicity of other chemicals by preventing the CYP enzymes from detoxifying the body [70].

Americans are definitely getting sicker in numerous ways highly correlated with adopting GM crops and rise in glyphosate use [67] and, as shown by all the testimonials from Moms across America, peoplesí health improves after removing GMOs and glyphosate residues from their foods by buying organic [63].

Environmental toxicity a concern for biodiversity, agriculture and sustainability

The spread of glyphosate-resistant weeds is increasingly compromising the effectiveness of the herbicide. There are now a reported 31 species of resistant weeds, up from 23 a year ago as recorded by the Weed Science organisation in the US [71]. In Brazil, an aggressive spread of weeds prompted a former DuPont agronomist to acknowledge the difficulties faced by farmers cultivating glyphosate-tolerant GM crops both in Brazil and Argentina [72]. Monsanto now recommends an ëintegrated weed managementí strategy that includes tilling the soil (of previously no-till land) and using multiple herbicides. The main selling points of Monsantoís Roundup Ready (RR) GM crop system was to reduce environmental damage through no-tillage agriculture and glyphosate use ñ a supposedly ësafeí herbicide compared to older chemicals. Not only is glyphosate toxic to health and the environment, but a cocktail of even more lethal herbicides have to be deployed to deal with glyphosate-resistant weeds, and an end to no till agriculture, resulting in further soil erosion. In short, we have an ecological and agronomic disaster.

Glyphosate toxicity to wildlife is well-documented. Many species, including aquatic organisms, reptiles, beneficial soil organisms including certain microbes and worms have been shown in scientific studies to be affected by glyphosate exposure (see [73] Ban GMOS Now, ISIS special report). This includes chronic and acute toxicity to the model aquatic organism Daphnia magna at below accepted thresholds for glyphosate presence in US freshwater [74]. Amphibians, the most endangered animals in the world, are so sensitive to glyphosate that 78 % of frogs died in one study on being exposed to Roundup herbicide [75]. Glyphosate has also been shown to stimulate the growth of soil fungi, increase the pathogenicity of soil pathogens such as Xylella fastidosa while numerous beneficial soil organisms have been decimated [76] (see [77] Scientists Reveal Glyphosate Poisons Crops and Soil, SiS 47). The latest study on soil organisms concluded that non-target organisms are at risk of local extinction after finding sub-lethal doses of glyphosate reduced fertility as well as survival of juvenile and adult E.fetida worms [78]. Monarch butterfly decline has been linked to glyphosate destruction of the milkweed in the US, the only food source for its larvae. Their migration from the US is at an all-time low and has been declining for the last 17 years (1994-5 to 2010-2011) (see [79] Glyphosate and Monarch Butterfly Decline, SiS 52) [80]. This decline has prompted a move to protect the butterflies under the Endangered Species Act by over 200 organisations and 40 scientists in November 2014 [81]. A new report on a Welsh nature reserve documents the decline in insects including beneficial pollinators such as bees as glyphosate levels increase (see [9] How Roundup Poisoned my Nature Reserve, SiS 64).

Not only are non-target organisms negatively affected, but also the target crops. Glyphosateís metal chelating properties reduce the micronutrients available to the plant, which it needs to maintain a fully-functioning immune system, thereby increasing its susceptibility to disease. This mechanism is thought to underlie the spread of over 40 crop diseases in glyphosate-tolerant GM crops (see [82] USDA scientist reveals All, SiS53). Indeed, USDA senior scientist Don Huber states that glyphosateís ability to kill plants is through the destruction of their immune system. This was clearly demonstrated by his experiments showing that non-GM plants grown in a sterile soil do not die when sprayed with glyphosate as the pathogens are not there to take advantage of the compromised immune system.

A reduction in mineral nutrients has health impacts on those eating the crops such as abnormalities in calves that are caused by manganese deficiency, which are on the rise and may well result from glyphosate chelation [83]. Farm animals are further suffering from other illnesses (and birth defects) as described by the Danish pig farmer earlier. Similar problems have been reported in Germany, where cows are suffering from chronic infections such as botulism [60] and in the US, with for example, the veterinarian Art Dunham reporting botulism in dairy cows, as well as reproductive problems, bloody bowels, rickets and viral diseases in hogs [84].

As a result of the problems faced by farmers, many are now moving away from GM and glyphosate-based systems. The US is seeing a growth in the non-GM seed market (see [85] Global Status of GMO and non-GMO

crops, SiS 62). Agriculture experts such as Howard Vlieger are helping 300-400 farmers in the US switch from GM to non-GM crops without glyphosate use due to its ill effects to soil, plants and animals [86]. Glyphosate-tolerant crops have also been shown to need more water and do worse in drought situations (see [87] GM Crops and Water ñ A recipe for Disaster SiS 56, and [88] GM Crops Destroyed by US Drought but non-GM Varieties Flourish, SiS56). This is consistent with their health being compromised by glyphosate.

While GM crops are causing problems for farmers, non-GM crops are leading the way in providing drought- and salt-tolerant varieties, which makes sense when one considers that the majority of traits are highly complex, involving multiple genes and pathways and therefore too complicated to mimic with crude genetic engineering techniques (see [89] Genetic Modification Trails Conventional Breeding By Far, SiS 64).

Regulatory science is corrupt
We MUST ban glyphosate locally

Glyphosate re-assessment by the EU commission was performed in 2014, not only re-approving glyphosate, but approving increased residue levels for food and feed, with the final decision expected in 2015. The reassessment was performed by industry, though Germany acted as the rapporteur state, submitting the renewal assessment report to the European Food Safety Authority (EFSA) (see [90]Scandal of Glyphosate Re-assessment in Europe(SiS63). This report relied on summary assessments provided by the Glyphosate Task Force which consists of Monsanto and other chemical companies such as Syngenta UK and Dow Italy. Assessments were made on glyphosate excluding commercial formulations most frequently used such as Roundup, and focused on studies showing less toxic results.

It has been well-documented and previously explained in Ban GMOS Now [73], that adjuvants present in glyphosate formulation products such as POEA, as well as glyphosate metabolites like AMPA have their own toxicity and moreover, that glyphosate and the adjuvants together are far more toxic than glyphosate alone. A new 2014 study by Professor S. Èralinìís group further confirms this, showing for the first time that glyphosate formulation products *(as well as insecticide and fungicides)* are far more toxic than glyphosate alone at concentrations well below agricultural dilutions [91]. Using human cell lines (HEK293, JEG3 and HepG2), they showed formulations to cause significant reductions in cell viability at concentrations 125 times less than glyphosate alone, challenging the relevance of the current acceptable daily intake (ADI). It is important to note that studies on the effects of pesticide cocktail mixtures, a far more likely scenario in real life, have yet to be properly investigated.

Using human cell lines
with names like HEK293, **JEG3** and **HepG2**,
they showed that these numerous Monsanto formulations caused
significant reductions in cell viability
at concentrations 125 times LESS!
than glyphosate alone

THIS **CHALLENGES** THE relevance
of the ***Acceptable Daily Intake***
(which should be zefuckingro).
It's also critical to note that studies on the **synergistic effects**
of **Pesticide Cocktail Mixtures**, the far more likely real-life scenario
have yet to be investigated.

Researching the effects of glyphosate and its singular affects on the human species is a slight of hand, a three-card-monte, the grift.

To conclude

The evidence of glyphosate toxicity to both human and animal health and the ecosystem has built up to such an extent that some governments are taking action. As mentioned earlier, both El Salvador and Sri Lanka have made steps towards banning the herbicide. The Netherlands successfully banned its sale to private individuals [92]. Russia has recently decided to ban the import and cultivation of all GM crops due to health and environmental concerns [93], while a section of the Chinese army has reportedly banned its consumption [94]. In Brazil a public prosecutor is also looking to suspend its use [95].

For those of us who are not being protected by our governments, it is time to start initiating our own campaigns, banning it first from our home, our community, our schools, local counties and Dr Eva Sirinathsinghji regions.

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There are 5 comments on this article so far

Feel free to add your own comment, no doubt it would be valued and respected.

Amyan Macfadyen Comment left 19th January 2015 18:06:50
/these facts seem undeniable and should be MUCH more widely disseminated. The big questino is how to do this without legal action by Monsanto and so as to lead to real acion, They woud have all the funds needed to resist such action, What is the legal position?

Naomi Z¸rcher Comment left 23rd January 2015 13:01:13
I agree with the first comment that such information needs to be widely distributed, Since Monsanto is the present devil incarnate, it behooves all of us to not allow the threat of legal action to disseminate this information

by whatever means is available to each of us. I will send this article to as many us elected officials that I can access in the hope that there is enough common sense and public caring left in one of them that they will take this and run with it. I also shared Sparc's contact information with the Cornucopia Institute - a fantastic US organization representing organic farming and farmers. Such organizations have established networks for dissemination of invaluable information such as this article. Thank you, Sparc.

Sherwood Botsford Comment left 6th February 2015 11:11:38
A consistent error throughout the article. A microgram per liter is a part per billion, not a part per trillion.

Will Murray Comment left 6th February 2015 11:11:35
Can you please send me addresses, emails to members of congress that I could write a letter to explaining that I oppose GMOs and the use of herbicides , pesticides and any solution with glyphosate? Thank you, William Murray

MaeWan Comment left 6th February 2015 11:11:31
Hi Sherwood, We are always pleased when readers point out errors to us. But please note that the error of equating ug/L with parts per trillion instead of parts per billion occurred only in one place, which is now corrected, the other ppts cited were correct. maewan

You can view Mae-Wan Ho's numerous awards, patents, books and inventions here: http://www.i-sis.org.uk/MWHcv.php

Anti-GMO Activist Mae-Wan Ho

Who Is Mae-Wan Ho?

by Jeff Prager

Mae-Wan Ho was born on November 12th, 1941 in Hong Kong and is a UK citizen. She is a world renowned geneticist known for her critical views on genetic engineering and neo-Darwinism. Ms. Ho has authored or co-authored a number of publications, including 10 books, such as 'The Rainbow and the Worm, the Physics of Organisms' (1993, 1998), 'Genetic Engineering: Dream or Nightmare?' (1998, 1999), 'Living with the Fluid Genome' (2003) and 'Living Rainbow H20' (2012).

Ms. Ho received a Ph.D. in Biochemistry in 1967 from Hong Kong University, was a Postdoctoral Fellow in Biochemical Genetics at the University of California, San Diego, from 1968 to 1972, Senior Research Fellow in Queen Elizabeth College, Lecturer in Genetics (from 1976) and Reader in Biology (from 1985) in the Open University, and since retiring in June 2000 she has been a Visiting Professor of Biophysics in Catania University, Sicily.

Ms. Ho is the director of the Institute of Science in Society, an interest group that campaigns against what it sees as unethical uses of biotechnology. The group published about climate change, GMOs, homeopathy, traditional Chinese medicine, and water memory.

Ms. Ho has expressed concerns about the spread of altered genes through horizontal gene transfer and that the experimental alteration of genetic structures may be out of control. One of her concerns is that the antibiotic resistant gene that was isolated from bacteria and used in some GM crops might cross back from plants by horizontal gene transfer to different species of bacteria, because "I*f this happened it would leave us unable to treat major illnesses like meningitis and E coli.*" Her views were published in an opinion article based on a review of others' research. The arguments and conclusions of this article were heavily criticized by prominent plant scientists and the claims of the article criticized in detail in a response that was published in the same journal. A review on the topic published in 2008 in the Annual Review of Plant Biology stated that "*These speculations have been extensively rebutted by the scientific community"*. Yet her claims have not been rebutted by the scientific community but rather, they've been proven time and again.

Ms. Ho, together with Joe Cummins of the University of Western Ontario, has argued that a sterility gene engineered into a crop could be transferred to other crops or wild relatives and that "*This could severely compromise the agronomic performance of conventional crops and cause wild relatives to go extinct*". They argued that this process could also produce genetic instabilities, which might be "*leading to catastrophic breakdown*", and stated that there are no data to assure that this has not happened or cannot happen. This concern contrasts with the reason why these sterile plants were developed, which was to prevent the transfer of genes to the environment by preventing any plants that are bred with or that receive these genes from reproducing. Indeed, any gene that caused sterility when transferred to a new species would be eliminated by natural selection and could not spread. Or so we hope.

Ms. Ho has also argued that bacteria could acquire the bacterial gene barnase from transgenic plants. This gene kills any cell that expresses it and lacks barstar, the specific inhibitor of barnase activity. In an article entitled Chronicle of An Ecological Disaster Foretold, which was published in an Institute of Science in Society newsletter, Ms. Ho speculated that if a bacterium acquired the barnase gene and survived, this could make the bacteria a more dangerous pathogen.

The Compiled Work of Mae-Wan Ho, PhD

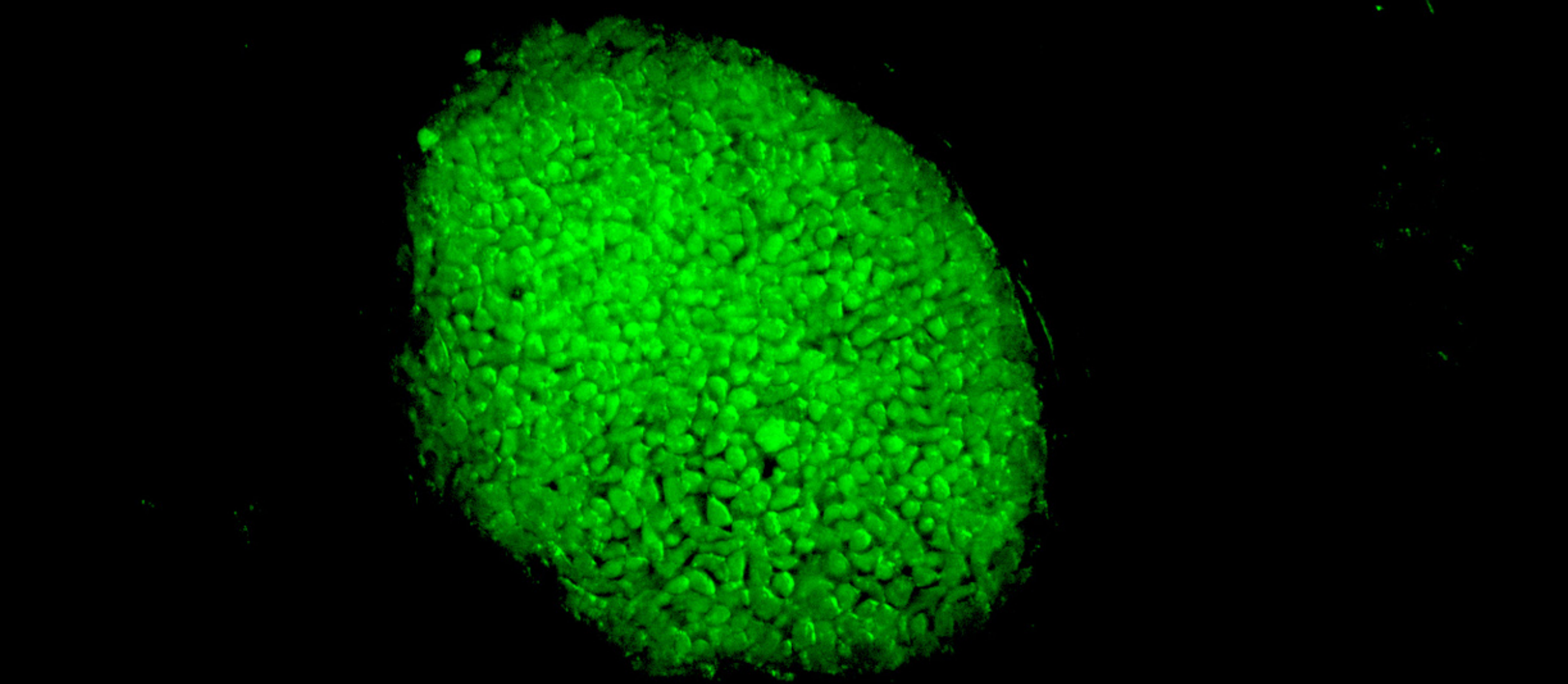
An incredible web site

http://gregorytaper.com/2014/11/14/the-compiled-work-of-mae-wan-ho-phd/

"…They're still fooled by the idea of genetic determinism; one gene determines one characteristic like a straightforward linear causal chain. Instead, everything is interconnected with everything else, and you cannot separate the environment from genetic influences."

— Dr. Mae-Wan Ho, "Human Genome:
The Biggest Sellout in Human History", 2000

Mae-Wan Ho, Open University and Institute of Science in Society, introduced an open letter, signed by more than 310 World Scientists, to all governments concerning GMOs. She said that the introduction of GMOs to developing countries will exacerbate inequality and prevent the essential shift to sustainable agriculture. And she's 100% correct.



A colony of about a thousand cells of the first human embryonic stem cell line called H1 genetically engineered with the jellyfish gene that glows in the dark. The white line *(at right)* shows the distance of one tenth of a millimeter.

Journal of Environmental & Analytical Toxicology

Detection of Glyphosate Residues in Animals and Humans

by Monika Krüger1, Philipp Schledorn1, Wieland Schrödl1, Hans-Wolfgang Hoppe2, Walburga Lutz3 and Awad A. Shehata1,4*

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Abstract

In the present study glyphosate residues were tested in urine and different organs of dairy cows as well as in urine of hares, rabbits and humans using ELISA and Gas Chromatography-Mass Spectroscopy (GC-MS). The correlation coefficients between ELISA and GC-MS were 0.96, 0.87, 0.97and 0.96 for cattle, human, and rabbit urine and organs, respectively. The recovery rate of glyphosate in spiked meat using ELISA was 91%. Glyphosate excretion in German dairy cows was significantly lower than Danish cows. Cows kept in genetically modified free area had significantly lower glyphosate concentrations in urine than conventional husbandry cows. Also glyphosate was detected in different organs of slaughtered cows as intestine, liver, muscles, spleen and kidney. Fattening rabbits showed significantly higher glyphosate residues in urine than hares. Moreover, glyphosate was significantly higher in urine of humans with conventional feeding. Furthermore, chronically ill humans showed significantly higher glyphosate residues in urine than healthy population. The presence of glyphosate residues in both humans and animals could haul the entire population towards numerous health hazards, studying the impact of glyphosate residues on health is warranted and the global regulations for the use of glyphosate may have to be re-evaluated.

Thoughts On The Report
"Detection of Glyphosate Residues in Animals and Humans"

by Jeff Prager

Glyphosate has been described as the newest environmental neurotoxin. Exposure of mammals to glyphosate can cause loss of mitochondrial transmembrane potential and result in oxidative stress to both the liver and brain. Both apoptosis (*cell death*) and autophagy (*cell degradation of unnecessary or dysfunctional cellular components*) are involved in glyphosate toxicity mechanisms. Numerous case reports indicate with clarity that exposure to glyphosate often results in rapid onset Parkinsonism, or Parkinson's Disease. Glyphosate residue now reaches humans through the food they eat at extraordinary levels and then is partially excreted in urine. Glyphosate does bioaccumulate. Presence of glyphosate in urine is less important than its accumulation in animal tissues which is alarming even at the lowest concentrations. Numerous unknown impacts of glyphosate on human and animal health as well as known glyphosate-caused neurological disorders and a plethora of known illnesses and diseases in humans linked to glyphosate and its additional ingredients warrants immediate, independent and fully transparent investigations of glyphosate residues, adjuvants found in Roundup® and all of the chemicals related to the wide variety of glyphosate-containing products. The global regulations governing the manufacturing, use and sale of glyphosate need to be swiftly and expeditiously re-evaluated by an independent civilian authority with subpoena and other grand jury power.

I'm also concerned about the animals because they spend more time in glyphosate contaminated areas than we do and they're more likely to ingest more glyphosate than humans. No one's watching out for us so it's perfectly obvious no one's watching out for the animals either.

This entire GMO program is supported by fabricated science, manipulated studies and reports, lax to nonexistent government regulations and a public that's far too busy to understand the serious medical dilemma that they and their offspring should expect to face and that millions of us are facing already.

Effects of field-realistic doses of glyphosate on honeybee appetitive behaviour

by Herbert LT1, Vázquez DE1, Arenas A1, Farina WM2.

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Abstract

Glyphosate (GLY) is a broad-spectrum herbicide used for weed control. The sub-lethal impact of GLY on non-target organisms such as insect pollinators has not yet been evaluated. Apis mellifera is the main pollinator in agricultural environments and is a well-known model for behavioural research. Honeybees are also accurate biosensors of environmental pollutants and their appetitive behavioural response is a suitable tool with which to test sub-lethal effects of agrochemicals. We studied the effects of field-realistic doses of GLY on honeybees exposed chronically or acutely to the herbicide. We focused on sucrose sensitivity, elemental and non-elemental associative olfactory conditioning of the proboscis extension response (PER), and foraging-related behaviour. We found a reduced sensitivity to sucrose and learning performance for the groups chronically exposed to GLY concentrations within the range of recommended doses. When olfactory PER conditioning was performed with sucrose reward with the same GLY concentrations (acute exposure), elemental learning and short-term memory retention decreased significantly compared with controls. Non-elemental associative learning was also impaired by an acute exposure to GLY traces. Altogether, these results imply that GLY at concentrations found in agro-ecosystems as a result of standard spraying can reduce sensitivity to nectar reward and impair associative learning in honeybees. However, no effect on foraging-related behaviour was found. Therefore, we speculate that successful forager bees could become a source of constant inflow of nectar with GLY traces that could then be distributed among nestmates, stored in the hive and have long-term negative consequences on colony performance: http://www.ncbi.nlm.nih.gov/pubmed/25063858

Glyphosate has "*long-term negative consequences on colony performance*"

GMO & Its Inherent Controversies

by Jeff Prager

Dr. Stephanie Seneff's first highly controversial peer reviewed report was shredded by the mainstream media, their in-house paid scientists with kids, house payments and car payments, and medical and scientific pseudo-researchers the world over. Stephanie Seneff and Anthony Samsel were vilified. Yet they survived intact and their Youtube videos are phenomenally educational. Dr. Seneff's numerous Youtube videos prove her success in her attempt to educate the public is apparent and growing.

I am including their two reports here precisely because of the controversy which was never once directed at the facts, the facts that Samsel and Seneff raised, discussed and offered up for free. So who is Stephanie Seneff and how was she vilified, disparaged and denounced? First, we'll examine Stephanie Seneff's more than outstanding biography.

Who Is Stephanie Seneff Anyway?

Stephanie Seneff is a Senior Research Scientist at the MIT Computer Science and Artificial Intelligence Laboratory. She received her B.S. degree in Biophysics in 1968, her M.S. and E.E. degrees in Electrical Engineering in 1980, and her Ph.D degree in Electrical Engineering and Computer Science in 1985, all from MIT. For over three decades, her research interests have always been at the intersection of biology and computation: developing a computational model for the human auditory system, understanding human language so as to develop algorithms and systems for human computer interactions, as well as applying natural language processing (NLP) techniques to gene predictions. She has published over 170 refereed articles on these subjects, and has been invited to give keynote speeches at several international conferences. She has also supervised numerous Master's and PhD theses at MIT. In 2012, Dr. Seneff was elected Fellow of the International Speech and Communication Association (ISCA).

In recent years, Dr. Seneff has focused her research interests back towards biology. She is concentrating mainly on the relationship between nutrition and health. Since 2011, she has written over a dozen papers (7 as first author) in various medical and health-related journals on topics such as modern day diseases (e.g., Alzheimer, autism, cardiovascular diseases), analysis and search of databases of drug side effects using NLP techniques, and the impact of nutritional deficiencies and environmental toxins on human health.

Here is a link to her extensive and simply amazing full biography and you'll quickly realize that she has the perfect credentials to investigate the innumerable disorders caused in part by glyphosate: http://people.csail.mit.edu/seneff/

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

by Anthony Samsel 1 and Stephanie Seneff 2,*

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Published: 18 April 2013

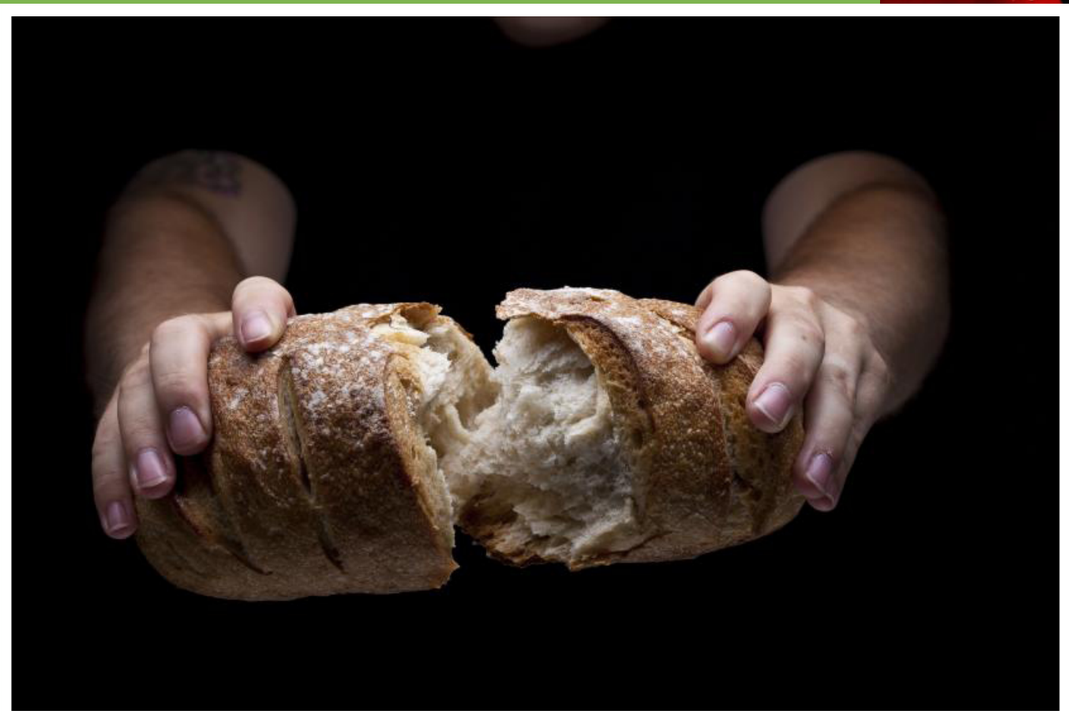
Abstract

Glyphosate, the active ingredient in Roundup®, is the most popular herbicide used worldwide. The industry asserts it is minimally toxic to humans, but here we argue otherwise. Residues are found in the main foods of the Western diet, comprised primarily of sugar, corn, soy and wheat. Glyphosate's inhibition of cytochrome P450 (CYP) enzymes is an overlooked component of its toxicity to mammals.

CYP enzymes play crucial roles in biology, one of which is to detoxify xenobiotics. Thus, glyphosate enhances the damaging effects of other food borne chemical residues and environmental toxins. Negative impact on the body is insidious and manifests slowly over time as inflammation damages cellular systems throughout the body.

Here, we show how interference with CYP enzymes acts synergistically with disruption of the biosynthesis of aromatic amino acids by gut bacteria,as well as impairment in serum sulfate transport. Consequences are 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.

We explain the documented effects of glyphosate and its ability to induce disease, and we show that glyphosate is the "***textbook example***" of exogenous semiotic entropy: the disruption of homeostasis by environmental toxins.



by Anthony SAMSEL 1 and Stephanie SENEFF 2

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2 Computer Science and Artificial Intelligence Laboratory, MIT, Cambridge, MA, USA
Received: 24 September 2013 • Revised: 10 November 2013 • Accepted: 12 November 2013

*Note: In the decades ahead this study will become known as the first exposure into the already known and hidden deadly hazards of these products. This study will be the 'gold standard' for judging the safety of genetically modified organisms and their pesticides.

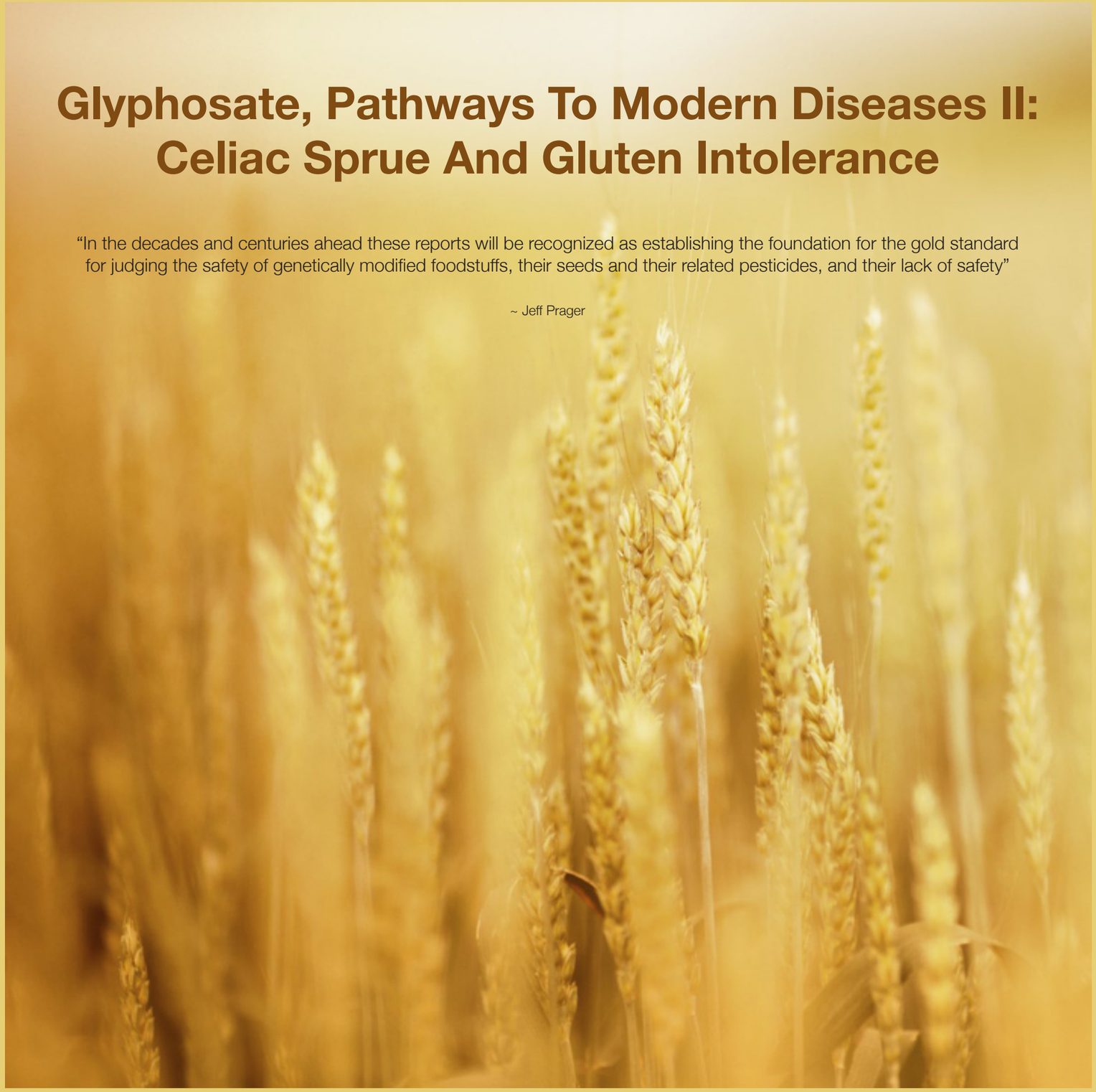
ABSTRACT

Celiac disease, and, more generally, gluten intolerance, is a growing problem worldwide, but especially in North America and Europe, where an estimated 5% of the population now suffers from it. Symptoms include nausea, diarrhea, skin rashes, macrocytic anemia and depression. It is a multifactorial disease associated with numerous nutritional deficiencies as well as reproductive issues and increased risk to thyroid disease, kidney failure and cancer. Here, we propose that glyphosate, the active ingredient in the herbicide, Roundup®, is the most important causal factor in this epidemic. Fish exposed to glyphosate develop digestive problems that are reminiscent of celiac disease. Celiac disease is associated with imbalances in gut bacteria that can be fully explained by the known effects of glyphosate on gut bacteria. Characteristics of celiac disease point to impairment in many cytochrome P450 enzymes, which are involved with detoxifying environmental toxins, activating vitamin D3, catabolizing vitamin A, and maintaining bile acid production and sulfate supplies to the gut. Glyphosate is known to inhibit cytochrome P450 enzymes. Deficiencies in iron, cobalt, molybdenum, copper and other rare metals associated with celiac disease can be attributed to glyphosate's strong ability to chelate these elements. Deficiencies in tryptophan, tyrosine, methionine and selenomethionine associated with celiac disease match glyphosate's known depletion of these amino acids. Celiac disease patients have an increased risk to non-Hodgkin's lymphoma, which has also been implicated in glyphosate exposure. Reproductive issues associated with celiac disease, such as infertility, miscarriages, and birth defects, can also be explained by glyphosate. Glyphosate residues in wheat and other crops are likely increasing recently due to the growing practice of crop desiccation just prior to the harvest. We argue that the practice of "ripening" sugar cane with glyphosate may explain the recent surge in kidney failure among agricultural workers in Central America. We conclude with a plea to governments to reconsider policies regarding the safety of glyphosate residues in foods.

Glyphosate, Pathways To Modern Diseases II: Celiac Sprue And Gluten Intolerance

"In the decades and centuries ahead these reports will be recognized as establishing the foundation for the gold standard for judging the safety of genetically modified foodstuffs, their seeds and their related pesticides, and their lack of safety"

~ Jeff Prager



by Jeff Prager

I believe it's important, and it was important to me, to take the time to understand each of the graphs from the Samsel and Seneff studies seen on the following pages.

Of course they're discussed in expansive detail in Seneff and Samsel's first study, "Glyphosate's Suppression of Cytochrome P450 Enzymes and Amino Acid Biosynthesis by the Gut Microbiome: Pathways to Modern Diseases," published in Entropy in 2013, and their second pivotal study, "Glyphosate, pathways to modern diseases II Celiac spruce and gluten intolerance," published less than a year later.

The intimacy of the mechanisms exposed and the direct correlations to the point of proving factual causation between GMO foodstuffs, their seeds and associated pesticides to almost every disease known to woman and man is so severely damaging that Seneff and Samsel were bullied, criticized and vilified by the mainstream media, They were crucified and absolutely shredded but we're here for the truth and Samsel and Seneff didn't just hit a nerve, they sliced right through a jugular and spilled the bloody truth across the entire planet.

You can't read their reports, following the science with a handy electronic dictionary and encyclopedia, read them slowly and carefully being certain to understand every nuance, every subtlety and all of the vast and numerous interactions—bacteria talking to our cells—without recognizing that Samsel and Seneff are right.

They're right about everything they've written. You'll find numerous and exceptionally entertaining videos on Youtube. Many more for Dr. Stephanie Seneff than Dr. Anthony Samsel but you'll find for both of them nevertheless!

Entropy **2013**, *15*, 1416-1463; doi:10.3390/e15041416

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Review

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

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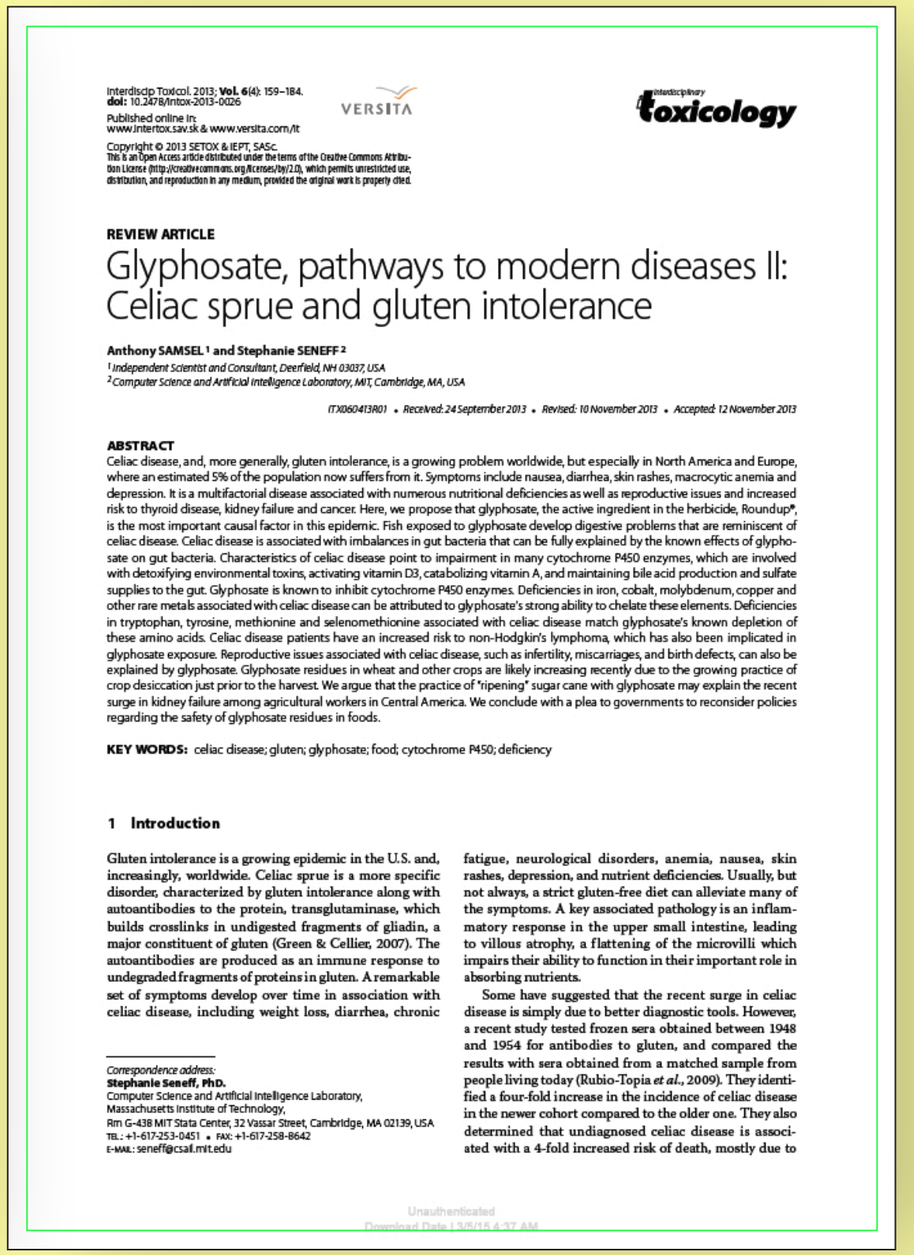
Keywords: glyphosate; cytochrome P450; eNOS; obesity; cardiovascular disease; cancer; colitis; shikimate pathway; gut microbiome; tryptophan; tyrosine; phenylalanine; methionine; serotonin; Alzheimer's disease; Parkinson's disease; autism; depression



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interdisciplinary toxicology

REVIEW ARTICLE

Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance

Anthony SAMSEL [1] and Stephanie SENEFF [2]

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ITX060413R01 • Received: 24 September 2013 • Revised: 10 November 2013 • Accepted: 12 November 2013

ABSTRACT

Celiac disease, and, more generally, gluten intolerance, is a growing problem worldwide, but especially in North America and Europe, where an estimated 5% of the population now suffers from it. Symptoms include nausea, diarrhea, skin rashes, macrocytic anemia and depression. It is a multifactorial disease associated with numerous nutritional deficiencies as well as reproductive issues and increased risk to thyroid disease, kidney failure and cancer. Here, we propose that glyphosate, the active ingredient in the herbicide, Roundup®, is the most important causal factor in this epidemic. Fish exposed to glyphosate develop digestive problems that are reminiscent of celiac disease. Celiac disease is associated with imbalances in gut bacteria that can be fully explained by the known effects of glyphosate on gut bacteria. Characteristics of celiac disease point to impairment in many cytochrome P450 enzymes, which are involved with detoxifying environmental toxins, activating vitamin D3, catabolizing vitamin A, and maintaining bile acid production and sulfate supplies to the gut. Glyphosate is known to inhibit cytochrome P450 enzymes. Deficiencies in iron, cobalt, molybdenum, copper and other rare metals associated with celiac disease can be attributed to glyphosate's strong ability to chelate these elements. Deficiencies in tryptophan, tyrosine, methionine and selenomethionine associated with celiac disease match glyphosate's known depletion of these amino acids. Celiac disease patients have an increased risk to non-Hodgkin's lymphoma, which has also been implicated in glyphosate exposure. Reproductive issues associated with celiac disease, such as infertility, miscarriages, and birth defects, can also be explained by glyphosate. Glyphosate residues in wheat and other crops are likely increasing recently due to the growing practice of crop desiccation just prior to the harvest. We argue that the practice of "ripening" sugar cane with glyphosate may explain the recent surge in kidney failure among agricultural workers in Central America. We conclude with a plea to governments to reconsider policies regarding the safety of glyphosate residues in foods.

KEY WORDS: celiac disease; gluten; glyphosate; food; cytochrome P450; deficiency

1 Introduction

Gluten intolerance is a growing epidemic in the U.S. and, increasingly, worldwide. Celiac sprue is a more specific disorder, characterized by gluten intolerance along with autoantibodies to the protein, transglutaminase, which builds crosslinks in undigested fragments of gliadin, a major constituent of gluten (Green & Cellier, 2007). The autoantibodies are produced as an immune response to undegraded fragments of proteins in gluten. A remarkable set of symptoms develop over time in association with celiac disease, including weight loss, diarrhea, chronic fatigue, neurological disorders, anemia, nausea, skin rashes, depression, and nutrient deficiencies. Usually, but not always, a strict gluten-free diet can alleviate many of the symptoms. A key associated pathology is an inflammatory response in the upper small intestine, leading to villous atrophy, a flattening of the microvilli which impairs their ability to function in their important role in absorbing nutrients.

Some have suggested that the recent surge in celiac disease is simply due to better diagnostic tools. However, a recent study tested frozen sera obtained between 1948 and 1954 for antibodies to gluten, and compared the results with sera obtained from a matched sample from people living today (Rubio-Topia *et al.*, 2009). They identified a four-fold increase in the incidence of celiac disease in the newer cohort compared to the older one. They also determined that undiagnosed celiac disease is associated with a 4-fold increased risk of death, mostly due to

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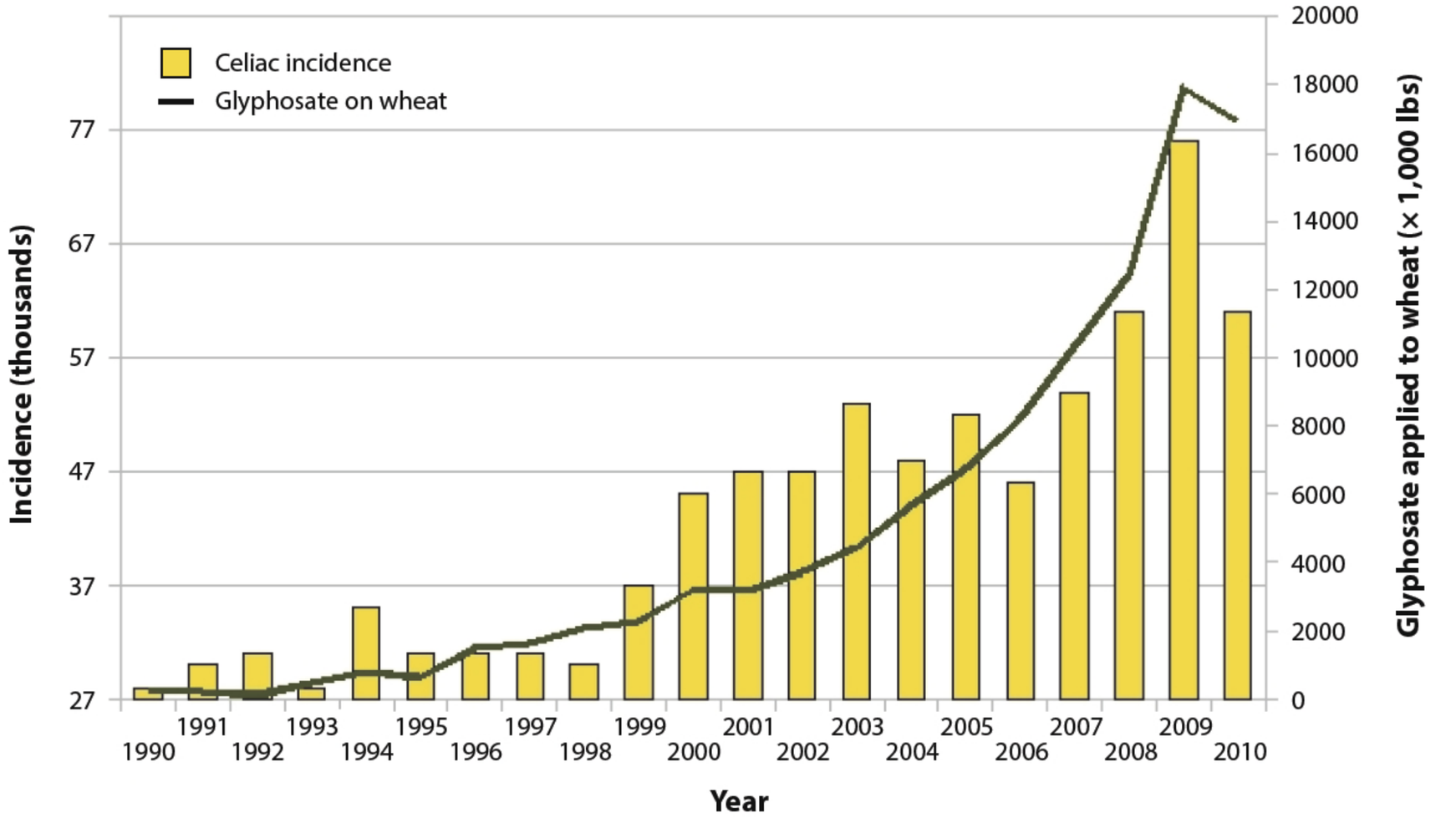
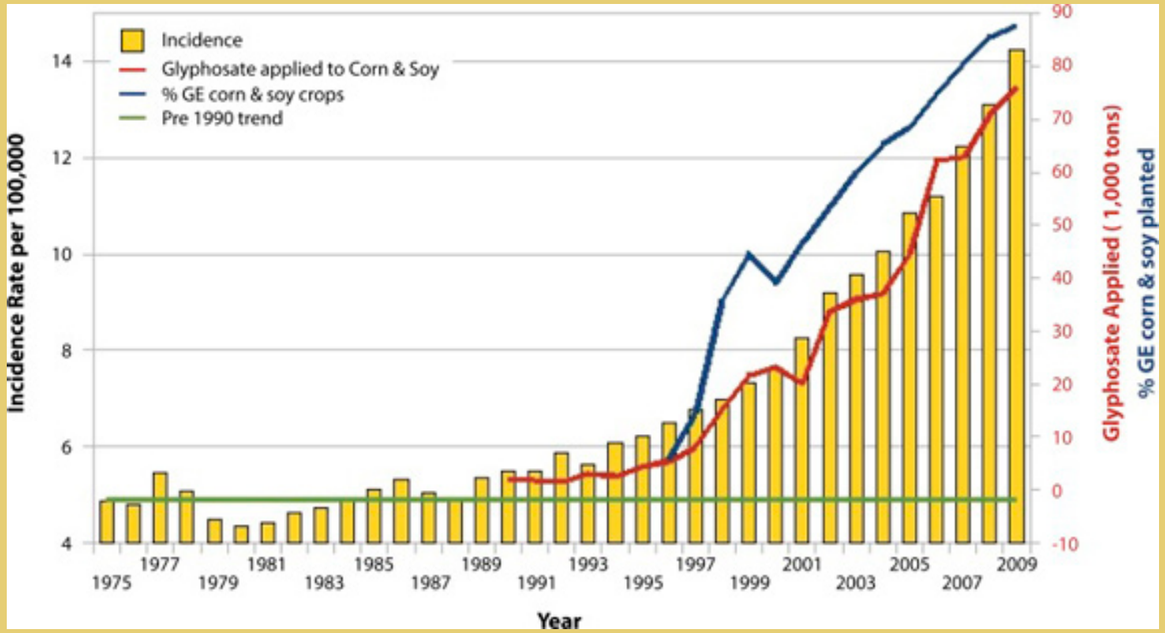
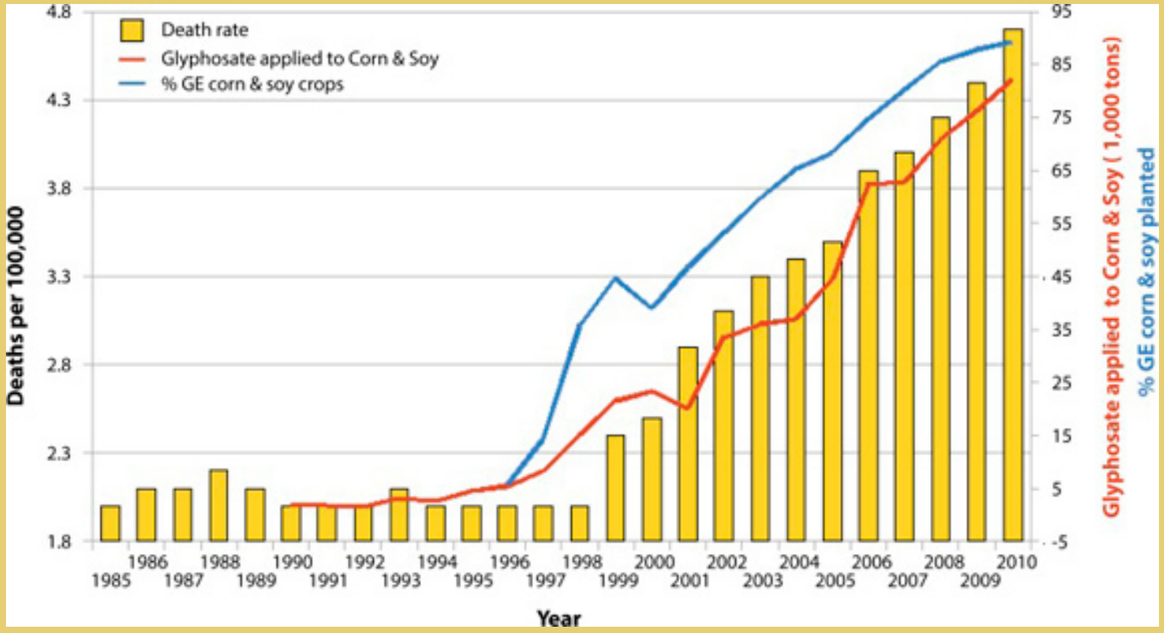
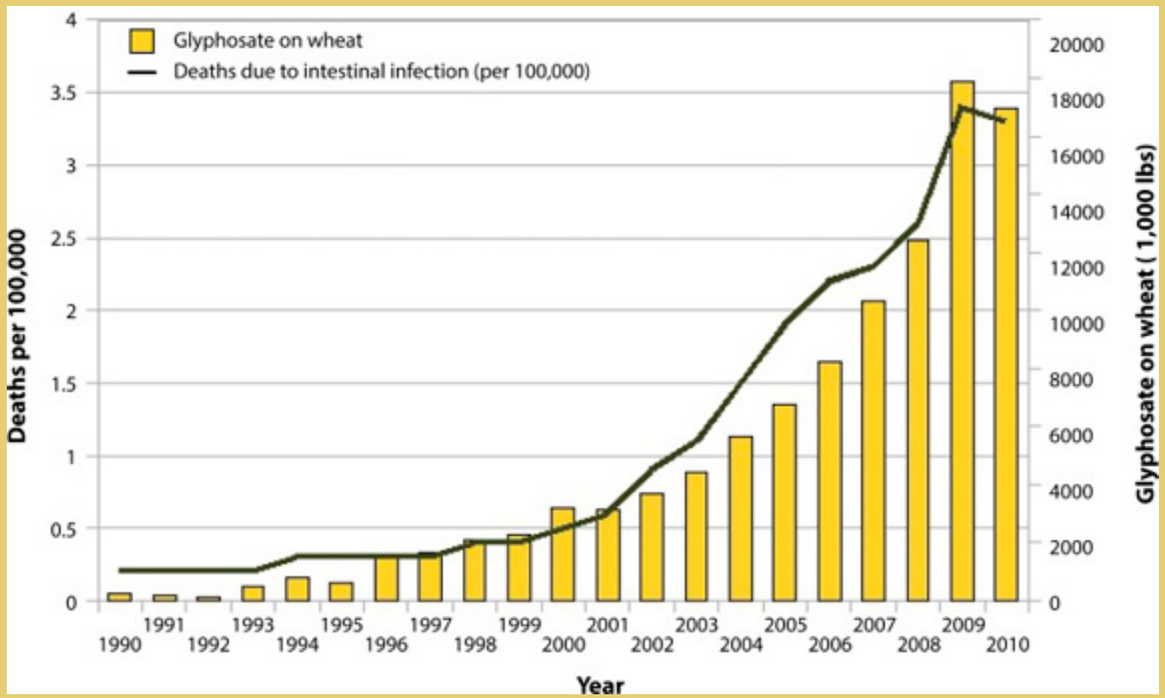


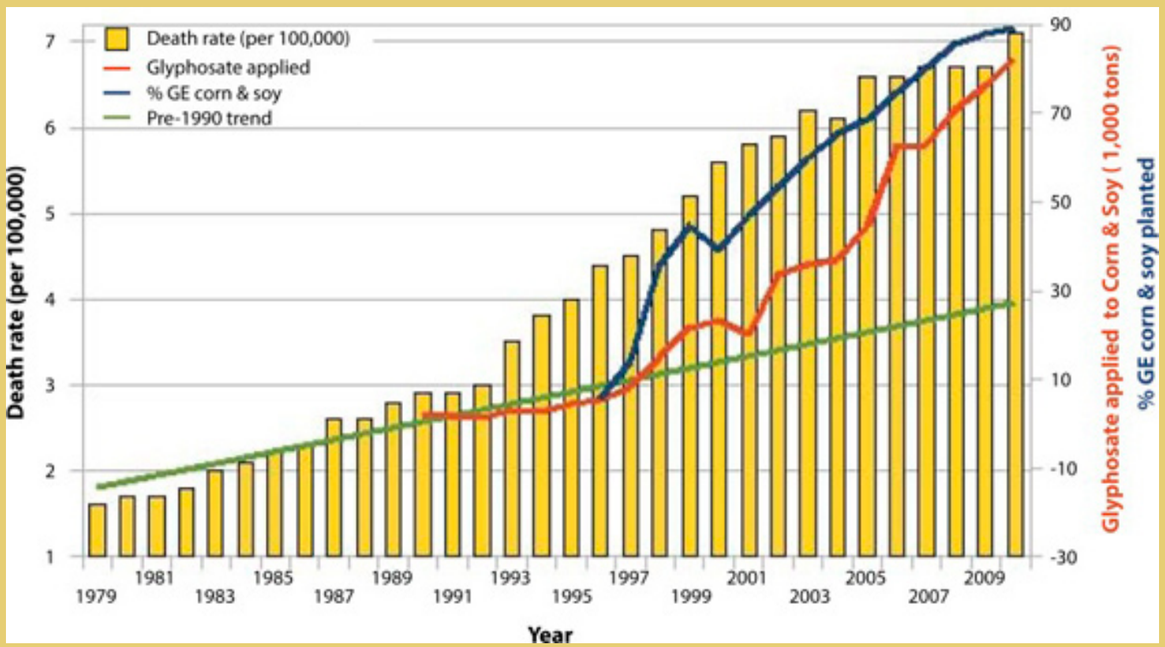
Figure 1. Hospital discharge diagnosis (any) of celiac disease ICD-9 579 and glyphosate applications to wheat (R=0.9759, $p \leq 1.862e\text{-}06$). Sources: USDA:NASS; CDC. (Figure courtesy of Nancy Swanson).

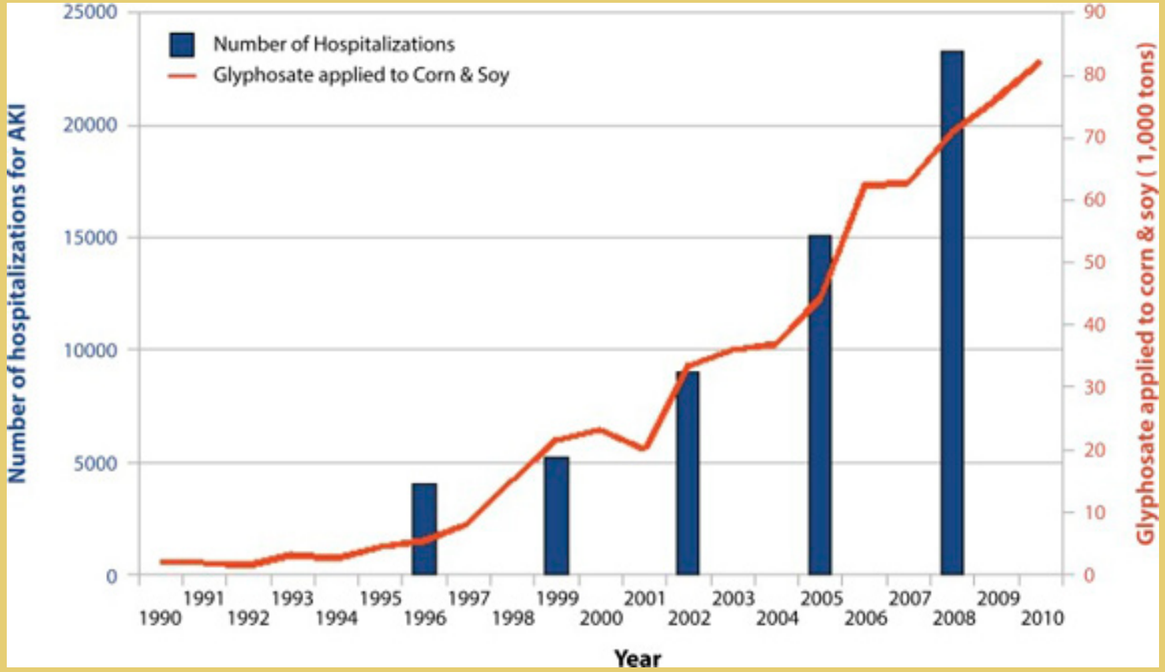
A recent study on glyphosate exposure in carnivorous fish revealed remarkable adverse effects throughout the digestive system (Senapati et al., 2009). The activity of protease, lipase, and amylase were all decreased in the esophagus, stomach, and intestine of these fish following exposure to glyphosate. The authors also observed "disruption of mucosal folds and disarray of microvilli structure" in the intestinal wall, along with an exaggerated secretion of mucin throughout the alimentary tract. These features are highly reminiscent of celiac disease. Gluten peptides in wheat are hydrophobic and therefore resistant to degradation by gastric, pancreatic and intestinal proteases (Hershko & Patz, 2008). Thus, the evidence from this effect on fish suggests that glyphosate may interfere with the breakdown of complex proteins in the human stomach, leaving larger fragments of wheat in the human gut that will then trigger an autoimmune response, leading to the defects in the lining of the small intestine that are characteristic of these fish exposed to glyphosate and of celiac patients. As illustrated in Figure 1, above, the usage of glyphosate on wheat in the U.S. has risen sharply in the last decade, in step with the sharp rise in the incidence of Celiac disease. We explain the reasons for increased application of glyphosate to wheat in Section 13 of this report.

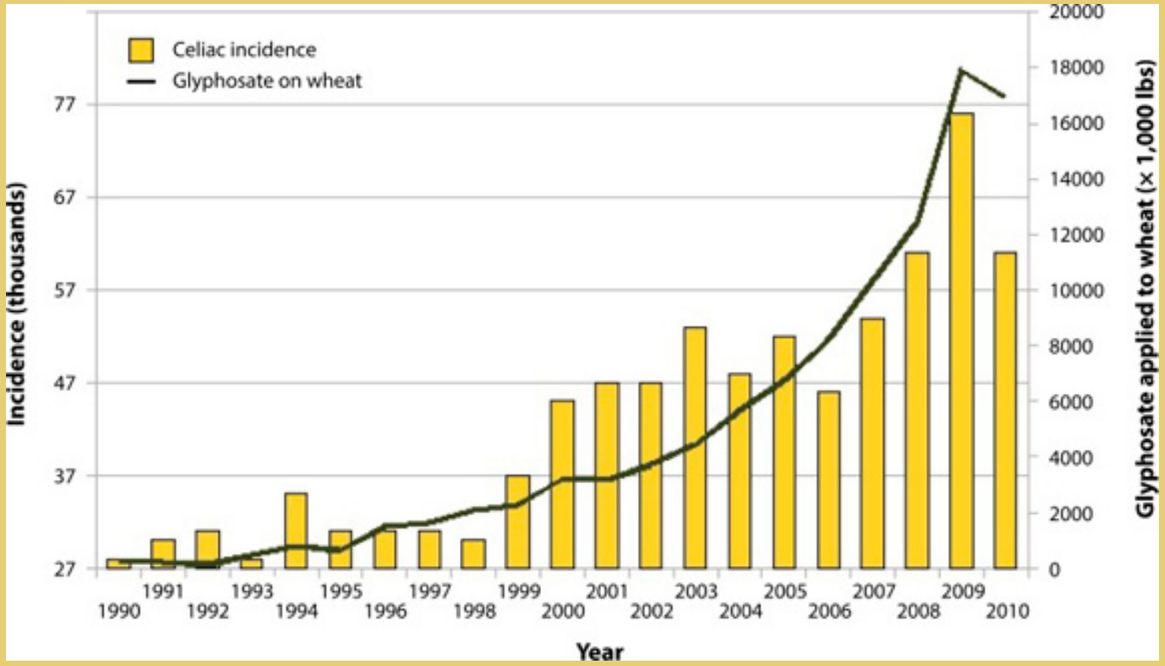

Incidence
Glyphosate applied to Corn & Soy
% GE corn & soy crops
Pre 1990 trend
Incidence Rate per 100,000
Glyphosate Applied (1,000 tons)
% GE corn & soy planted
Year

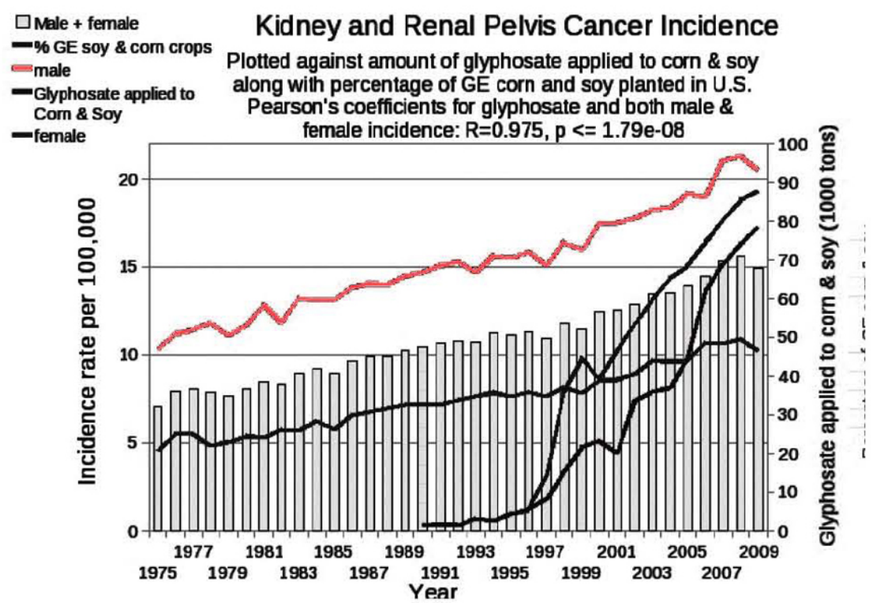

Death rate
Glyphosate applied to Corn & Soy
% GE corn & soy crops
Deaths per 100,000
Glyphosate applied to Corn & Soy (1,000 tons)
% GE corn & soy planted
Year

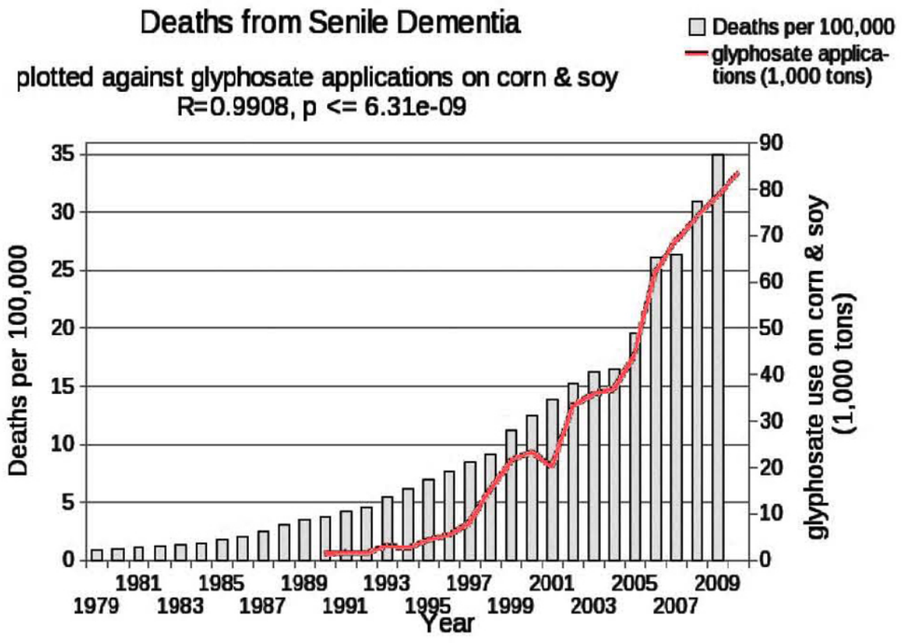

Glyphosate on wheat
Deaths due to intestinal infection (per 100,000)
Deaths per 100,000
Glyphosate on wheat (1,000 lbs)
Year

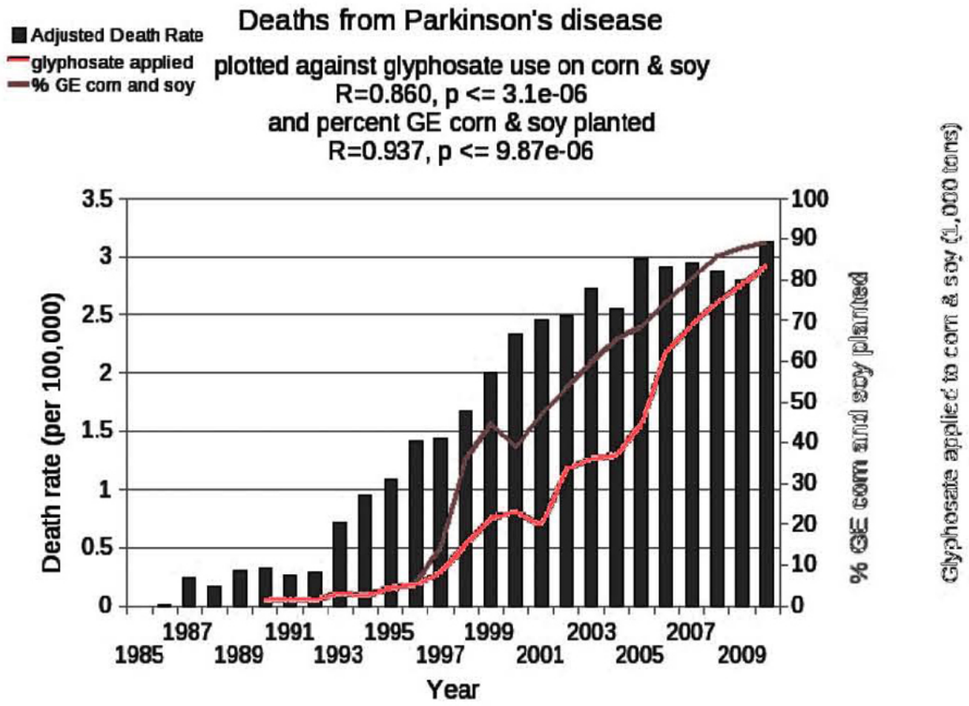

Death rate (per 100,000)
Glyphosate applied
% GE corn & soy
Pre-1990 trend
Death rate (per 100,000)
Glyphosate applied to Corn & Soy (1,000 tons)
% GE corn & soy planted
Year

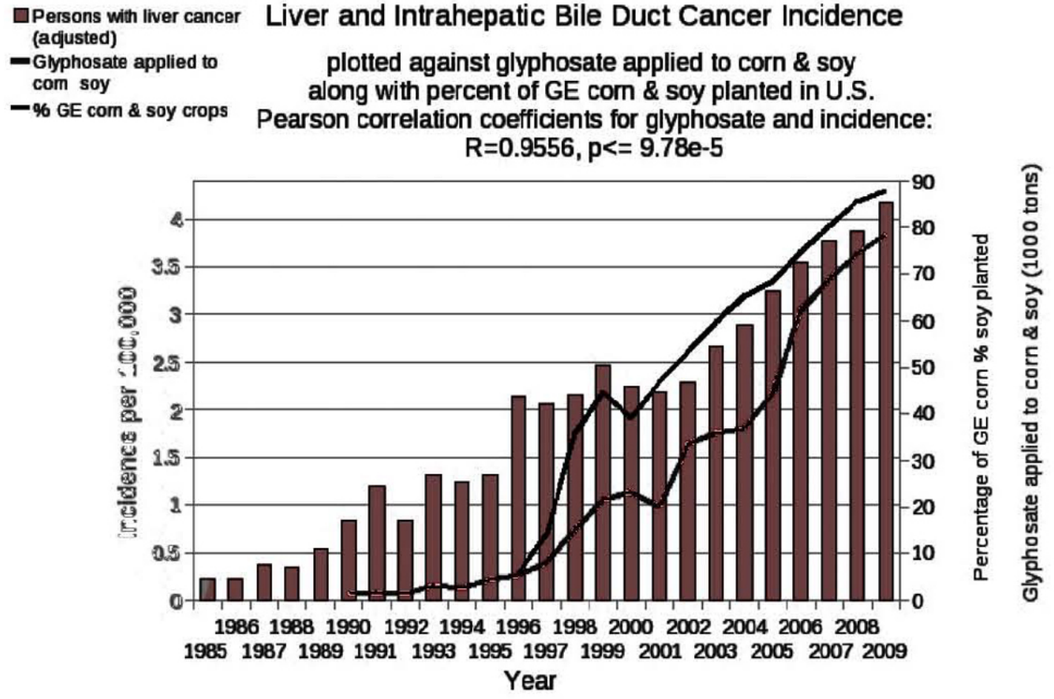

Number of Hospitalizations
Glyphosate applied to Corn & Soy
Number of hospitalizations for AKI
Glyphosate applied to corn & soy (1,000 tons)
Year

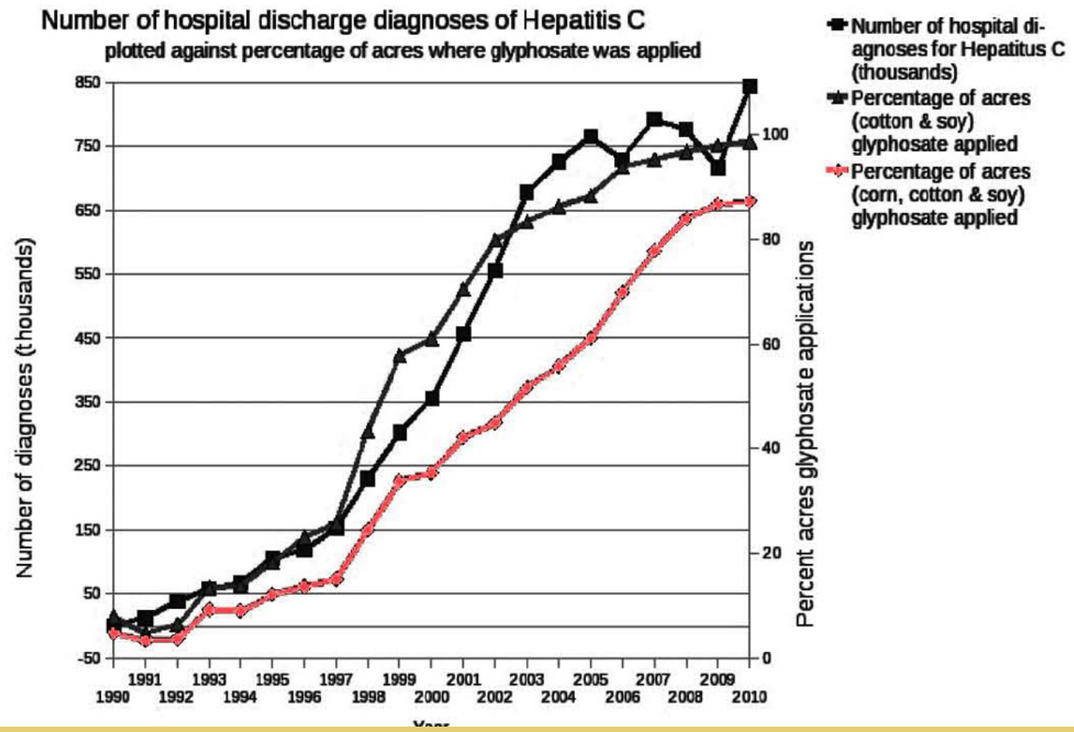

Celiac incidence
Glyphosate on wheat
Incidence (thousands)
Glyphosate applied to wheat (× 1,000 lbs)
Year

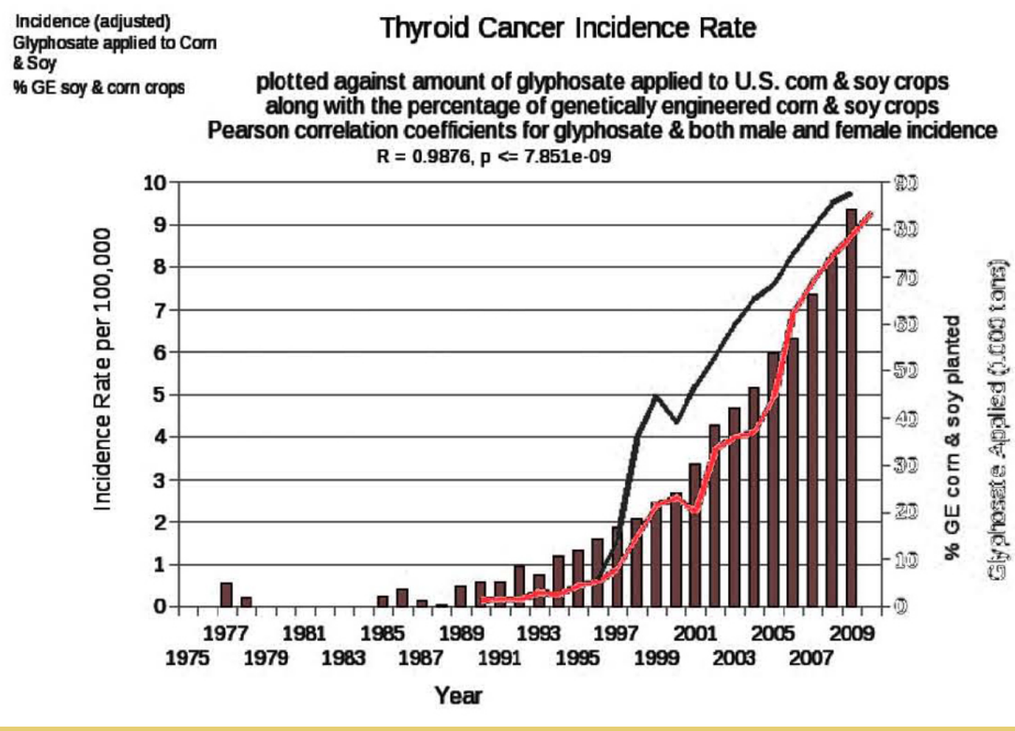

Male + female
% GE soy & corn crops
male
Glyphosate applied to Corn & Soy
female
Kidney and Renal Pelvis Cancer Incidence
Plotted against amount of glyphosate applied to corn & soy along with percentage of GE corn and soy planted in U.S.
Pearson's coefficients for glyphosate and both male & female incidence: R=0.975, p <= 1.79e-08
Incidence rate per 100,000
Glyphosate applied to corn & soy (1000 tons)
Year


Deaths from Senile Dementia
plotted against glyphosate applications on corn & soy
R=0.9908, p <= 6.31e-09
Deaths per 100,000
glyphosate applications (1,000 tons)
Deaths per 100,000
glyphosate use on corn & soy (1,000 tons)
Year


Deaths from Parkinson's disease
Adjusted Death Rate
glyphosate applied
% GE corn and soy
plotted against glyphosate use on corn & soy
R=0.860, p <= 3.1e-06
and percent GE corn & soy planted
R=0.937, p <= 9.87e-06
Death rate (per 100,000)
% GE corn and soy planted
Glyphosate applied to corn & soy (1,000 tons)
Year


Persons with liver cancer (adjusted)
Glyphosate applied to corn soy
% GE corn & soy crops
Liver and Intrahepatic Bile Duct Cancer Incidence
plotted against glyphosate applied to corn & soy
along with percent of GE corn & soy planted in U.S.
Pearson correlation coefficients for glyphosate and incidence:
R=0.9556, p<= 9.78e-5
Incidence per 100,000
Percentage of GE corn % soy planted
Glyphosate applied to corn & soy (1000 tons)
Year


Number of hospital discharge diagnoses of Hepatitis C
plotted against percentage of acres where glyphosate was applied
Number of hospital di-agnoses for Hepatitus C (thousands)
Percentage of acres (cotton & soy) glyphosate applied
Percentage of acres (corn, cotton & soy) glyphosate applied
Number of diagnoses (thousands)
Percent acres glyphosate applications


Incidence (adjusted)
Glyphosate applied to Corn & Soy
% GE soy & corn crops
Thyroid Cancer Incidence Rate
plotted against amount of glyphosate applied to U.S. corn & soy crops
along with the percentage of genetically engineered corn & soy crops
Pearson correlation coefficients for glyphosate & both male and female incidence
R = 0.9876, p <= 7.851e-09
Incidence Rate per 100,000
% GE corn & soy planted
Year

Monsanto's Glyphosate & Aluminum Cocktail Consequences Exposed by MIT Scientist

A Conversation With Dr. Stephanie Seneff

By 2025, half the kids born in the U.S. will be diagnosed with autism, according to Dr. Stephanie Seneff, Senior Research Scientist at the MIT Computer Science and Artificial Intelligence Laboratory.

She, like many others says autism isn't just genetic – it is almost surely due to environmental factors. Just a couple of those factors are Monsanto's RoundUp (glyphosate) and heavy exposure to a cocktail of heavy metals, including aluminum.

Dr. Seneff isn't respected by the ivory towers of the pharmaceutical medicine paradigm or industrial agriculture, but she has something to say about autism. She is a computer scientist who transitioned into biology and toxicology, so people like to attack her credentials, but what Dr. Seneff has to say is key, and many other mainstream researchers have been negligent in reporting these findings.

She has been studying autism for over 7 years, along with the environmental factors that lead to the disease. Decreased exposure to sunlight, poor diet, vaccines *(specifically aluminum and mercury)*, as well as glyphosate toxins from RoundUp are causing skyrocketing rates of autism. She explains this in a two-hour presentation given recently at Autism One.

Aluminum and Glyphosate

Aluminum and glyphosate specifically interrupt the workings of the pineal gland (*melatonin sulfate*), leading to high rates of autism. She outlines this fact in pinpointing detail in her research, which can be found here.

Furthermore, glyphosate chelates manganese. Dr. Seneff believes that just the absence of appropriate amounts of manganese can help to cause autism. Glyphosate also promotes aluminum uptake into our tissues, and interrupts an important path for amino acid uptake called the shikimate pathway, into our guts.

"*The way glyphosate works is that it interrupts the shikimate pathway, a metabolic function in plants that allows them to create essential amino acids. When this path is interrupted, the plants die. Human cells don't have a shikimate pathway so scientists and researchers believed that exposure to glyphosate would be harmless.*"

In fact, industrial claims don't match the science on RoundUp. It is often used because it is considered one of the 'safest' of all herbicides. This claim is touted by Monsanto and other chemical pushers, but it turns out that RoundUp is one of the least safe herbicides on the market. Incidentally, scientists were mistaken about a human shikimate pathway, and we rely upon it for many important functions in our body, including ridding our body of poisons like RoundUp as well as other herbicides and pesticides.

"*The problem is that bacteria DO have a shikimate pathway and we have millions of good bacteria in our guts – our 'gut flora.' These bacteria are essential to our health. Our gut isn't just responsible for digestion, but also for our immune system. When glyphosate gets in our systems, it wrecks our gut and as a result our immune system.*"

She says: "*The effects are insidious. You won't notice when you eat a food that contains glyphosate, but over time you will enter an old-age state before you should.*"

It's Time for Chemical Reform

Though Dr. Seneff's findings are in the research stages, there are plenty of families that have autistic children who have chosen to drastically change their children's diets, eliminating all pesticides, herbicides and as many neurotoxins as possible while eating organic food.

They often experience some incredible results, seeing improvement in their children's speech patterns, cognitive abilities, and social skills in weeks, not years. This amounts to circumstantial evidence, but it supports Dr. Seneff's claims.

The rate at which diseases like autism (*along with Parkinson's, Alzheimer's and others*) are growing

Paenibacillus is a genus of facultative anaerobic, endospore-forming bacteria, originally included within the genus Bacillus and then reclassified as a separate genus in 1993.[2] Bacteria belonging to this genus have been detected in a variety of environments such as: soil, water, rhizosphere, vegetable matter, forage and insect larvae, as well as clinical samples in humans.

would be unheard of just 50 years ago. You can't simply discount this phenomenon as the result of 'better screening and diagnosis.' In the past 5 years alone, autism rates have increased from 1/150 to 1/50. This is an environmental epidemic; it isn't genetic.

When you factor in the levels of glyphosate being found in women's breast milk is ten times that which is allowed in European drinking water, and people in 18 different countries were found to have glyphosate in their blood, you have to question the rise in autism from another perspective, aside from the genetic one, and connect the dots.

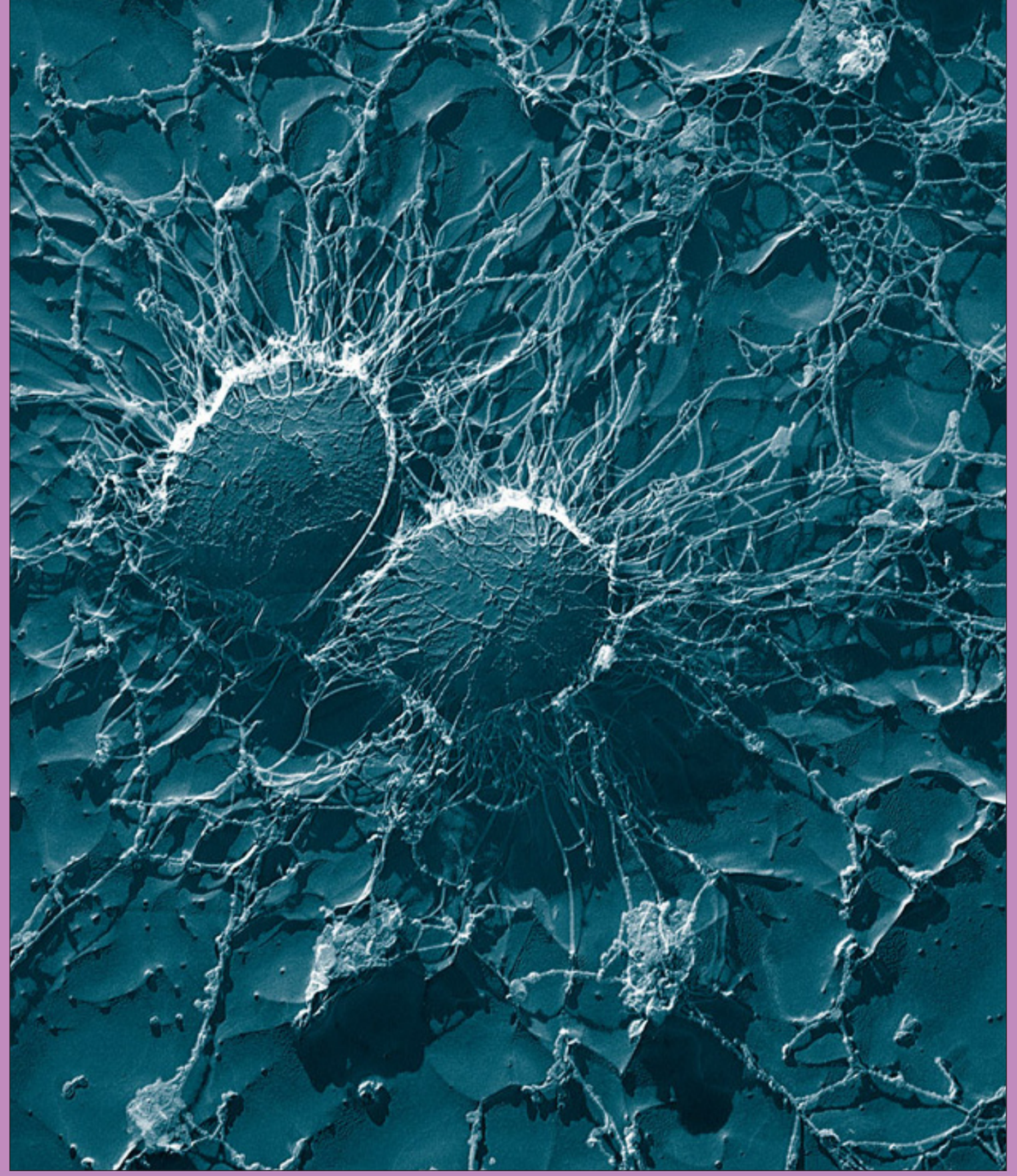
This leads to glyphosate as a synergistic compound that works with other suggested autism causes – like vaccines (*controversial, I know*).

"*Ordinarily the body is quite good about keeping aluminum out. The gut will absorb very little of what's in the diet…assuming you have a healthy gut. Glyphosate produces a leaky gut, and that's going to help the aluminum get in. What I believe now is that the aluminum in the vaccine is far more toxic as a consequence of the glyphosate that's also in the blood. The two of them are synergistic, because the glyphosate forms a cage around the aluminum and keeps it from getting expelled. The aluminum ends up accumulating, getting trapped with the glyphosate, and then the aluminum ends up in the pineal gland, and messes up sleep, and causes a whole cascade of problems in the brain. The glyphosate and aluminum are working together to be much more toxic than they would be, acting alone.*"

RoundUp chemicals are the most used chemicals in numerous lived-in cities such as New York City, not just on American farms. In just ten years, the use of RoundUp chemicals on American farms grew more than 89%. More than 80,000 tonnes are currently used on GMO corn, soy and other crops. We are being poisoned by the truckload. This isn't Big Ag against the masses anymore, it looks like pure genocide.

Additionally, all of Dr. Seneff's papers can be studied to corroborate her assertions that glyphosate and aluminum, among other environmental toxins, are synergistically causing autism:

"Anthony Samsel and Stephanie Seneff, "Glyphosate's Suppression of Cytochrome P450 Enzymes and Amino Acid Biosynthesis by the Gut Microbiome: Pathways to Modern Diseases" Entropy 2013, 15(4), 1416-1463; doi:10.3390/e15041416



Staphylococcus aureus, above, is a Gram-positive coccal bacterium that is a member of the Firmicutes, and is frequently found in the human respiratory tract and on the skin. It is positive for catalase and nitrate reduction. Although S. aureus is not always pathogenic, it is a common cause of skin infections (e.g. boils), respiratory disease (e.g. sinusitis), and food poisoning. Disease-associated strains often promote infections by producing potent protein toxins, and expressing cell-surface proteins that bind and inactivate antibodies. The emergence of antibiotic-resistant forms of pathogenic S. aureus (e.g. MRSA) is a worldwide problem in clinical medicine.

Robert M. Davidson, Ann Lauritzen and Stephanie Seneff, "Biological Water Dynamics and Entropy: A Biophysical Origin of Cancer and Other Diseases" Entropy 2013, 15, 3822-3876; doi:10.3390/ e15093822

Stephanie Seneff, Ann Lauritzen, Robert Davidson and Laurie Lentz-Marino, "Is Encephalopathy a Mechanism to Renew Sulfate in Autism?" Entropy 2013, 15, 372-406; doi:10.3390/e15010372

Stephanie Seneff, Ann Lauritzen, Robert Davidson and Laurie Lentz-Marino, "Is Endothelial Nitric Oxide Synthase a Moonlighting Protein Whose Day Job is Cholesterol Sulfate Synthesis? Implications for Cholesterol Transport, Diabetes and Cardiovascular Disease." Entropy 2012, 14, 2492-2530; doi:10.3390/e14122492

Stephanie Seneff, Robert M. Davidson and Jingjing Liu, "Is Cholesterol Sulfate Deficiency a Common Factor in Preeclampsia, Autism, and Pernicious Anemia?" Entropy 2012, 14, 2265-2290; doi:10.3390/e14112265

Samantha Hartzell and Stephanie Seneff, "Impaired Sulfate Metabolism and Epigenetics: Is There a Link in Autism?" Entropy 2012, 14, 1953-1977; doi:10.3390/e14101953

Stephanie Seneff, Robert M. Davidson, and Jingjing Liu, "Empirical Data Confirm Autism Symptoms Related to Aluminum and Acetaminophen Exposure," Entropy 2012, 14, 2227-2253; doi:10.3390/e14112227

Robert M. Davidson, and Stephanie Seneff, "The Initial Common Pathway of Inflammation, Disease, and Sudden Death," Entropy 2012, 14, 1399-1442; doi:10.3390/e14081399

Stephanie Seneff, Glyn Wainwright, and Luca Mascitelli, "Nutrition and Alzheimer's Disease: The Detrimental Role of a High Carbohydrate Diet," European Journal of Internal Medicine 22 (2011) 134-140; doi:10.1016/j.ejim.2010.12.017

Stephanie Seneff, Glyn Wainwright, and Luca Mascitelli, "Is the Metabolic Syndrome Caused by a High Fructose, and Relatively Low Fat, Low Cholesterol Diet?" Archives of Medical Science, 2011; 7, 1: 8-20; doi:10.5114/aoms.2011.20598

Stephanie Seneff, Robert Davidson, and Luca Mascitelli, "Might cholesterol sulfate deficiency contribute to the development of autistic spectrum disorder?" Medical Hypotheses, 8, 213-217, 2012.

Hidden Viral Gene Revealed in GMOs

Claims that GM technology is 'predictable and safe' has been shaken by the discovery of viral gene sequences in many GM crops according GM Freeze.

Two thirds of GM crops approved in the US contain the hitherto unidentified viral gene, but although regulators have insufficient information to determine if it is safe for human consumption EFSA has opted for a retrospective review rather than a ban.

The existence of the Gene VI viral gene was revealed in a study authored by EFSA staff and published in the journal GM Crops and Food. The gene is in many widely-grown GM crops, including Monsanto's RR MON810 soya, NK603 maize and other crops imported to the EU for food and animal feed. Recently, co-founder of the anti-GM movement Mark Lynas said GM technology could in fact deliver safe food with less impact on the planets' resources at a recent lecture.

"*I realised genetic engineering technology could be a powerful tool to address planetary boundaries, such as issues with the nitrogen cycle,*" said Lynas.

He said food production was limited by nitrogent availability, '*but we had overcome this by synthesising around 120bn tonnes of atmospheric nitrogen a year into fertilisers'*.

"*This is a good thing because it keeps more than half of humanity alive, but it has doubled the nitrogen cycle on land.*"

"*Environmental impacts include eutrophication and the release of nitrous oxide, a powerful greenhouse gas, into the atmosphere. Not using GM technology is risky in itself. It is regulated out of existence in most of Africa. It is effectively illegal to use this technology in any environmentally beneficial way in most of the world except in very specific applications.*"

Researchers found Gene VI in 54 of the 86 GM crops currently approved in the US. It is linked to the Cauliflower Mosaic Virus promoter gene used in many of the GM traits already in crop plants, but the gene may affect other aspects of the genetic performance of the plant with unknown, unintended consequences. Scientists are concerned the gene could disturb the normal functions of crop plants, and while there is insufficient data available to determine what impacts this might have, researchers have already identified three potential mechanisms for plant function to be disrupted:

• The gene sequence could make plants more susceptible to some pathogens and less to others. This could have a serious impact on crop health.

• Interference with messenger RNA, which relay information from the plant's DNA to the structures that build proteins. This means the sequence could induce plants to produce novel proteins with unknown impacts on plant, human or animal health.

• Gene silencing, which could lead to genes that are normally turned on being turned off, which could in turn interfere with plant's defences.
Gene VI was tested against known toxins and allergens, but such evaluation will miss novel proteins and/or toxins being produced by the gene in plants. It is impossible to determine if these are present or harmful without further study.

Commenting Pete Riley of GM Freeze said: "*This discovery of this previously unidentified gene in GM crops raises serious concern about the safety of GM food and feed. It totally undermines claims that GM technology is safe, precise and predictable.*"

"*The very existence of Gene VI has been missed for many years, so we don't know what implications it might have*."

"*It is impossible to say if this has already resulted in harm to human or animal health, and since there is still no GM labelling in places like the US where GM is more common the diet, no epidemiological studies can be carried out.*"

"*Possible harmful effects of GMOs could easily be lost in the general morass of ailments which vets and medics have to deal with on a daily basis, especially if these were as result of low level exposure over several years, and the link to GM could take many years to establish that way*."

"*This is a clear warning the GM is not sufficiently understood to be considered safe. EFSA cannot continue to take risks with public health. Authorisation for these crops must be suspended immediately, and they should be withdrawn from sale, until a full and extended review of their safety has been carried out.*"

PARTING SHOTS


Liquid concentrate
ROUNDUP
WEEDKILLER
KILLS WEEDS to ROOTS
Fully degrades in soil


Bayer Garden
Glyphosate
Concentrate
Kills weeds & roots
1L


Bayer Garden
Super Strength
Glyphosate
kills weeds & roots

SMOKING
IS HEALTHIER THAN
FASCISM