

# Pusztai affair

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The **Pusztai affair** is a controversy that began in 1998 after protein scientist Arpad Pusztai went public with research he was conducting at the Rowett Institute with genetically modified (GM) potatoes. The potatoes had been transformed with the *Galanthus nivalis agglutinin* (GNA) gene from the Galanthus (snowdrop) plant, allowing the GNA lectin protein to be synthesised. This lectin has been shown to be toxic to some insects. Rats were fed on raw and cooked genetically modified potatoes, using unmodified Desiree Red potatoes as controls. Twelve feeding experiments were conducted, ten short-term (10 days) and two long-term (110 days). Rats fed raw or cooked potato modified with the GNA gene showed statistically significant thickening of the stomach mucosa compared to rats fed the unmodified potato. As these effects were not observed in rats fed control potatoes injected with GNA protein, Pusztai concluded that the differences were a result of the transformation procedure.

In a short interview on Granada Television's current affairs programme World in Action Pusztai said that rats fed the potatoes had stunted growth and a repressed immune system. This resulted in Pusztai and the Rowett Institute receiving numerous phone calls from government, industrial, NGO and media organisations. Following the media frenzy, Pusztai was suspended and misconduct procedures were used to seize his data and ban him from speaking publicly. His annual contract was not renewed. The Rowett Institute and the Royal Society reviewed Pusztai's work, concluding that the data did not support his conclusions. The data was published in the *The Lancet* in October 1999, and reported significant differences in the thickness of the gut epithelium of rats fed genetically modified potatoes (compared to those fed the control diet), but no differences in growth or immune system function were suggested. After publishing, it was criticised on the grounds that the unmodified potatoes were not a fair control diet, and that any rats fed only on potatoes will suffer from a protein deficiency. Pusztai responded to these criticisms by stating that all the diets had the same protein and energy content and that the food intake of all rats was the same.

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## Background

Prior to 1995, no peer-reviewed studies had been published investigating the safety of genetically modified food using human or animal feeding trials.<sup>[1]</sup> In 1995 the Scottish Agriculture Environment and Fisheries Department commissioned a £1.6 million three-year research study to assess the safety of genetically engineered Desiree Red potatoes.<sup>[2]</sup> The potatoes had been developed by biochemist<sup>[3]</sup> John Gatehouse at Cambridge Agricultural Genetics (later renamed Axis Genetics) and had recently completed two years of field trials at Rothamsted Experimental Station.<sup>[2]</sup> The *Galanthus nivalis agglutinin* (GNA) gene from the Galanthus (snowdrop) plant was inserted into the potato allowing the GNA lectin protein to be synthesised.<sup>[4]</sup> This lectin has been shown to be toxic to some insects.<sup>[5]</sup>

Twenty-eight study proposals were presented with eight being selected for peer review by the Biotechnology and Biological Sciences Research Council. From these eight the Rowett Research Institute's proposal was chosen and a combined team of academics from the Scottish Crop Research Institute, the Durham University Department of Biology and the Rowett Institute was set up with Arpad Pusztai coordinating the study.<sup>[2]</sup> Although the potatoes used were not a commercial variety and not intended for human consumption<sup>[6]</sup> a contract was signed with Cambridge Agricultural Genetics, which included a profit-sharing agreement, if potatoes developed using this technology were approved and released commercially.<sup>[2]</sup> This was one of the first animal feeding studies conducted with genetically modified foods to be independently peer reviewed.<sup>[1]</sup> Pusztai had previously studied the effect GNA had on rats in ten-day feeding trials and concluded that it did not significantly affect the rats growth, although there was some hypertrophy of the small intestine and a slight decrease of gut enzyme activity.<sup>[7]</sup>

## The experiment

The potatoes were chosen because they were deemed substantially equivalent to non-GM Desiree Red potatoes.<sup>[8]</sup> The Rowett study aimed to examine the substantial equivalence of the modified potatoes and to test for any adverse effects on rats fed the potatoes for ten days and three months.<sup>[9]</sup> The study used two transgenic lines of potato, both with the GNA gene inserted, and they were grown in the same conditions along with the non-GM parent plant.<sup>[9]</sup> According to Pusztai the potatoes were not substantially equivalent, as one of the transgenic lines contained 20 percent less protein than the other<sup>[10]</sup> and the starch and sugar contents varied by up to 20 percent between the three lines.<sup>[11]</sup> In Pusztai's opinion the lack of substantial equivalence was reason enough to discontinue any further experimentation with the potatoes.<sup>[11]</sup>

Rats were fed on raw and cooked genetically modified potatoes, using unmodified Desiree Red potatoes as controls. One of the controls consisted of an unmodified Desiree Red potato spiked with the GNA snowdrop lectin.<sup>[4]</sup> Twelve feeding experiments were conducted, ten short-term (10 days) and two long-term (110 days).<sup>[9]</sup> Before the experiment Pusztai and his team said they expected there to be no differences between the rats fed modified potatoes when compared to rats fed the non-modified ones.<sup>[12][13]</sup> Their experiment however showed a statistically significant difference in the thickness of the stomach mucosa. The mucosa of rats fed raw or cooked potato modified with the GNA gene was thicker than that of rats fed the unmodified potato.<sup>[4]</sup> The crypt length in the jejunum was greater on rats fed the raw modified potato, although there was no statistical difference observed in the rats fed the cooked potato.<sup>[4]</sup> As these effects were not observed in rats fed the control potatoes spiked with GNA, Pusztai concluded that the differences were not due to the presence of GNA, but were a result of the transformation procedure.<sup>[4][13]</sup> Stanley Ewen, who collaborated with Pusztai on the experiment, said that the cauliflower mosaic virus used as a promoter could be the likely cause of the changes observed.<sup>[14]</sup>

The experiment as reported in *The Lancet* - if taken at face value - found that the transformation event or the gene construct produced one compound that is heat stable and that made the jejunum proliferate but had no effect on the caecum. And it also found that - at the same time - the transformation event or the gene construct produced another compound that is heat activated that had an *anti*-proliferation effect on the caecum but no effect on the jejunum.<sup>[4]</sup>

## Announcement

On June 22, 1998 Pusztai revealed his research findings during an interview on Granada Television's current affairs programme *World in Action*<sup>[15]</sup> titled "Eat up your genes".<sup>[16]</sup> He was given permission to do the interview by Rowett Institute Director Philip James and their press officer was present at the start of filming. During the interview Pusztai said that he had "concerns that some of the testing techniques are not up to what we thought it was necessary to do, and therefore we should have more testing."<sup>[17]</sup> When asked why he felt concerned he said "it was because we had done some experiments which made us feel concerned" and discussed his results with the programme in general terms based on his experiences.<sup>[17]</sup> Pusztai later said that at the time of the interview he was not sure if he should reveal results from experiments that had not been completed and did not think that the programme would be hostile towards genetically modified food. He estimated that the experiments were 99 percent complete when the interview was conducted.<sup>[17]</sup>

The show aired seven weeks later on Monday August 10, with the Pusztai interview lasting 150 seconds. On the show he said that the rats in his experiments suffered stunted growth and had suppressed immune systems and that more safety research was required.<sup>[18]</sup> He also said that "If you gave me the choice now, I wouldn't eat it"<sup>[18]</sup> and it was "very, very unfair to use our fellow citizens as guinea pigs".<sup>[19]</sup> A press release from *World in Action* was issued the day before the broadcast,<sup>[20]</sup> resulting in Pusztai and the Rowett Institute receiving numerous phone calls from government, industrial, non-governmental and media organisations. James says he was dismayed that unpublished data had been released and withdrew Pusztai from any further media commitments on Monday morning.<sup>[17]</sup> He eventually ended up suspending Pusztai, used misconduct procedures to seize his data, banned him from speaking publicly and did not renew his annual contract.<sup>[6]</sup>

At the time there was confusion over just what experiments had been conducted. In his interview Pusztai had mentioned two lines of genetically modified potatoes, meaning the two GNA lines, and this was reported by the media. The Rowett institute mistakenly assumed the media was talking about a second line transformed with concanavalin A (ConA), a Jack Bean lectin which is toxic to mammals. Transgenic ConA Potatoes had been developed, but they had never been tested.<sup>[17]</sup> Two press releases issued by the Rowett Institute on the 10th and 11th praised Pusztai's research<sup>[21]</sup> and supported increased safety tests on genetically modified food.<sup>[17]</sup> The press releases also said that the potatoes were modified with ConA, adding to the confusion. Pusztai says he never saw the press release before it went out, so had no opportunity to correct the mistake. James says that he drafted it and Pusztai rewrote a whole section, but did not see the final copy.<sup>[17]</sup> The mistaken belief that the ConA gene was inserted into the potato led scientist Sir Robert May and Agricultural Minister Jack Cunningham to release statements to the media saying

that the findings were not surprising as a known poison had been added to the potato<sup>[20]</sup> and some scientists still dismiss Pusztai's work due to this.<sup>[6]</sup>

An audit of Pusztai's work was conducted by the Rowett Institute on the 22nd October, 1998, and it concluded that the data did not support his conclusions.<sup>[22][23]</sup> In February 1999, 22 international scientists from 13 countries, organised by the environmental group Friends of the Earth,<sup>[24]</sup> published a memo responding to the audit.<sup>[25]</sup> It says that their independent examination of the data supports Pusztai's conclusions and he had a right to be concerned by his findings. On 19 February the Royal Society publicly announced that a committee would review his work. World in Action reporters Laurie Flynn and Michael Sean Gillard say that this was an unusual step as the Royal Society does not normally conduct peer reviews.<sup>[26]</sup> The data was sent to six anonymous reviewers<sup>[6]</sup> and the resulting review was published in June 1999.<sup>[27]</sup> It stated that Pusztai's experiments were poorly designed, contained uncertainties in the composition of diets, did not have a large enough number of rats, used incorrect statistical methods and lacked consistency within experiments. Pusztai responded by saying they had only reviewed internal Rowett reports, which did not include the design of the experiments or methodology used.<sup>[2]</sup>

## Publishing

Pusztai's experiment, co-authored by Stanley Ewen, was eventually published in 1999 as a letter in *The Lancet*.<sup>[4]</sup> Due to the controversial nature of his research the letter was reviewed by six reviewers - three times the usual number. Four reviewers found it acceptable after revisions. A fifth thought it was flawed, but wanted it published "to avoid suspicions of a conspiracy against Pusztai and to give colleagues a chance to see the data for themselves". The sixth, John Pickett of the Institute of Arable Crops Research, also thought it was flawed.<sup>[28]</sup> After consulting with the Royal Society, Pickett publicly criticised the *Lancet* for agreeing to publish the study. The study, which used data from a follow-up study conducted by Stanley Ewen<sup>[29]</sup> and was not subject to a veto on Pusztai's work,<sup>[6]</sup> reported significant differences between the thickness of the gut epithelium of rats fed genetically modified potatoes (compared to those fed the control diet) but did not mention any stunted growth or immunity issues.<sup>[4]</sup>

After publishing, it was criticised on the grounds that the unmodified potatoes were not a fair control diet and that any rats fed only on potatoes will suffer from a protein deficiency.<sup>[30]</sup> Pusztai responded to these criticisms by stating all the experimental diets had the same protein and energy content, and that the food intake of all rats was the same.<sup>[31]</sup> In an interview, Pickett later stated that Richard Horton (the *Lancet* editor) had a political motive for publishing the paper, because the "referees" had rejected it. According to Pusztai this claim was repeated by academic critics who assumed that Pickett's use of the plural suggested that the study had failed peer review.<sup>[2]</sup>

Horton says he received a "very aggressive" phone call calling him "immoral" and threatening him that if he published the paper it would "have implications for his personal position" as editor.<sup>[26]</sup> Peter Lachmann, the former vice-president and biological secretary of the Royal Society and president of the Academy of Medical Sciences, admits making the call but denies that he threatened Horton and says the call was to "discuss his error of judgment" in publishing the letter.<sup>[26][32]</sup> Following publication, co author Dr Stanley Ewen, says he found his career options "blocked at a very high level" and retired.<sup>[20]</sup>

## Follow up

Investigative journalist Andrew Rowell<sup>[33]</sup> wrote in his 2003 book *Don't worry, it's safe to eat: The true story of GM food, BSE and foot and mouth* that pressure to sack Pusztai had been applied to the institute from Monsanto, a multinational company that owns 90 percent of GM seed technology.<sup>[20]</sup> According to Rowell, professor Robert Orskov, who was working at Rowett at the time, heard that US President Clinton rang Prime Minister Blair who then rang James to tell him to silence Pusztai. Pusztai's colleague Stanley Ewen says he heard the story from another Rowett researcher, Asim Duttaroy.<sup>[34]</sup> In 2008 James Randerson, *The Guardian's* environment and science news editor,<sup>[35]</sup> telephoned Orskov and Duttaroy and emailed James.<sup>[34]</sup> Orskov said that while he would not be surprised if the calls had occurred, he had no personal knowledge of them. Duttaroy remembers his conversation with Ewen, but does not remember making any statements about political manipulation. In 1999 James had denied receiving any phone calls from Government or Cabinet, but later stated to Randerson that he was phoned by "the science officer in the Department of Agriculture in the Scottish Office".<sup>[34]</sup> He says the conversation played no role in his decision to suspend Pusztai.<sup>[20]</sup>

A survey by the European Food Safety Authority GMO Panel Working Group on Animal Feeding Trials concluded that "Results obtained from testing GM food and feed in rodents indicate that large (at least 100-fold) 'safety' margins exist between animal exposure levels without observed adverse effects and estimated human daily intake. Results of feeding studies with feed derived from GM plants with improved agronomic properties, carried out in a wide range of

livestock species, are discussed. The studies did not show any biologically relevant differences in the parameters tested between control and test animals.<sup>[36]</sup> In 2005 Pusztai was given a whistleblower award from the Federation of German Scientists.<sup>[6]</sup>

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## External links

- Findings of Royal Society Reviewers (<http://www.ask-force.org/web/Pusztai/Royal-Society-Experts-1-7-19990510.pdf>) Royal Society
- Timeline of the affair (<http://www.guardian.co.uk/news/1999/feb/12/food.science1>) *The Guardian*
- GM FOOD SAFETY: Scientific and Institutional Issues (<http://www.tandfonline.com/doi/pdf/10.1080/09505430120115734>) Full account of the affair by Arpad Pusztai.

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