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Full Length Research Paper

Pathology reports on the first cows fed with Bt176 maize (1997–2002)

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Accepted

On an independent modern farm followed by certified veterinarians, dairy cows (mean of 62 per year) were maintained in optimized milk production for 3 years each. From 1997 to 2002, just after the commercial release of the first GMO (genetically modified organism) in Europe, genetically modified (GM) Bt176 maize grown on the farm was progressively introduced in controlled diets. The results are described in the following account, which has an historical value as it is the longest and first on-farm observation of mammals, performed by an experienced farmer and veterinarians, during a period of unusual pathological problems in cows receiving a GMO-rich diet. Thus it was not designed as a scientific experiment. Over the years, and coinciding with regular increases in GMO content of the diet (0–40%), the proportion of healthy cows with high milk yield diminished from 70% (normal rate) to only 40%. At the peak of mortalities in 2002, 10% of the cows died, preceded by a long-lasting paresis syndrome without hypocalcemia or fever, but with kidney biochemical failure and mucosa or epithelial problems. No microbial origin was identified, though intensively investigated. The GM maize, subsequently withdrawn from the market, was at the time the only intended managerial change for the cows. It is proposed that it provoked long-term toxic effects on mammals, which are not observable in most common conditions of intensive farming with high and rapid animal turnover and with no specific labels on GM feed (identifying amount and precise identity of GMO content). More long-term assessments during GMO feeding trials should be performed.

Key words: GMO; pesticides; dairy farm; toxicity; Bt176 maize.

INTRODUCTION

This study was not designed as a scientific experiment. It is a detailed observation of a conventionally managed technologically advanced dairy farm, with access to detailed raw data, which were collected because of unusual pathological problems. These observations were made during the progressive introduction (1997–2002) of the first genetically modified (GM) maize Bt176 into the European market and into animals' feeding rations. Thus this is the first and longest formal observation of the feeding of cows with an agricultural GMO. It is unusually detailed due to the research by the experienced and qualified farmer into the origin of the pathologies observed, because the GMOs were not believed to be responsible at first. This case was rapidly reported by the German press at the time, and in books, but was not scientifically documented and based on access to the raw data. This is the first scientific explanation of these observations. Other cultivations of GMOs were performed previously on the same farm, without the feeding of animals, because that was not the goal at the time. It is

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Abbreviations: BSE: bovine spongiform encephalopathy; **Bt:** Bacillus thuringiensis – its mutated insecticidal toxin gene is inserted in the modified maize. **GM**: genetically modified; **GMO**: genetically modified organism.

also one of the conventional farms where the feed was produced on site. There were also numerous analyses in blood, urine, feed, and milk. The Bt maize was grown and used raw to make silage on the farm.

To date there is an ongoing debate on the need for long-term toxicity studies with GM plants (Séralini et al., 2011, 2013, 2014). However, in considerably shorter-term studies, no side effects of Bt maize on dairy cows were published (Aulrich et al., 2001; Barrière et al. 2001; Donkin et al., 2003; Faust et al., 2007; Folmer et al., 2002; Steinke et al., 2010). The second-longest exposure after the present study (Steinke et al., 2010) was 2 years long (compared with 3 years per cow in the present report), but that study did not test the same Bt maize; it tested a different genetic construct and insertion. No study has been performed with Bt176 that is longer than the one described below.

Bt176 GM maize was never grown on a wide scale. It was replaced by Bt11 and MON810, because of governmental restrictions (from 2000 in Germany) or national moratoria (like in France). After little use, it was definitively and officially withdrawn from the European market in 2007. It was genetically engineered to produce a specifically mutated and truncated active insecticidal Bt toxin from the natural Cry1Ab gene (Mesnage et al., 2013). In *in vitro* experiments, this and comparable Bt toxins have been found to affect human cells, both alone and in combination with herbicide residues (Mesnage et al., 2013).

The following observations were performed because of severe pathologies and deaths in the animals fed Bt176 GM maize. Several investigations were made by official laboratories and are summarized below. We wanted here to investigate, at a scientific level for the first time, all the compiled raw data that were released as a result of a court case, which will be described elsewhere (Séralini, 2016).

MATERIALS AND METHODS

Plants and feed composition

The GM Bt176 (Pactol Cb GM variety) maize seeds, as well as the seeds for the conventional counterpart (Pactol), were bought from Novartis Seeds, Saint-Sauveur, France. They were grown in Weidenhof, Wölfersheim, Hessen, Germany each year from 1997–2001. The feed harvested each year was ensiled and used until the next year. Maize silage was fed to dairy cows on the same farm. The feed composition was conventionally analyzed for glucides, proteins, fibers, ash, and minerals by RWZ, Colonia, Germany, and in April 2002 also by Lufa-ITL, the institute for animal health and food quality in Kiel, Germany. Both analyses included pathogens and mycotoxins. Amino acids were measured in grains by Supramol, Rosbach-Rodheim, Germany.

The Cry1Ab was independently measured by ELISA in GM maize silage (official test material and sampling) in July 2002 by the State Education and Research Institute for Agriculture (SLFA), Biotechnological Crop Protection Section. The feed was composed of an average of 40% maize silage, 24.5% grass silage, 15.5% malt draff, 7.8% barley, 7.8% wheat, 4% soy, and 0.4% minerals. The diet thus contained around 40% maize silage (conventional variety Pactol), cultivated on the same land only for these animals. As soon as the GM Bt maize was commercially available in 1997, it progressively replaced each year the conventional counterpart: 5% of 10 ha in 1997, then 10% in 1998, 50% in 1999, and 100% of the maize surface area in 2000. At this time the 40% of maize in the diet consisted entirely of GM Bt176 maize.

Animals and feeding

The dairy cows were registered in the herd record books as Holstein Friesian, Schwarzbunt variety. Dates of birth, names, numbers, milk production, identification details, genealogy, breeding values, body mass indexes, number and births, sexes of calves, complete pedigree, were all recorded in these books. Around 62 cows per year were regularly followed by several certified veterinarians. The healthy cows had no problems with fertility, legs, milk yield, or udder infections. The general physiology and metabolism were good. The cows were replaced every 3 years or after disease with new animals in order to maintain high yield in milk production, as is usual in dairy herd management. Up to 2002 the animals were thus fed amounts of Bt maize increasing from 2–40% in the total feed (Figure 1).

Microbial and biochemical analyses in mammals

All analyses were ordered by certified veterinarians at the request of the farmer over the years, and were performed in accredited laboratories, or at sites indicated by the German government, after its inclusion in the research on the origin of pathologies, as well as Syngenta. Syngenta was informed by the farmer in August 2001 that investigations had been opened, and again officially in February 2002, when the hypothesis of the involvement of the GMOs in the pathologies became clear. The following analyses were specifically being investigated.

The usual analyses of milk and blood compositions were performed regularly in the herd, each year in representative samples chosen by the veterinarian (11–20 animals). More detailed analyses were performed in disabled cows or after their death in the veterinary laboratory. In blood, different parameters were tested and measured by routine and classical methods in representative samples of healthy cows, namely: bovine

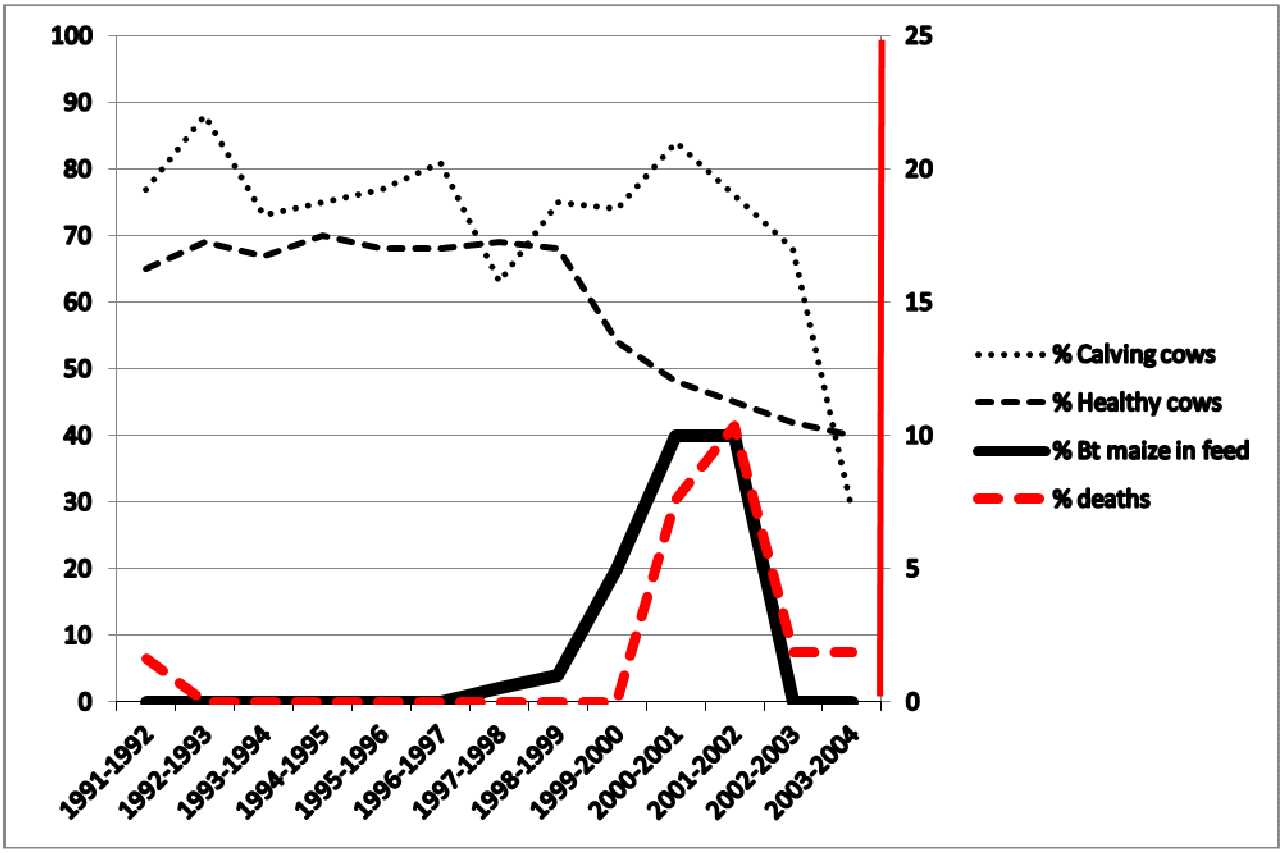

Figure 1. Percentage on the farm of calving cows, healthy cows, Bt maize in feed (left axis) and on the right axis percentage of deaths.

herpes virus 1, viral antigens and antibodies of bovine viral diarrhea and mucosal disease; bacteria coxiella burnetii, chlamydia, leptospira antigen and antibodies, listeria; and parasites in feces, all by the University Justus-Liebig in Giessen (Germany), Institute for Veterinary Pathology. Bacterial analyses of the uterus, stomach, and milk were carried out; and blood cells were counted. In animals that had died, clostridium botulinum was searched for in feed, blood and various organs (liver, stomach, kidney, and intestine) by the University Georg-August in Göttingen, Germany. Assays for bacteria in the stomach were performed at the Technical University of Munich, Germany. BSE was systematically tested for by the State Veterinary of Hessen, Germany. At a biochemical level, in blood and/or urine, different parameters were assayed: urea, triglycerides, cholesterol, ketone, glucose, glutamate dehydrogenase, aspartate aminotransferase, bilirubin, and minerals (Na, K, Ca, Mg, and P); these assays were also performed using standard methods at the veterinary laboratory of the University of Justus-Liebig in Giessen, Germany.

The quality and composition of the milk was constantly monitored (fat, proteins, lactose, bacteria, cells), at HVL in Alsfeld, Hessen, Germany by classical methods. In addition, in 2000, a 211 bp specific fragment of the Bt176 DNA and a 509 bp plus a 180 bp specific fragments of the EPSPS gene (present in GM Roundup tolerant soya) were assessed by PCR in whole milk from the farm, twice, once in October and once in December. This was performed using the Dr R. Einspanier method (PCR template preparation kit for DNA extractions from Roche) at the Institute of Physiology, Weihenstephan Research Centre for Milk and Food, Technical University of Munich.

Farming experience

The equilibrated diet was given to dairy cows, rising from 45 cows in 1989 up to 70 in 1999, on a modern biotechnological conventional farm rebuilt in 1986. During the observation of unusual pathologies, the GM toxicity hypothesis was not investigated at first since the reputation of GMOs on the farm was good. GMOs were positively tried by the farmer cooperating with industry, at a cultivation level, but never at a feeding level before this observation, because this was not officially authorized yet. Before the introduction of GMOs, one cow from the farm in 1997 was given an award by the German Holstein Friesian Herd Book Organization for high milk production

(114 tons) over the course of its life, in which it gave birth to 14 calves. The farm itself received the German Food Society award in Frankfurt for 10 years' worth of high yield and good quality milk production from 1991 to 2000.

The technologically advanced farm was managed by an independent and qualified farmer, trained at the Agricultural School in Friedberg, Germany as a state-certified agronomist (1982) and Master of agriculture (1986). Thus he was licensed to train apprentices (7 in total). The highest standards of hygiene and animal husbandry were followed in modern stall barns. The herringbone stalls for milking were for 2 x 4 animals simultaneously. In general, animals had free access to grassland.

The farmer was working with biotech companies and was one of the first farmers to perform small-scale trials (1995-1997) of glufosinate-tolerant GM maize LL (Liberty Link). However, this trialled maize was not used for feed or food and was not grown on the future Bt176 maize land.

RESULTS AND DISCUSSION

All data were documented in the herd record books. Few cows have been fed over a long-term period with this GMO event (which has now been withdrawn from the market) and subsequently analysed. Published long-term experiments are scarce for all GMOs and non-existent for this particular GMO. Feed analyses included pathogens and mycotoxins, which were in all cases absent or below regulatory thresholds. Nutrient content was normal; however, a 12% higher protein content was measured in the Bt silage in comparison to conventional. 19% less free amino acids were measured in Pactol Cb grains. No conclusions were drawn from that. The GM feeding was stopped in February 2002 because of serious health problems in the herd, which had begun in the second year of Bt feeding. At this time the percentage of Bt maize in the diet had increased from 2 to 40% in total during the observation years (Figure 1). It contained 8.3 ng/g modified CryIAb Bt toxin in the silo 1.5 years after harvest, corresponding for the last 2 years to a minimal exposure of approximately 0.15 mg/cow ration/day. In the case of another somewhat similar Bt maize variety, MON810, approximately 1 µg/g of the modified Bt toxin was found in grains and around 10 µg/g in leaves (Szekacs et al., 2009). This was compatible with what could be in the silo after 1.5 years. In 2000, milk tested positive for the Bt176 DNA specific fragment. It was detected 2 times in milk fat and once in cells, proving that the animals were fed Bt maize, and, under European law, providing grounds for labelling the milk as coming from GM-fed animals. In addition, traces of the small fragment of the specific probe for the Roundup Ready tolerance gene EPSPS from GM soy (the amount of soy in the feed was 10 times less than the maize) were found once, in milk cells.

Productivity on the farm

The mean age of the healthy cows was constant (4.7–5.3 years), as well as the time between 2 calvings (402–417 days) for inseminated cows, and the milk yield per year (6–8 tons/cow/year). The fat and protein content of the milk was good (4 and 3.4% respectively). The only variations were in the number of healthy cows recorded by the certified veterinarian and the deaths, which were closely linked to the Bt content in the diet (Figure 1).

The number of calving cows represents an indicator of the fertility of the herd; their number decreased approximately one year (pregnancy length 282 days) after the maximum level of Bt maize was reached in the diet (Figure 1). However, the total number of cows in the herd was maintained at a constant level by introducing new cows previously fed another diet to replace the dead and unhealthy animals, for economic reasons. This is the normal way of functioning of a productive farm, but it is different from a scientific experiment, where animals must not be replaced mid-way through the study period. The replacement of animals could have resulted in an underestimate of the toxic effects. This paper documents a real observation in an agricultural context, like an environmental study in field conditions.

First pathology report in 2001

In 2001, the Bt maize content in the diet reached its maximum level (from 20% the year before to 40%). Because of 5 abnormal deaths between May and August 2001 out of 66 cows (7.6%) – the first such occurrence on the farm during its entire history – careful examinations were performed for bacterial and viral infections, as well as the presence of parasites and mycotoxins. Samples were taken in August. There was no viral infection and no Coxiella burnettii bacteria (which are responsible for Q fever). Chlamydia antibodies were found in 5 cases but not in disabled animals: 3 uteri tested positive for chlamydia, and in one uterus leptospira antibodies were found, but the feces had no known pathogenic bacteria. One healthy cow had coccidia. The deaths were not linked to infectious or genetic diseases. Because of these diseases or signs of weaknesses, as a preventive measure, 52% of cows (34 in total) were removed from the dairy milk production programme. The first diagnosis of the pathologies was a paresis, comparable to what is observed after calving, but lasting much longer; later, disabled cows had difficulty standing up. The veterinarian tested the hypothesis of postparturient hypocalcemia, a disease of dairy cows, and immediately performed classical infusions of glucose,

Table 1. Symptoms of diseases and parameters disturbed in the farm.

Parameters disturbed and symptoms	Before trial	Oct. 1999 - Sept. 2000 20% Bt maize	Oct. 2000 –Sept. 2001 40% Bt maize	Oct. 2001–Feb. 2002 (5 months) 40% Bt maize
% abnormal deaths	0	0	7.6	10.3
% removed cows	32	46	52	55
Paresis	no	no	++	++
Liver metabolism				
Beta-carotene	no ab.	no ab.	low	no ab.
Triglycerides	no ab.	normal	low	normal
Bilirubin	no ab.	no ab.	normal	low
Liver disease	no ab.	no. ab.	no. ab.	yes
Kidney metabolism				
Plasma sodium	no ab.	normal	low to very high	no ab.
Urine sodium	no ab.	normal	very high	very high
Urea in plasma	no ab.	no ab.	high	very high
Kidney disruption	no ab.	no ab.	yes	yes

(1) Removed cows are unhealthy or aged. The normal removal rate from dairy production after aging is around 30% on the commercial farm, because the cows are changed after three years. Above 30% are unusual unhealthy cows.
no ab.: no abnormality reported. All other parameters were normal.
Very high : 2-8 times the norm, high is over the norm (less than 2 times).

calcium borogluconate and magnesium (500 ml/day). This was not sufficient. A cow was euthanized after 5 days of paresis. All known tests for pathologies, including in the organs, were negative. Bovine spongiformencephalopathy (BSE) was tested for but not detected in any case.

Similar pathologies became more frequent in other cows. Symptoms were atypical in that they recurred irregularly for months. At a biochemical level, the calcium norm in blood is between 9 and 12 mg/dl. The mean on the farm in 2001 was in the norm, 9.67 mg/dl in blood, and 9.97 mg/dl in urine, i.e. 2.49 mm/l. Before these results became known, the prescribed infusions were partially effective; probably because of low glucose levels in disabled cows that were eating less than normal, but improvements were only short-term. Blood magnesium levels were also within the norm, as were phosphate, potassium, glucose, and urea levels. There was not enough beta-carotene in the plasma, and triglycerides in plasma were also low in general in disabled animals, from 0 to the lowest norm (15 mg/dl). The urine contained no ketone bodies. Sodium was 400–700% over the upper limit in general (10 mmol/l), 100% more in one other case, and in a few cases it was almost undetectable. This indicated kidney problems. Disrupted parameters are summarized in Table 1. Some animals were analyzed in more detail before or following their deaths and their cases are further reported below.

CASE STUDY

The cow Gisela died on Aug 13, 2001 from chronic pleuritis, endometritis, and severe paresis. She had been biochemically analyzed (see “Materials and methods”) in the general screening 12 days before, and therefore presented an interesting case for investigation of the reasons for death in a subsequent analysis. She tested negative for BSE, viruses, chlamydia in blood and uterus, and other pathogenic bacteria or parasites; she had no genetic disease or malformations. In the plasma, minerals and glucose were normal; however, urea was at the maximum level in comparison to all animals measured (35 mg/dl) 12 days before death. There was at this moment high Na in urine (5 times higher than the normal upper limit); this was the only mineral at an abnormal level. Potassium was 2 times under the norm (350 mmol/l in urine). The kidneys appeared to be dysfunctional.

Pathology report in 2002

In 2001–2002 (from October to September), six new animals died – an extremely unusual occurrence for the farmer. The GMO content was 40% of the diet and continued at this level until February 2002, when official advice was given by the farmer’s lawyer, due to the lack of a clear answer from the authorities, to stop the diet due to the problems observed, although no mycotoxins or other known pathogens were found. The veterinary examination in July concluded that 8 cows had chronic paresis, liver disease, and mucosa problems evidenced by a dry, white muzzle and tongue. In addition, the cows exhibited abnormal behaviour in that in all cases, they continued lying down after the calving period. They only temporarily recovered for a short period after glucose, calcium and magnesium infusions, probably because of the temporary boost in energy. However, their plasma calcium level was not low (a characteristic sign of parturient paresis) but normal (9.62 mg/dl); urine calcium

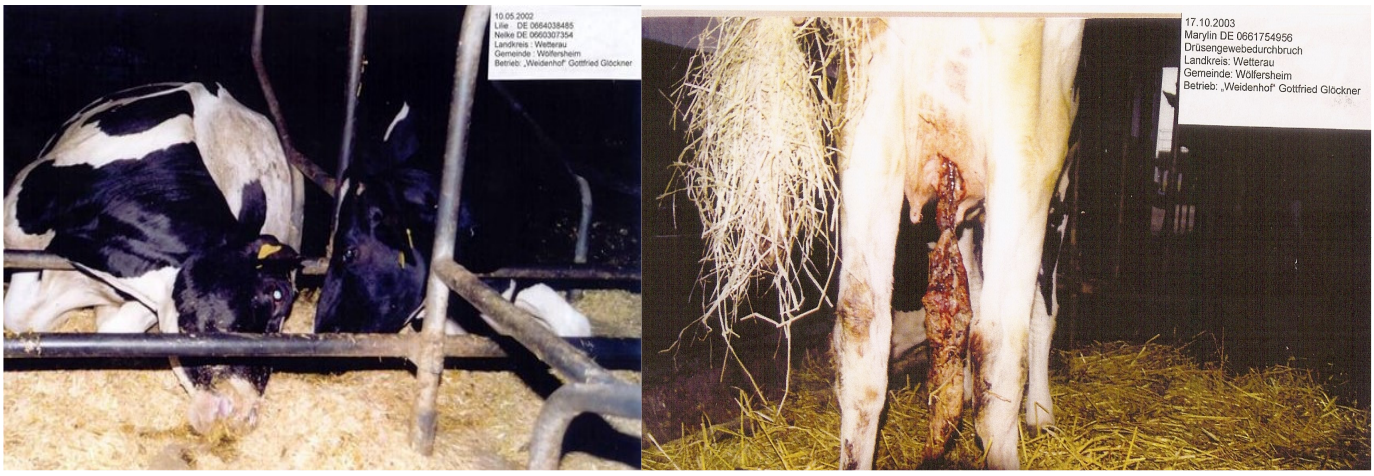

Figure 2. Characteristic symptoms of the pathology observed. Paresis in animals (on the left, 2002) and mammary gland break (on the right, 2003), epithelial disruptions together with mucosal problems.

level was also normal (8.2 mg/dl). Mg, triglycerides, GLDH, AST and cholesterol were also within the norm. The bilirubin level was low (4 µm/l). The plasma glucose level was normal; there were no abnormal or high levels of blood cells in milk, and no viral or bacterial infections. Levels of urea in plasma were 2 times above the norm (around 60 mg/dl); urine ketones were normal but urine Na was again elevated, in general 3–15 times more than the normal upper limit, indicating a kidney leakage. The urinary potassium was half the level of the upper limit.

Other cases

One other animal, Lilie, died at the veterinary clinic at Giessen, in May 2002 after a similar paresis (Figure 2). In common with another cow in the same shed (Nelke, Figure 2), she lay down often, was tired, and had irregular heart function and muscle paresis, including of the tongue. It had a very low calcium level in plasma at death (0.2 mmol/l). A calcium-rich infusion did not ameliorate the problem.

Another cow, Liesel, died on 27 June 2002; she was euthanized because she could not stand up, and was always sleeping, with no energy in the muscles, and suffered from paresis. Eleven months before, in August 2001, she had no sign of pathology; she was tested in the regular programme and proved negative for viruses, positive for chlamydia antibodies but, like 4 other healthy animals, negative for bacteria in blood; in the vestibulum of the uterus, like 4 other animals, she had chlamydia, but no visible infection. Phosphorus and calcium levels in plasma were normal; liver markers GLDH and AST were close to the norm (slightly above the upper level, 50 and 25%, respectively). Glucose and cholesterol were normal; triglycerides were 2 times below the norm; urea in plasma was high (41% more than the norm); Na in urine was low (80% less than the norm); K was normal, and Mg was at the highest level in plasma (4.2 mg/dl) among all animals tested, possibly because of infusions. Again, the kidney function appeared the most disturbed.

Analyses after removal of Bt maize from the diet

On 17 June 2003, a new analysis was performed because some unusual symptoms were still observed in the herd after the removal of Bt maize from the diet, even though only one cow died. Still no infection was visible or detected, urea in plasma was still double the norm, and 4 animals had high ketone levels in urine (4 mg/dl). The livers were normal for all parameters, and the urine Na was below the norm (70–90% less because sodium was no longer added to the feed, because of previous hypernatremia in urine), except for 2 animals (2.5 and 3.8 times over the norm). However, some double openings of the teats and mucosa and epithelial problems in the mammary gland (in one case heavily cracked and bleeding, Figure 2) were observed. The exposure to the mutated Bt toxin or other GM maize metabolites during the fetal life of these animals may have induced a malformation of the mammary gland; the epithelial tissue may have been affected during its first differentiation.

The fourth analysis on August 2004 was performed more than 2.5 years after Bt maize was removed from the diet. These animals had been exposed to Bt maize only during their fetal life. Only one death (with characteristic abnormal symptoms) occurred, and no infection was detected in any of the cows. The plasma urea was high only in one case, and levels of minerals, glucose, and cholesterol were normal. The liver function had recovered, but some cases of diarrhea were noticed, apparently due to the consumption of grass silage, which replaced the maize.

OBSERVATIONS AND COMMENTS

At the maximum, 10% of the cows in this herd fed GM maize feed died abnormally with comparable symptoms, and 30% were unhealthy. Comparable levels of sickness and death were unknown on this farm since its creation in 1986. The symptoms were heavy paresis, with no fever or infection, and there was always a disruption of the Na/K equilibrium in urine together with other kidney biochemical failures, high urea in the blood (see above), and some liver toxicity. In addition, some mucosal dryness and epithelial problems, illustrated in the most serious case by a break in the mammary gland (Figure 2), were observed.

Interestingly, when this GM Bt maize was first developed, Novartis (subsequently Syngenta) performed an initial trial for the authorities in the USA. Only 4 cows were fed with the maize over a 2-week period (1996 report from Iowa State University for Novartis, rendered public by Court, see Annex). One cow died in the middle of the experiment with electrolyte and mucosal problems, and surprisingly, was removed from the protocol. This information was not public at the time, but one of the authors of this article (GES) had access to the file as an expert on GMOs for the French government. Animal feeding trials were not at the time compulsory before commercial releases of GMOs. That is still the case especially in America, where most agricultural GMOs are produced. The company concluded that no specific toxic effect was noticed. However, even with these inadequate data and controversial results, the company still requested the commercialization of this maize. Commercial cultivation began on the farm featured in this report in 1997. Syngenta did not officially conclude on the possible origin of the pathologies described in our report, but said that the link with Bt maize was not relevant for any disease (see Annex). These comments, without any explanation, are not scientifically justifiable. Thus when Syngenta also concluded that there was no Bt protein in the silage of the farm, which was made from maize modified to make a Bt toxin, it was not possible to take this result seriously (see Annex), since the SLFA independent state laboratory had concluded that there was 8.3 ng/g of Bt toxin in the same sample (see Annex and above). Moreover, Syngenta recognized the quality of the farmer's silage, but asked him not to dispose it on grassland (see Annex). This contradictory information from the company and the court case that followed are described elsewhere (Séralini, 2016).

As a possible scientific explanation for these pathologies, it is known that the cadherin family of transmembrane proteins play an essential role in the bovine kidney (Kartenbeck et al., 1991), as well as during gestation (Caballero et al., 2014) and in epithelial cells. It was recently discovered that some cadherins are involved in the mechanism of toxicity for Cry1Ab (Gomez et al., 2014), the toxin produced by this GM Bt maize. This hypothesis may explain some symptoms at the level of the kidneys and mucosa or epithelia. This does not exclude other possibilities, such as the presence of new toxic metabolites in the GM maize. The insecticidal protein may be degraded to some extent in the gastrointestinal tract (Lutz et al., 2005), unless weaknesses are present in some animals at this level. In a recent and comprehensive review of the effects of Cry toxins on mammals (Rubio-Infante et al., 2015), it was shown that these insecticides may induce kidney and liver toxicities even when fed even for subchronic periods.

CONCLUSION

In conclusion, biochemical kidney disruptions such as those observed in this work have been already linked to Bt maize consumption in subchronic tests in mammals. Biochemical disruptions in the liver have also been observed (Séralini et al., 2007, 2011, Spiroux et al., 2009; Rubio-Infante et al., 2015). Biochemical disruptions have been reported in *in vitro* studies on embryonic kidney cells exposed to Bt maize (Mesnage et al., 2013). The *in vivo* effects may have been inappropriately neglected (Séralini et al., 2009). Altogether in the farm-level observations described above, 10% of the cows died abnormally, preceded by a long-lasting paresis syndrome without hypocalcemia or fever, but with kidney biochemical failures and problems at the mucosal and in some cases epithelial levels. No microbial origin was identified, though intensive searches for pathogens were performed.

The GM maize, subsequently withdrawn from the market, was at the time the only intended managerial change for the cows. It is proposed that it provoked long-term toxic effects on mammals, which are typically not observed in the usual high-turnover (more rapid than 3 years) conditions of intensive farming, especially as GM feed carries no specific labels. More long-term feeding trials should be performed before other market releases of GM Bt-producing plants, as well as Roundup-tolerant GMOs, as previously noted (Séralini et al., 2014).

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as other cited documents are given in the Annex, in the interests of full transparency.

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