COMMENTARY

Genetically modified foods: "absurd" concern or welcome dialogue?

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"The attempt of single-interest groups, supported by the tabloid press and now by others who should know better, to declare this whole [genetically modified] technology as dangerous and immoral is sad for the UK, but is also absurd".[1] So wrote the president of the UK's Academy of Medical Sciences, Peter Lachmann, after *The Lancet* criticised Arpad Pusztai for announcing the results of his experiments with genetically modified (GM) potatoes on television. Lachmann had less to say about the journal's additional and equally important concern—namely, that those in government, the food industry, and science had badly miscalculated the level of public anxiety about this new biotechnology.[2]

Richard Sykes, chairman of GlaxoWellcome, also marginalised the public's concern. In his presidential address to the British Association for the Advancement of Science on Sept 13, 1999, he noted that "It is now very possible that the outcomes of the present anti-GM food campaign will be detrimental to this country. It will lead to a failure to develop new UK companies based upon the technology developed here, loss of technical expertise as funding by major international companies is withdrawn, and disadvantage for British agriculture". This state of affairs was even more starkly summed up by Roger Gosden, the scientist acclaimed for the first successful ovary graft,who is emigrating from the UK to Canada in a blaze of publicity about the brain drain, who said that "With all the fuss over GM food and so on,it is difficult to be a scientist in Britain. One does not feel proud of being a scientist any longer".[3]

The trigger for much of this despondency was the public debate that followed Pusztai's television revelations. The data on which this media furore was founded are published for independent assessment in this week's issue of *The Lancet*, 18 months after their first public release. The Research Letter by Stanley Ewen and Pusztai was received by the journal towards the end of 1998. Since then, it has been peer reviewed by six specialist advisers—a nutritionist, a human pathologist, a veterinary pathologist, an agricultural geneticist, a plant molecular biologist, and a statistician—who had several requests for clarification about the design of the study, the laboratory methods used, and the statistical tests applied. Some advised rejection; others encouraged us to go ahead and publish.The authors revised their letter three times to try to meet our reviewers' criticisms. The Royal Society's own internal review of the Pusztai data had led to the damning verdict that the study "is flawed in many aspects of design, execution, and analysis and that no conclusions should be drawn from it". So why publish the paper?

The answer lies partly in a February, 1999, statement from the UK's chief scientific adviser, Robert May.[4] While criticising the researchers' "sweeping conclusions about the unpredictability and safety of GM foods", he pointed to the frustration that had dogged this entire debate: "Pusztai's work has never been submitted for peer review, much less published, and so the usual evaluation of confusing claim and counter-claim effectively cannot be made". This problem was underlined by our reviewers, one of whom, while arguing that the data were "flawed", also noted that, "I would like to see [this work] published in the public domain so that fellow scientists can judge for themselves . . . if the paper is not published, it will be claimed there is a conspiracy to suppress information". Publication of Ewen and Pusztai's findings is not, as some newspapers have reported,[5] a "vindication" of Pusztai's earlier claims. On the contrary, publication of a paper after substantial review and revision provides a report that deserves further scientific attention. Such wider appraisal begins in this week's *Lancet* with the commentary by Harry Kuiper and colleagues.

Once the sketchy details of these data had been revealed last year, several respected scientists and scientific institutions called for more careful government scrutiny of research into GM food. For example, the Royal Society's own statement on GM plants[6] recommended that "any further increase in the number of antibiotic-resistant micro-organisms resulting from transfer of antibiotic-resistance markers from GM food should be avoided". The report supported labelling of foods containing GM material (a practice introduced last month in the UK) and threw its weight behind the idea of "an over-arching body or 'super-regulator'" to oversee all government advisory bodies on GM technology. The Royal Society also recommended further research into alternative markers to antibiotic-resistance genes, the impact of virus-resistant and insect-tolerant plants on the ecosystem, and the unpredictable genetic effects resulting from gene insertion into a GM plant.

These concerns were echoed in Robert May's 1999 statement,[4] which concluded that "there can be questions of health and safety associated with some GM foods, particularly if we introduce genes coding for production of toxins against certain kinds of pests".The Chief Medical Officer of England, Liam Donaldson, together with May, wrote that although "There is no current evidence to suggest that the GM technologies used to produce food are inherently harmful . . . nothing can be absolutely certain in a field of rapid scientific and technological development.[7] Donaldson and May urged the UK government to develop a comprehensive research strategy

into GM food technology, including study of its potential effects on health.

These responses reflect an appropriately cautious approach towards the science of genetic modification. They reflect the real concern expressed by both "single-interest groups" and a wider public. These anxieties may seem odd, even irrational, given that GM foods were introduced in the USA without any sign of consumer anxiety. Why? Because Europe now lives in a post-BSE (bovine spongiform encephalopathy) age, one in which society has learned that the epidemic of BSE was brought on by unchecked industry-driven changes in farming practices and that the denials of risk by government and scientific authorities were worthless. That concern is now spreading beyond the UK. Recognition of this deeply ingrained public scepticism about food technology has led Monsanto to rethink its entire GM-food strategy.[8,9]

The comments by Lachmann, Sykes, and Gosden are therefore disappointing because they reflect a failure to understand the new, and apparently unwelcome, dialogue of accountability that needs to be forged between scientists and the public. Risks are not simply questions of abstract probabilities or theoretical reassurances. What matters is what people believe about these risks and why they hold those beliefs. Ewen and Pusztai's data are preliminary and non-generalisable, but at least they are now out in the open for debate, as are the results, also published in today's *Lancet*, of Brian Fenton and colleagues. Only by welcoming that debate will the standard of public conversation about science be raised. Berating critics rather than engaging them—and criticising reports of research, as the Royal Society did with the Pusztai data,before those data were reviewed and published in the proper way—will only intensify public scepticism about science and scientists.

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Adequacy of methods for testing the safety of genetically modified foods

See pages 1353, 1354

An issue that has been prominent in the current debate on the health risks of genetically modified (GM) foods is whether there are adequate methods of testing for the safety of these foods. One view is that the safety assessments of these foods are not as rigorous as those for new chemicals or drugs. Today's *Lancet* carries two Research Letters reporting work on the potential risks to human health of the lectin *Galanthus nivalis* agglutinin (GNA), a compound that may be useful in protecting food plants from attacks by insects. These letters raise issues about the design of studies on safety.

Stanley Ewen and Arpad Pusztai report that, when fed to rats, GM potatoes containing the GNA lectin have proliferative and antiproliferative effects on the gut. They suggest that several of these effects are due to alterations in the composition of the transgenic potatoes, rather than to the newly expressed gene product. However,data on the composition of the different diets are not reported in the letter. Pusztai has released some of these details on the internet (http://www.rri.sari.ac.uk/gmo/ajp.htm). These details indicate that the content of starch, glucose polymers, lectin, and trypsin and chymotrypsin inhibitors in GM potatoes differed from that of the parental line. Unfortunately, these differences have not been examined further by analysis of an extended range of lines, for evidence on whether these differences are attributable to the genetic modification or to natural variations. Another shortcoming of the study is that the diets were protein deficient; they contained only 6% protein by weight. There is convincing evidence that short-term protein stress and starvation impair the growth rate, development, hepatic metabolism, and immune function of rats.[1,2]

Ewen and Pusztai say that the significant differences between diet groups in variables such as mucosal thickness or crypt length are evidence of the biological effects of the GM foods. Such a claim is easy to make but difficult to prove, because no consistent patterns of changes were observed in the study. Ingestion of potatoes may be associated with several adaptive changes in the gut because of the low digestibility of raw or partly refined potato starch. In rats caecal hypertrophy is a common response to short-term feeding of various poorly digestible carbohydrates, such as raw potato starch.[3,4] A physiological response of this nature is probably of little toxicological significance. Dose-response studies would have helped in the assessment of consistency of response.

The experiments done by Ewen and Pusztai were incomplete, included too few animals per diet group,[5] and lacked controls such as a standard rodent diet containing about 15% protein (lactalbumin) as a balanced source of aminoacids[6] and a test diet with potatoes containing an "empty" vector. Therefore the results are difficult to interpret and do not allow the conclusion that the genetic modification of potatoes accounts for adverse effects in animals. Similar criticisms of this work have been made by the Royal Society (http://www.royalsoc.ac.uk/ st_pol54.htm).

In the second Research Letter, Brian Fenton and colleagues provide data that indicate strong binding of GNA to human white blood cells in vitro. Binding per se of a lectin does not automatically imply cell activation. Nevertheless, such findings emphasise the need for further studies. Attention should not be confined to the gastro-intestinal tract, but should also be paid to the bioavailability of these compounds and their potential toxic effects once they have entered the systemic circulation. Such investigations will be of paramount importance for future generations of GM foods (see below). An extensive toxicological study of this type has been done with a GM tomato containing an insecticidal protein derived from *Bacillus thuringiensis*.[7]

What about the adequacy of existing test methods and strategies for the assessment of the safety of GM foods?