

# CORRESPONDENCE

## Health risks of genetically modified foods

Sir—It is profoundly depressing to follow the public debate on genetically modified (GM) crops. As the passion of the arguments increase, their scientific content diminishes correspondingly. It is a sad day for UK medicine when first the BMA and then *The Lancet*, in your May 29 editorial,<sup>1</sup> align themselves with the tabloid press in opposition to the Royal Society and the Nuffield Council on Bioethics. It is also disturbing and unusual for an editorial in *The Lancet* to be factually so inaccurate.

I imagine the first paragraph refers to maize made resistant to stem boring insects. This crop is not sterile and there is no difficulty in planting the GM seeds. The “Gene Use Restriction Technology”, called the “terminator gene” by the press is so far merely a patent claim and has not yet been produced. This device to prevent the formation of fertile seed from a GM crop, would also prevent the spread of the inserted gene to other plants. Surprisingly, this idea has found no favour with the opponents of GM organisms who concentrate entirely on the rights of the farmer to save seed.

Farmers currently have to use new seed with the conventionally bred F1-hybrid crops that are increasingly used worldwide, because F1-hybrid seeds do not produce F1 progeny. Their yield is so much higher that, in many cropping systems, F1-hybrids are highly advantageous.

There is no experimental evidence nor any plausible mechanism by which the process of genetic modification can make plants hazardous to human beings. Individual introduced genes may not be a great idea. For example, the use of a nut protein to enhance the protein content of a cereal may be a hazard to people who are allergic to nuts, but this danger would be the same if the nut protein were simply added to the cereal. The practice of leaving antibiotic-resistant markers in the GM plant has attracted criticism from the Royal Society among others since there is a hypothetical risk that antibiotic resistance could spread to gut flora.

The Scottish Crop Research Institute initiated an entirely sensible study to see whether lectins which make some plants unpalatable to insects could be introduced into other plants for the same purpose. The study used potatoes only

to make the experimentation easier. These particular potatoes were never intended to be developed as a food crop. Some assessment of the transgenic potatoes was made at the Rowett Institute. One of their scientists announced on television last autumn that feeding these transgenic potatoes to rats had caused abnormalities of organ growth and had damaged their immune systems. These remarks were seized upon by the tabloid press and engendered a hysterical reaction that has not died down. The Royal Society produced a careful peer review of all the available data on this work and concluded that the experiments were badly designed, poorly carried out, and inaccurately interpreted. Your editorial's comment that it is impertinent of the Royal Society to review the data because they may not be in their final form is incomprehensible. A scientist invites expert scrutiny by making his work public through the media and the worldwide web.

One reason for welcoming GM technology is that intensive agriculture, on which the world's food supply now depends, is in the long term both unsustainable and potentially harmful. It is unsustainable because it relies on the consumption of fossil fuels and consumes more energy than the food produces. The high levels of nitrogen and phosphate fertilisers used are a potential hazard to human health when these ions appear in the water supply. There are also potential concerns about the residues of pesticides and herbicides. Any technology that may enable better yields to be obtained with less external input should be welcomed.

It is also an illusion that there ever was a time when the food supply was entirely safe. All those who, in previous centuries, died of ergot poisoning and those who still develop liver disease from aflatoxin in their food are forgotten, especially by the enthusiasts for organic farming. Bacterial food poisoning always was a serious problem.

It is wrong to regard the introduction of resistance to insects or herbicides as the only long-term goals of genetic manipulation. This is the “horse-less carriage” stage of development of this new technology. Looking rather further into the future, other goals include developing plants that can grow in saline-polluted soil, a major issue in some parts

of the world. Similarly, it may be possible to develop plants that need less water input. Finally, there is the prospect of developing plants with an increased efficiency of the photosynthetic process itself. If this efficiency could be increased several fold agriculture would be able to meet not just the food but also the energy needs of the world.

The attempt of single interest groups, supported by the tabloid press and now by others who should know better, to declare this whole technology as dangerous and immoral is sad for the UK, but is also absurd. 300 million Americans and a billion Chinese eat genetically modified food with neither ill effects nor hysteria. On the world scale, what happens in the UK may not be of overwhelming importance. However, what this campaign of vilification does to the science base and the prosperity of the UK may be serious.

*Peter Lachmann*

The Academy of Medical Sciences, London  
SW1Y 5AH, UK

1 Editorial. Health risks of genetically modified foods. *Lancet* 1999; 353: 1811.

Sir—Your editorial<sup>1</sup> on genetically modified (GM) crops would never have passed the rigorous refereeing which you normally use for the contents of the rest of your journal. Of course the motive behind the commercial production of anything is added shareholder value. No farmer is compelled to buy any seed from any company. They can always continue to use traditional crops if they feel it is to their benefit. Farmers are just as driven by the profit motive as anybody else, whether in developing countries or not. There are many parts of India where cotton farmers have gone bankrupt through insect depredation, whereas North American cotton growers are now able to guarantee increased yields of cotton accompanied by a 70% reduction of chemical-based insecticides.

Although antibiotic-resistance markers are used for some plant biotechnology products to “select” for the presence of a desired trait, the antibiotic markers in these products were selected on the basis of their frequent occurrence in nature, their efficacy as a marker, and the limited clinical importance of the antibiotics which they inactivate. The potential effect on human health of these markers

is carefully evaluated during the safety assessment regulatory review process in the UK and other countries. Further, it is recognised that the increased frequency of bacterial resistance to antibiotics is mainly attributable to the widespread use and misuse of antibiotics in human and veterinary applications, not to genetically modified crops. Experts and regulatory bodies that have assessed the probability that antibiotic markers used in genetically modified plants will impact antibiotic efficacy have concluded that this likelihood is remote. Nonetheless, alternative markers should be and are being developed for use in future genetically modified crops.

It is unusual for the Royal Society to take a judgment on an independent scientist's unpublished data. Unfortunately, it was clear that the mythology surrounding these experiments was having a major impact on public perception of this technology. Although the data were not refereed by the usual channels, they had been made available to the world via the internet. It was therefore perfectly appropriate that any scientist or group of scientists should comment on the false conclusions being drawn.

The British Medical Association did not need to recommend a moratorium on the commercial planting of GM crops. Such a moratorium already exists. No permission for commercial planting has been given nor will it be given until ACRE is satisfied on the various issues which have been widely discussed.

Of course the Government should take an interest in any possible health risks associated with any new food and indeed this is exactly the role which the Advisory Committee on Novel Foods and Processes takes. Nobody, however, has been able to identify any potential health risk associated with consumption of lecithin, or soya oil, or soya starch obtained from a GM crop, compared with traditional crop. In the absence of any hypothesis, the design of a sensible experiment is impossible.

It is not true that the population of the USA had been eating genetically modified ingredients. The ingredients they have been eating have not been modified in any way whatsoever. It is the crops from which the ingredients were derived that have been modified. There has not been one example of any identifiable medical condition induced in the 250 000 000 Americans who have consumed such material during the past 3 years.

Alan D B Malcom

Institute of Biology, 20 Queensberry Place,  
London SW7 2DZ, UK

1 Editorial. Health risks of genetically modified foods. *Lancet* 1999; 353: 1811.

Sir—Your May 29 editorial<sup>1</sup> misleads readers by saying biotechnology companies and government officials “have paid little evident attention to the potential hazards to health of genetically modified foods”. You ignore thousands of scientific studies, environmental risk assessments, and the field trials undertaken worldwide before the commercial introduction of transgenic crops.

Before the approval of the first transgenic *Bacillus thuringiensis* (BT) corn in the USA, the Department of Agriculture (USDA) conducted an environmental assessment in 1995 that analysed data on risks to insects beneficial to agriculture and other non-target insects as risks to endangered organisms—from bobwhite quail to certain species of butterflies. Tests to find out if endangered aquatic organisms were threatened examined the impact of BT corn pollen blown into water. The USDA concluded the data showed no significant potential to adversely affect organisms other than the targeted pest that destroys corn.

Scientific inquiry, however, has not ended there. Researchers continued to examine transgenic corn, such as scientists who explored the impact on beetles, flower bugs, and lacewings, all of which feed on corn borers. These predators also eat corn pollen. In a paper published in April 1997, the researchers reported they found no detrimental effects on the beneficial insects. In fact, they observed more of them in BT corn fields than in non-BT corn fields.<sup>2</sup>

As for the safety of transgenic corn and other biotech crops in food, the US Food and Drug Administration (FDA) undertook its own exhaustive studies and concluded in 1992 and again in 1995, “It is not aware of information that would distinguish genetically engineered foods as a class from foods developed through other methods of plant breeding”.<sup>3</sup> The fact is, the FDA observed, because recombinant DNA techniques are used to introduce only one or a few genes into a crop, agricultural scientists avoid a major difficulty of conventional cross hybridisation, which is the multiple introduction of undesirable genes.

Results of all studies by the USDA, FDA, and the Environmental Protection Agency—the three US agencies charged with monitoring biotech crops and foods—are produced with public input and available for perusal when completed.

A 1996 report from the Food and Agricultural Organisation of the United Nations and WHO also explored in depth the safety of foods derived from biotech crops. Those two groups

concluded: “Food safety considerations regarding organisms produced by techniques that change the heritable traits of an organism, such as recombinant DNA technology, are basically of the same nature as those that might arise from other ways of altering the genome of an organism, such as conventional breeding.”<sup>4</sup> The report also noted, “The presence in foods of new and introduced genes per se was not considered to present a unique food safety risk.”

It is one thing for *The Lancet* to urge caution in introducing genetically modified foods. Everyone agrees continued vigilance is necessary. It is an egregious error, however, for you to imply potential health hazards have been overlooked by industry and regulatory agencies. In doing so, it dismisses decades of dedicated scientific work that clearly proves otherwise.

Carl B Feldbaum

Biotechnology Industry Organization, Washington,  
DC 20006, USA

- 1 Editorial. Health risks of genetically modified foods. *Lancet* 1999; 353: 1811.
- 2 Pilcher CD, Obyrcki JJ, Rice ME, Lewis LC. Preimaginal development, survival, and field abundance on insect predators on transgenic *Bacillus thuringiensis* corn. *Environmental Entomology* April 1997; Vol. 26, no 2, 446–54.
- 3 FDA's policy for foods developed by biotechnology contained in the proceedings of the American Chemical Society Symposium, series no. 605, 1995, by Maryanski JH, Strategic Manager for Biotechnology, Centre for Food Safety and Applied Nutrition, FDA.
- 4 Biotechnology and food safety, report of a joint consultation of the food and agricultural organisation of the United Nations and WHO, Rome, Italy, 30 September to 4 October 1996.

Sir—As chairman of the Dutch Committee on Genetic Modification (COGEM), the main adviser to the government in our country on the safety of genetic modifications, I and others stand accused in your editorial of May 29<sup>1</sup> of badly mishandling important health issues.

The safety of genetic modification is a serious topic and the quality of the decision-making process can only improve by the input from as many sources as possible. However, these contributions should be based on the data collected by the cautious step-by-step approach during the 20 years of genetic modification. Although uncertainties remain, there is no reason to ignore the information that is available. Your editorial fails to make a continuing argument against the opinion of the US Food and Drug Administration that genetic modification does not constitute a risk in itself.

Phenotypic characteristics such as the presence of an antibiotic resistance in

plants may be considered harmful, but you ignore the reports and other scientific evidence on this topic. It would for example, be interesting to know your reaction to the criteria used by the Dutch COGEM to assess the risks of antibiotic resistance gene in crops. Our approach is based on the assumption that antibiotic resistance may spread from plants to microorganisms.

You also fall short of supporting the moratorium on introduction of genetically modified crops, as advocated by the British Medical Association and other organisations. In my opinion there is at present no rationale for a moratorium. Those who argue in its favour have to formulate the specific reasons why and what they want to achieve. They have to quantify the current risks and to what extent these risks have to be reduced to be acceptable and to terminate the moratorium.

Learned societies and journals, mainly in the UK, seem to have lower scientific standards with regard to the genetic modification of plants than other topics. If the assumption is correct that the reasons for this unbalanced approach lie outside science, there is more at stake than the future of genetic modification of plants.

*H Schellekens*

Dutch Committee on Genetic Modification,  
2912 BH Nieuwerk, Netherlands

1 Editorial. Health risks of genetically modified foods. *Lancet* 1999; **353**: 1811.

Sir—Peter Mitchell and Jane Bradbury's May 22 news item (p 1769)<sup>1</sup> reports the Royal Society's judgment that Arpad Puztai's study on the potential toxic effects of genetically modified (GM) potatoes is "flawed in many aspects of design, execution and analysis and that no conclusions should be drawn from it". The society rightly says that research scientists should expose their new results to peer review before releasing them.

The episode at the Rowett Research Institute highlights just how important the integrity of the peer-review process is to the maintenance of high standards in science. Our experience<sup>1</sup> with trial data on recombinant bovine somatotropin (rBST, an injectable hormone which raises milk yield in dairy cows) suggests that increased vigilance, perhaps through some mechanism of formal audit, may be needed to preserve such standards.

In that case, official regulatory authorities accepted the manufacturer's unpublished analysis. We previously identified the shortcomings in this analysis, and did

our own, but we were unable to publish it because the company concerned withheld consent. Here the peer-review process was compromised, partly by the pressures on the existing regulatory process and partly by the requirement for commercial scientists to deliver the product to market. In general, if preapproval studies are not published, any questionable conclusions may go unchallenged. Put another way, if applicants are able to argue successfully that disclosure would cause commercial harm, then peer scrutiny may be restricted.

A process that bears the hallmarks of these difficulties led to the approval of rBST for farm use by the US Food and Drug Administration in 1994. rBST is unlicensed in Canada and the European Union. The company seeking to market this productivity aid gave us data from eight randomised controlled trials. We did a meta-analysis and found evidence for a pro-mastitic effect due to rBST. The report was sent to the company and to a UK peer-review journal. Although our report passed the peer review, the company refused permission for its publication on the basis that the trial investigators would soon submit their own analysis for publication. In the following 3 years, no such report appeared. We resubmitted our paper to a US journal and then to another UK journal. On each occasion the paper received peer approval but could not be published because the company alleged they had copyright over our analysis of their data. We were eventually able to publish our findings as a response to a public accusation of plagiarism by a company representative, but only after FDA approval for rBST had been given.

There is no method of recourse in such situations. We therefore support the recent recommendation contained in the first report of the Commons Select Committee on Science and Technology<sup>2</sup> for further openness in the regulatory process in the UK and elsewhere for new foods, with the rapid publication of papers and data (<http://www.publications.parliament.the-stationery-office.co.uk/pa/cm199899/cmselect/cmsctech/286/28602.htm>; accessed June 10, 1999).<sup>2</sup> This approach would substantially strengthen the peer-review process.

\*Eric Brunner, Erik Millstone

\*Department of Epidemiology and Public Health, University College London Medical School, London WC1E 6BT, UK; and Science Policy Research Unit, Sussex University, Brighton

1 Millstone EP, Brunner EJ, White IR. Plagiarism or protecting public health. *Nature* 1994; **371**: 647–48.

2 House of Commons Select Committee on Science and Technology. Scientific Advisory System: genetically modified foods. First Report of Session 1998–99 (HC 286). London: HM Stationery Office, 1999.

## Antiphospholipid antibodies and thrombosis

Sir—M Greaves (April 17, p 1348)<sup>1</sup> notes the difficulties in laboratory diagnosis of antiphospholipid syndrome. Antiphospholipid antibodies (APAs) have been found in drug-induced syndromes, cancer, certain infectious diseases, and in small groups of apparently normal individuals. An APA test may be misleadingly negative at the time of thrombosis in some patients, and an association of the thrombotic disorder with the presence of APAs may be omitted. Before antibodies to  $\beta_2$ -glycoprotein I could be measured in clinical practice,<sup>2</sup> Drenkard and colleagues<sup>3</sup> reported concentrations at the time of a thrombotic event in patients with systemic lupus erythematosus, compared with antibody concentrations before and after the vaso-occlusive episode. In several of these patients concentrations fell into the normal range. Therefore, when diagnostic suspicion is high, caution may be necessary in interpreting negative results if the test is done at the time of active thrombosis.

Francisco José Fernández-Fernández  
Department of Internal Medicine, Hospital Arquitecto Marcide, 15405 Ferrol, Spain

- 1 Greaves M. Antiphospholipid antibodies and thrombosis. *Lancet* 1999; **353**: 1348–53.
- 2 Cabral AR, Amigo MC, Cabiedes J, Alarcon-Segovia D. The antiphospholipid/co-factor syndromes: a primary variant with antibodies to  $\beta_2$ -glycoprotein-I but no antibodies detectable in standard antiphospholipid assays. *Am J Med* 1996; **101**: 472–81.
- 3 Drenkard C, Sanchez-Guerrero J, Alarcon-Segovia D. Fall in antiphospholipid antibody at time of thromboocclusive episodes in systemic lupus erythematosus. *J Rheumatol* 1989; **16**: 614–17.

Sir—M Greaves<sup>1</sup> reviews antiphospholipid antibodies and thrombosis. We noted a special pattern of antiphospholipid syndrome in a woman aged 42 years who was admitted to our intensive care unit because of sudden severe respiratory failure. Computed tomography scan on day 2 revealed ground-glass opacity, interstitial, reticular, and confluent infiltrates, peripheral pulmonary thromboembolism, pleural