GENETICALLY MODIFIED FOOD AND ITS IMPACT ON ANIMAL HEALTH
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Disclosure
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Objectives
To introduce the veterinary health professional to the evidence that clearly demonstrates that genetically-modified foods pose a potential health threat to veterinary patients and clients.

INTRODUCTION
GM foods or organisms are plants or animals that have, through technological manipulation, had the DNA of one species inserted into the DNA of another species for the purpose of creating a specific effect in the genetically-modified individual.

Starting in the mid-1970’s scientists were able perform these insertions, with the intention of creating crops that 1) could withstand higher applications of an herbicide called glyphosate (Roundup™), and 2) that endogenously created their own pesticides. The stated purpose of these genetic modifications was to increase crop yields, and better provide food for the population of the earth.

Genetically modified organisms were presented to the public that they offered the promise of feeding the world, cleaning up the environment, reducing manufacturing waste, and turning fields into factories that would produce anything from life-saving drugs to insect-resistant plants.

Other GM organisms were created for some rather bizarre effects. For instance: Spider genes were inserted into goat DNA in an attempt for the milk to contain spider web protein to be used in bullet-proof vests; cow DNA was inserted into pig DNA with the intention of having the pigs create cow skin; Jellyfish DNA caused pig noses to have bioluminescence, or glow in the dark; arctic fish genes gave tomatoes and strawberries frost tolerance; potatoes would glow in the dark when thirsty; human genes were inserted into corn to manufacture spermicide; pharmaceutical companies inserted DNA into bacteria, making them living factories to produce drugs; seed companies gave new traits to planted crops.

Genetic engineering takes artificial combinations of genes that have never existed together in nature, forcibly inserts them into random locations in the host genome and then clones the results. (1) This is a process that is clearly different than natural breeding.

Fares et al (1998) in their study of structural changes to the ilium of mice fed transgenic potatoes summarize the main problem with GM crops:
“Traditional breeding methods have been based on natural reproductive processes and involve selection at the level of the organism, the precise orchestration of thousands of genes, relatively infrequent mutations, and products that have been selected for safe use over thousands of years. By contrast, GE crop technology abrogates natural reproductive processes, selection occurs at the single cell level, the procedure is highly mutagenic, and frequently breeches genera barriers, and the technique has only been used commercially for 10 years. Furthermore, normal breeding never introduces a cassette of bacterial genes for drug resistance along with strong…promoters to express foreign proteins at high levels in all parts of the plant.” (2)

How are GM organisms manufactured?
To create a GM organism, scientists first identify the gene and analyze its sequence. Bacterial DNA is slightly different than plant DNA, so the sequence needs some alteration when coming from bacterial sources. To the end of the gene in question, a “promoter sequence” is added, which turns on the gene. GM crops most commonly use a promoter called CaMV 35S which will force the gene to continually produce a high volume of protein. To the opposite end of the gene, engineers insert a “terminator sequence”. This sequence of DNA code tells the DNA that the “transgene ends here—stop reading”. A “marker gene” is also added at this step, which usually is a gene that codes for antibiotic resistance.

This sequence of promoter/transgene/terminator/marker DNA is termed the “Gene Cassette”, which goes on to be replicated by the millions after it is placed into a bacterial plasmid, which is a circular loop of DNA, which can reproduce multiple times in bacteria. In the early days of genetic engineering, the entire plasmid DNA was inserted into the target plant’s DNA while these cells were being grown in in vitro in tissue culture. Most recently, technological advancements have allowed the genetic engineers to remove the extraneous plasmid DNA and insert only the gene cassette into the plant DNA.
Once the gene cassette is inserted into the plant cells, which are grown in tissue culture, the plant cell undergoes multiple mutations, which are unpredictable, and uncontrollable. The actual insertion of the DNA is performed according to two different techniques.

The first technique involves a bacterium (Agrobacterium tumefaciens) that under normal conditions infects a plant by inserting a specific portion of its own DNA into the plant DNA. This DNA, when functioning normally in the plant DNA, causes the plant to grow tumors. The genetic engineers replace the tumor-creating portion of the bacterial DNA with one or more of the gene cassettes, thus allowing this bacterium to infect the plant DNA with these foreign “transgenes”.

A second technique of inserting the gene cassette into the plant cell genome is called the “gene gun” or “particle insertion” method. Miniscule particles of tungsten or gold are coated with gene cassettes and then “shot” into millions of plant cells in tissue culture. Only a few plant cells, out of the many millions that have been “shot” with the gene cassette coated particles of tungsten or gold will have the gene cassettes incorporate the foreign transgenes.

The few plant cells in tissue culture that incorporate the gene cassettes, whether inserted via the bacterial DNA or the gene gun, are detected as a result of the marker DNA that is part of the gene cassette. By applying the specific antibiotic for which resistance has been coded in the gene cassette to the plant tissue culture, cells that do not contain the gene will die, leaving only the plant cells that have survived the gene splicing. These surviving cells are then grown on a different tissue culture that allows for their maturation into entire plants. The transgenic plant is then propagated via their seeds or by making more clones through tissue culture.

Each plant grown from separate gene insertions is unique. The location of the transgene in the host DNA, and the consequences of that insertion are different with each insertion. All the plants grown from a single insertion are termed an “event”, which means that the integration of the transgene cassette is not reproducible or repeatable.

**Benefits of GM foods**

GM crops have been touted as being able to deliver on the promise of greater harvests, and subsequently, feed more people. Statistics do not confirm this fact. GM crops have been modified to make them resistant to the herbicide glyphosate (Roundup™) or to produce a pesticide endogenously, Bt, or to be more resistant to drought. By inserting the gene cassette into the plant cell genome is called the “gene gun” or “particle insertion” method. Miniscule particles of tungsten or gold are coated with gene cassettes and then “shot” into millions of plant cells in tissue culture. Only a few plant cells, out of the many millions that have been “shot” with the gene cassette coated particles of tungsten or gold will have the gene cassettes incorporate the foreign transgenes.

In a 2004 report presented at the Midwest Soybean Conference it was reported that soybean yields from 1995 -2003 had “flattened”, and the report goes on to incriminate GM soybean as the problem. Additionally aphids had never been a problem on soybeans prior to the introduction of GM soy, but following the GM seed introduction in 1995, aphids had become a problem, which also affected plant yields. (3)

Industry, university and state sponsored surveys summarized by Benbrook (4) and Martinez-Ghersa (5) showed that Roundup Ready (RR) soybean yields averaged 5%-10% less than conventional soybeans in the period from 1995-2000.

There are similar reports regarding lower yields from GM canola and cotton. In a study published in 2005 of 87 villages in India over a period of 3 years, it was found that non-GM cotton yielded about 10% more than the Bt variety. Some farmers complained that they were not able to grow other crops after Bt because it had altered their soil. The overall average return over 3 years to these farmers was 60% less, and 71% of farmers who used Bt cotton ended up with financial losses. (6) Many of these cotton farmers (>100,000) in India who suffered complete financial loss associated with the failure of their GM cotton crops committed suicide as a result of their sudden and unexpected losses.

The currently available evidence does not support the contention that GM crops will increase yields and thereby better feed the world’s population. Other studies, not quoted here have produced data supporting the fact that sustainable agriculture holds a much greater potential to increase crop yields. Furthermore, it has been reported that the world does not currently suffer from a food production problem anyway. There is reported to be enough food in the world to provide 3500 kcal daily to every person on the planet. The real issue is of distribution, and cost of the food materials. In fact, 78% of all malnourished children under five in the developing world live in countries with food surpluses. (7) (8)

**Documented and Identified Health Risks Associated with eating GM foods**

1. **Roundup-Glyphosate Problems**
Glyphosate, the patented active ingredient in Roundup manufactured by Monsanto, is an herbicide that has long term soil persistence and can cause nutrient deficiencies in food crops to which it is applied. Even sub-herbicidal doses can create these same problems.

Glyphosate’s mechanism of action is to chelate cations such as calcium, magnesium, iron, manganese, zinc, copper and cobalt. As a result it will reduce the mineral and amino acid content of the crops it is applied to. It takes twice the amount of water to grow the same amount of crops when glyphosate is applied. On necropsy of food animals fed crops where glyphosate has been used they find lesions consistent with a manganese deficiency. It also reduces the healthy microbial content of the soils it is applied to.

When glyphosate is applied late in a crop’s cycle, it will accumulate in the fruit and seed. For this reason, the brewing industry avoids glyphosate crops because it can kill the yeast necessary for brewing. The seed that has accumulated glyphosate cannot be used because it will create abnormal growth. Potatoes grown on glyphosate have significantly reduced harvest size. Crop rotation will exacerbate this effect.

As a result of glyphosate application, in crops that are genetically modified to be more resistant to its herbicidal effects, an increase of as much as 50% in allergies to soy have been documented. Increases in mycotoxins such as aflatoxins are also seen in crops grown on glyphosate. It also has an adverse effect on the endocrine system resulting in infertility. One positive result of this is a 30% drop in teen pregnancies. It affects the fertility of both males and females.

As a result of the widespread application of glyphosate, it is the most common pollutant found in our air, water and food. A recent report from Germany found 5-20 times the allowable amount of glyphosate in the urine than allowed in the drinking water. It has become ubiquitous. There even are reports of a new pathogen emerging that is prion-like that is associated with the use and over-use of glyphosate. Some weeds are becoming more resistant through natural mutations to glyphosate, necessitating the application of increased amounts of glyphosate. The use of glyphosate has been linked to an increase in birth defects (increased by 70% since 1996), celiac disease and a number of other chronic diseases such as IBD in humans, allergies and cancer. In low doses, glyphosate has also been shown to be an endocrine disruptor (14). Neurologic and behavioral pathology in both the human and animal species exposed to glyphosate has also been documented. (9)

2. Genetic Material from the GMO can be transferred to the animal or human eating the GM food

Bacterial toxin (Bt)

Bacillus thuringiensis is a soil bacterium that produces a toxin that is used commercially as a pesticide, applied topically to crops. Solutions that contain the bacteria are sprayed on plants as a means of insect control, commonly used by organic farmers. The sequence of genes that produce the toxin from this bacterium, termed, Bt-toxin, were modified and inserted into plant DNA. Unfortunately, Bt-toxin when used topically is not always safe. There are reports of reactions from humans to the spray that are allergic or flu-like in nature. Eye, nose, throat and respiratory irritation have been noted. Allergic symptoms range from sneezing, runny nose, watery eyes, dermatitis, pruritis, swelling, erythema, conjunctivitis, asthma exacerbations, angioedema. (10)

Bt-toxin spray elicits an immune response as potent as cholera toxin, causing the immune system to become overly sensitive to other compounds, and as a result eliciting both systemic and mucosal immunologic responses. (11)

Bt-toxin produced by GM crops is made in every cell of the plant on a continuous basis, not just applied only during high insect infestation emergencies. Sprayed Bt-toxin dissipates within a few days, and can be washed from the leaves by rainfall or watering. Plants produce 3000-5000 times the amount of the toxin as the spray. Bt-toxin is exempted from regulatory limits as far as how much can be expressed in GM food. These higher levels of Bt-toxin are by design, in order to reduce the potential for Bt-toxin resistant pests. (12)

The evidence is supportive of the assertion that Bt-toxin genes can be incorporated by gut bacteria, thus producing this toxin in both human and animal gastrointestinal tracts. This is may be one mechanism whereby increased intestinal permeability can occur. With increased intestinal permeability, or Leaky Gut, substances get into the systemic circulation inappropriately, leading to systemic effects and chronic disease issues. A similar mechanism may occur with the transmission of the gene for antibiotic resistance, a marker that is commonly used in GM organisms. Bt-toxin has also been found in the blood of pregnant and non-pregnant women and their babies. (13)

Increased production of allergenic foreign proteins by GM organisms
Genes inserted into crops can carry with them allergenic properties. This was first reported in the New England Journal of Medicine in 1996 following the insertion of a gene from the Brazil nut into soy DNA so as to increase production of the amino acid that is typically low in soy and other legumes, methionine. (15)

A 1999 study in UK tested 4500 people for allergic reactions and sensitivities to a wide range of foods. Their findings showed that allergies to soy had increased markedly from 10% to 15%. Prior to this time, soy had not been placed in the top ten most allergenic food substances for the prior 17 years of these studies. Symptoms in this human population included acne, eczema, irritable bowel syndrome, other digestive problems, chronic fatigue, headaches and lethargy. GM soy had been introduced to the UK several years prior to this study.

Another study found a different immunological reaction to non-GMO soy versus GMO soy protein, indicating that there are different proteins in GMO soy, causing reactions to the GMO soy protein in some individuals who did not have reactions to the non-GMO soy. (16)

**GMO Facts and Statistics**

**GM Crops (figured quoted, when available, as of 2013)**
- Alfalfa
- Corn (85%)
- Sugar Beets (95%)
- Crook neck squash (small amount)
- Zucchini (virus resistant) (13%)
- Hawaiian papaya (80%)
- Soybean (91%)
- Canola (75%)
- Tobacco
- Cotton (88%)
- Non-browning Arctic Apple
- Tomatoes
- Milk (rGBH) (20%)
- Plum
- Wheat
- Rice
- Cantaloupe
- Flax
- Potato
- Radicchio

**GM Foods and Animal Health**

**Effect on Embryonic development**
Antoniou in his review article (17) on the teratogenic effects of glyphosate and the lack of appropriate regulatory decisions cites a number of studies in experimental animals such as the frog, chicken, rat, rabbit and mouse in which multiple teratogenic effects were found. Antoniou notes that many of these defects are due to disruption of the retinoic acid signalling pathway, as glyphosate is an endocrine disrupter. These side-effects from the application of glyphosate in high dosages to GMO crops that are genetically modified to have less toxicity to the herbicide Roundup™ (glyphosate) are listed here:

1. Malformation of embryo
2. Microcephaly
3. Microphthalmia
4. Cyclopia
5. Embryonic deaths
6. Increased skeletal, visceral and cardiac malformations
7. Increased death of mothers
8. Unossified sternebrae
9. Early fetal resorption and deaths

**Histopathological and Organ changes in studies of animals fed GM foods**
1. Young rats fed GM potatoes with Bt toxin genetically encoded, developed proliferation of the gastric mucosa and jejunal hyperplasia resulting in crypt lengthening accompanied by increased epithelial T lymphocyte infiltration into the mucosal wall. (21)

2. Rats fed GM corn for 90 days were observed to develop significant adverse impact on their liver and kidneys. (19)

3. Rats fed GM corn for 2 years. All treated groups had 2-3 times more mortality than controls, and more rapidly. All results were gender dependent. 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 congestion and necrosis were 2.5-5.5 times higher. Marked and severe kidney nephropathies were also generally 1.3-2.3 times greater. Males presented 4 times more often with 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 genders. 76% of the altered parameters were kidney related. The authors conclude: “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.” (20)

4. Rats fed GM soy had differences in plasma amylase levels and a transient depletion of zymogen stores in the pancreas with increase in pancreatic acinar cell disorganization, similar to what is seen with pancreatitis. (18)

5. Mice, in another study where the mothers were also fed GM food, found that the pancreatic acinar cells had increases in the number of fibrillar centers (FC) in the GM fed mice but the FC were smaller than normal. FC are found in the nucleolus. (18)

6. Hepatocytes from GM-fed mice had irregular shaped nucleoli and their nucleoli were also irregular and less compact. Differences in FC were also observed. In this same study, the groups of GM fed mice with irregular shaped nuclei and nucleoli were then fed non-GM food, the changes that were seen in the GM fed group diminished, indicating a possible reversibility for some of the observed effects of feeding GM foods. They also fed the control group that had not previously received GM foods, and were adults, GM foods, and then were able to observe the changes occur rapidly in the nuclei and nucleoli of their hepatocytes.

7. Male mice fed GM soy or conventional soy had observable differences in Sertoli cells of the seminiferous tubule, spermatogonia and spermatocytes. Sertoli cells had enlarged vesicles of the smooth endoplasmic reticulum in the GM-fed group. (18)

8. Rats fed on a GM potato diet that produces a pesticide, or conventional potatoes, found thicker mucosal linings of the stomachs on those fed GM-feed. Crypt lengths of the jejunum were greater in rats on GM potato, and not on conventional potato supplemented with the lectin pesticide) (18)

9. Rats were fed GM corn, and found to have GM—feed-specific physiological changes in the liver, kidney, pancreas and bone marrow, some of which were sex specific. Liver alkaline phosphatase and ALT and AST activities differed by 8-23% in GM and non-GM fed groups. (18)

10. Sheep fed GM hay developed significantly different levels of proliferation of ruminal epithelium basal cells in ewes fed GM corn. Hepatocytes and pancreatic acinar cells revealed smaller irregularly shaped cell nuclei with increased amounts of heterochromatin and perichromatin granules. (18)

11. Rabbits fed GM soy or conventional soy had significantly higher levels of LDH, ALT and GGT in kidneys than animals on the conventional diet. LDH was also significantly elevated in heart muscle. (18)

12. Chickens fed Liberty Link corn, engineered to resist the herbicide glufosinate, had twice the mortality rate as those chickens fed non-GMO corn. In this study, 140 chickens were divided up into 4 pens of 35 chickens each and allowed to consume as much GMO corn as they could. An equal number of chickens also divided into four other pens were fed a commercial corn diet. Ten chickens from the GM group (7.14%) and 5 from the non-GM group (3.57%) died. The industry average for deaths is 4%. The GM-fed group also gained less weight and had far greater body weight variability. Their feed intake was also erratic. (28)

**SUMMARY of FINDINGS:**
1. Nephropathies
2. Hepatopathies
3. Neoplasia
4. Changes in the mucosal wall of the stomach and small intestine
5. Pancreatic changes
6. Birth defects and stunted growth
7. Reduced fertility and alteration in testicle size

Reports of GM feeds affecting livestock (News events, not in controlled studies)

- Cattle herd in Texas 15 out of 18 head died eating Tifton 85 GM Bermuda grass June 2012, near Austin, TX. Had been eating the grass for 15 years with no problems. Necropsy results indicate the grass began producing cyanide gas which likely killed the cattle. (KEYE-TV (Austin, Texas) http://www.weareaustrin.com/news/top-stories/stories/vid 2393.shtml)
- 71 shepherds report that 25% of their sheep died from grazing on Bt cotton plants. Among 29 herds consisting of 2,168 sheep total, 549 (25%) died. Farmers estimate the total number of sheep deaths in this area of India was around 10,000. Similar reports came from neighboring communities. The sheep developed cough and nasal discharge, reddish erosive oral lesions, bloat, blackish diarrhea, and occasional hematuria. Death occurred in 4-7 days usually in the younger adults and lambs. Post-mortem pathology found black patches in the intestine and enlarged bile duct and black patches on the liver. (22) (23) (24)
- 100 Filipinos in a village adjacent to a field of Bt corn, fell sick when the corn was pollinating. Symptoms included headaches, dizziness, extreme stomach pain, vomiting, chest pains, fever and allergies, as well as respiratory, intestinal and skin reactions. (25)
- In the UK soon after GM soy was introduced with skin hypersensitivity testing positive in a patient for GM soy. (1)
- Swine fertility dropped from 80% to 20%. Most animals had false pregnancies. This was in Iowa in 2001. The swine producer is an animal nutrition consultant and his veterinarian did extensive testing and ruled out common causes of infertility. Numbers of other swine producers in Iowa complained of the same thing. He had started feeding GM corn in 1997. Analysis of the corn found possible endocrine disrupters in it that effect fertility. (26)
- A farmer in Germany’s cattle began getting ill after he started feeding only GM feed from the year 2000 on. The GM corn was designed to produce the Bt toxin. 5 cows died in 2001 and another 7 died in 2002. Milk production was also decreased in some cows, and some cows were slaughtered due to an unidentified illness. Common errors in feeding and infectious causes had been ruled out as the cause of death. Inadequate testing was performed on the dead cattle or corn to definitively assign a cause to these deaths. The company, Syngenta that manufactured the corn compensated the farmer but did not claim responsibility for the deaths. (27)

Potential Problems of Feeding GM Foods in Companion Animals

Most people feed their pets commercially processed dry food, which contains high percentages of corn and soy, two grains that have been genetically modified the most. Pet foods also contain meat, which most probably has been derived from livestock fed from GM crops. From the information presented earlier in this paper, even meats that are fed GM foods can pass on GM DNA. GM foods tend to be higher in glyphosate or glufosinate, two herbicides that have been shown to have potential for creating a number of problems in the species that consume them, including infertility, kidney and liver problems and even cancer.

GM foods have the potential to create or maintain certain problems in companion animals. It has been determined that the DNA from GM crops can become part of the animals’ DNA that consumes it. This is a principle called epigenetics, and although it does not follow the accepted means of transfer of genetic material from one individual to another, it has been proven to be a means whereby the foreign DNA of a plant (GMO) can incorporate itself into the DNA of an different Kingdom. It has also been proven that the proteins and the allergens that are created in GM plants, and in animals that consume them can be different than the proteins and allergens that they would normally produce. This means that pets with a tendency for food allergies or intolerances may become sensitive to GM plants and meats from animals fed GM crops, even for foods that historically that animal was not sensitive to.

For animals of breeding age, if they are intended for breeding, then the potential for feeding GM foods and the increased glyphosate or glufosinate residues found in GM foods, and in non-organic crops may cause difficulties in conception and pregnancy, and have the potential to cause birth defects. Certainly animals with impaired liver and kidney function should also steer clear of GM foods, of meats from animals fed GM foods, and should, in general be fed organic foods to avoid pesticide and herbicide residues which could exacerbate existing renal or hepatic insufficiencies in the veterinary patient.
Recently, there has been an “explosion” in the pet food market for diets that are “grain free”. Most veterinary dermatologists and nutritionists can’t adequately explain why so many pet owners are finding benefit in feeding their pets these grain-free diets, when these pets are not testing positive for allergies to these foods, and don’t have gluten enteropathies or celiac disease. It is possible the answer lies in the amount of herbicide residues and the different proteins that are being created by the genetically engineered DNA of the GM crops.

For the veterinarian, when presented with a complicated chronic disease such as allergies that doesn’t have a clear cut etiology, it makes sense to try and eliminate all GM foods and non-organic foods from the patient’s diet. This usually means a home prepared meal, being the only way to absolutely be sure all of the ingredients in the diet are non-GMO and are organic. It may not be as important what the actual food ingredients are, as long as they are non-GMO. In today’s world, it is increasingly becoming more difficult to find non-GM corn or soy, since over 90% of each of these are GM crops. This is one good reason why it is important to have laws that insist on the correct labeling of foods as being non-GMO and organic.

**What to Do?**

It's difficult to stop the practice of planting and harvesting GM crops. The practice is ubiquitous, and many farmers are locked into contracts with Monsanto for glyphosate and seed. Seed is patented which doesn't allow farmers to use other seeds. The best approach is public awareness. This author wasn't aware of the problems with GM foods until attending seminars, reading articles, discussing the matter with individuals more knowledgeable on the subject.

- Awareness, share this information with friends and colleagues and clients.
- Legislate labeling of foods containing GM ingredients to allow consumer to make choices
- Communicate with the pet food industry about the importance of providing GM-free foods and labeling those diets as “GMO-free”.
- They are already going grain-free/gluten-free/organic -- why not?
- Home-prepared diets especially for those patients with chronic disease complaints

**REFERENCES**

24. Ramanjaneyulu and Ramdas (ANTHRA), letter to Shri Bir Singh Parsheera, India, July 28, 2006