Risk Assessment and "Fact –free Models"

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The Precautionary Principle

- "*When an activity raises threats of harm to human health or the environment, precautionary measures should be taken, even if some cause and effect relationships are not fully established scientifically*"
  'Wingspread Statement on Chemically-Induced Alterations to immune system.' Environmental Health Perspectives, 104:4, August 1996.

	Pharmaceuticals	Food
Development costs	US$ 400,000,000	?
Duration of exposure	Usually days or weeks	Lifelong
Dose	µg or milligrams per day	kilograms per day
Choice	Yes and usually for good indications	None
Lifetime exposure	a few grams	tonnes

The US experiment!

- No baseline data – where did we start from?
- No exposure data – who eats what?
- Uncontrolled experiment!!
- If GM food was causing changes to common conditions (e.g. allergy, auto-immune disease, cancer) there is absolutely no way that we could know!
- (We can however observe that people don't seem to drop dead from acute toxicity)

Precautionary principle stifles discovery

Sir — The so-called 'precautionary principle' (PP) has gained currency in discussions about environmental protection and genetic manipulation, but it should be treated with caution.

The principle has been endorsed in international treaties, including the consolidated version of the treaty establishing the European Union. In many of these documents the PP has not been explicitly defined, but the Wingspread conference attempted to define it[1]. We believe the following definition would be accepted by most proponents:

"When an activity raises threats of serious or irreversible harm to human health or the environment, precautionary measures that prevent the possibility of harm (for example, moratorium, prohibition) shall be taken even if the causal link between the activity and the possible harm has not been proven or the causal link is weak and the harm is unlikely to occur."

In our view, there are problems with the PP as so defined. The PP tells us to balance evidence in a specific way. The weight given to evidence is ordinarily thought to be a function of its epistemic warrant (the degree to which we have reasons for believing the evidence). The PP instructs us to change this normal balancing by giving evidence pointing in one direction more importance than evidence pointing in the other direction, even in cases where the evidence has the same epistemic warrant. Such discounting will distort our beliefs about the world, and will lead us to hold false beliefs. The PP cannot therefore be a valid principle for evaluating evidence.

As a principle of rational choice, the PP will leave us paralysed. In the case of genetically modified (GM) plants, for example, the greatest uncertainty about their possible harmfulness existed before anybody had yet produced one. The PP would have instructed us not to proceed any further, and the data to show whether there are real risks would never have been produced. The same is true for every subsequent step in the process of introducing GM plants. The PP will tell us not to proceed, because there is some threat of harm that cannot be conclusively ruled out, based on evidence from the preceding step. The PP will block the development of any technology if there is the slightest theoretical possibility of harm. So it cannot be a valid rule for rational decisions.

This fatal weakness of the PP illustrates a common problem in attempting to convert moral choices into legislation. The temptation is great to try to find one absolute and easily applicable principle, but such a principle will often be simplistic and will, when applied, lead to unjustifiable conclusions. Many moral choices are complex, and in making political decisions we should not lose sight of this complexity.

Søren Holm, John Harris

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1. http://www.wajones.org/wingcons.html

Sensible precautions make good science...

Sir — Søren Hòlm and John Harris strongly criticize the precautionary principle but they seem not to understand it (*Nature* **400**, 398; 1999). They complain that it is not valid for evaluating evidence, when that is not what it is for. It is a tool for decision-making, and, like many such tools, deals in expectations rather than probabilities.

The point is that it requires us to take into account not just the probability that a technology will be hazardous, but also the benefits if it succeeds and the costs if things go wrong. There may have been a very small probability that a large ship travelling at high speed in the North Atlantic would hit an iceberg, but the captain of the *Titanic* should have thought more about what could happen if it did — and all the more so because it didn't really matter if the voyage lasted a few hours more.

Holm and Harris argue that the precautionary principle would have stopped us developing genetically modified organisms (GMOs) because the greatest uncertainty about their possible harmfulness existed before anybody had produced one. But the principle does not demand that we halt research if we cannot be certain the end result will be safe (though common sense suggests it is unwise to make large investments if the end result is likely to be dangerous). It is to be applied at each stage in the process, weighing the risks in going one step further against the likely benefits if the project is successful.

That is why we and many others are arguing not for a complete ban on research into GMOs but for a five-year moratorium on field trials and commercial planting. There is a lot more research to be carried out in the relative safety of a closed laboratory first. This is always good practice, but it is especially important in the case of GMOs because of the irreversibility that is inherent in the technology. If a new drug proves to be harmful we can withdraw it, but once genes have left the laboratory there is no calling them back. The experiments in which GM milkweed was found to harm the monarch butterfly were performed in contained conditions; had this been discovered in field trials, the gene might already be spreading through the environment.

Our objection to the current field trials of GM crops is based not on whether commercial planting would be safe (though we are concerned about that), but on whether the trials themselves are safe — and whether they are well enough designed to be worth the risk. Neither has been shown to be the case. At the end of a moratorium, a much better-informed risk assessment should be possible.

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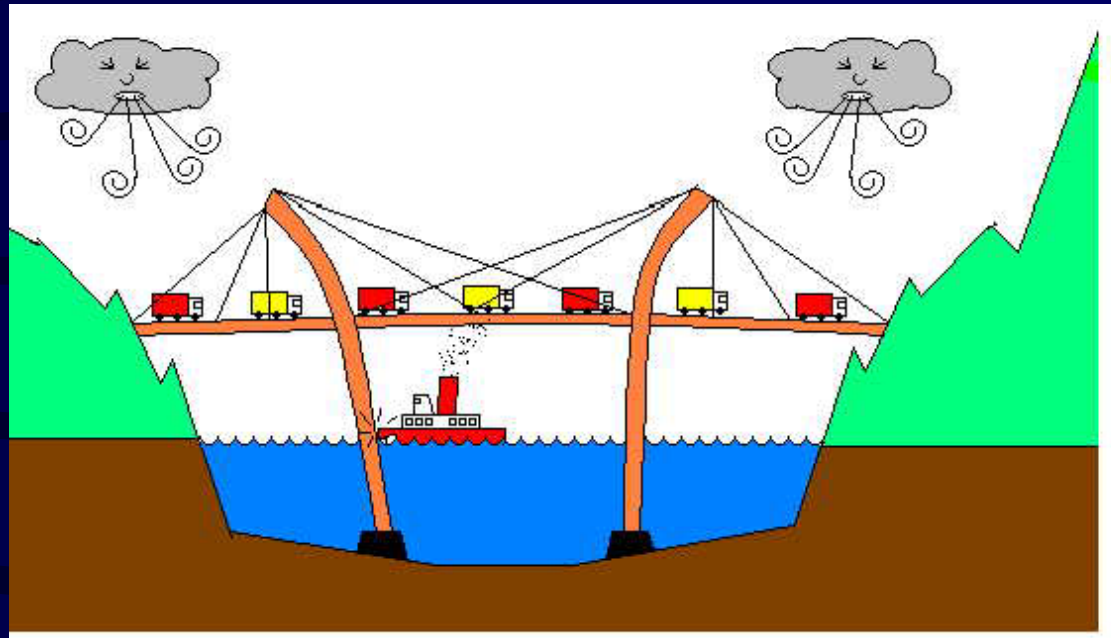
Risk Assessment

- The main tool used to stop the implementation of the Precautionary Principle
- Used as ‘proof’ that technologies are safe
- Largely, in my experience, misunderstood by decision makers



Risk assessment was designed by engineers to assess the reliability of engineered structures, where most of the facts are known or can be measured.

Risk Assessment – Invented by Engineers

- Used to assess the integrity of structures
- Most information required is available
- Realistic risk assessments possible
- Lead to over design of structures
  - Bridges and buildings typically x 5
  - Aircraft typically x 1.1 to 1.2

  The tighter the margin – more research required

Risk assessment in engineering is not foolproof

- Despite sophisticated models based on hard data and years of experience unpredictable events still happen
- This represents either a failure of hazard identification or of hazard assessment

Risk Assessment – 4 phases

- **Hazard identification** – requires insight and understanding of the system in question
- **Hazard assessment** – costs time and money for hard science – positive findings require action
- **Exposure assessment** – can be very expensive and, for human exposure, complex
- **Risk assessment** – depends totally on the 1st three steps

Complex Systems

- Risk assessment is now being applied to very complex systems - such as ecosystems
- It is impossible to have comprehensive hazard data for such systems
- Missing data is often provided by ‘data models’, but these can be subjective
- Sometimes the whole risk assessment can be based solely upon data models

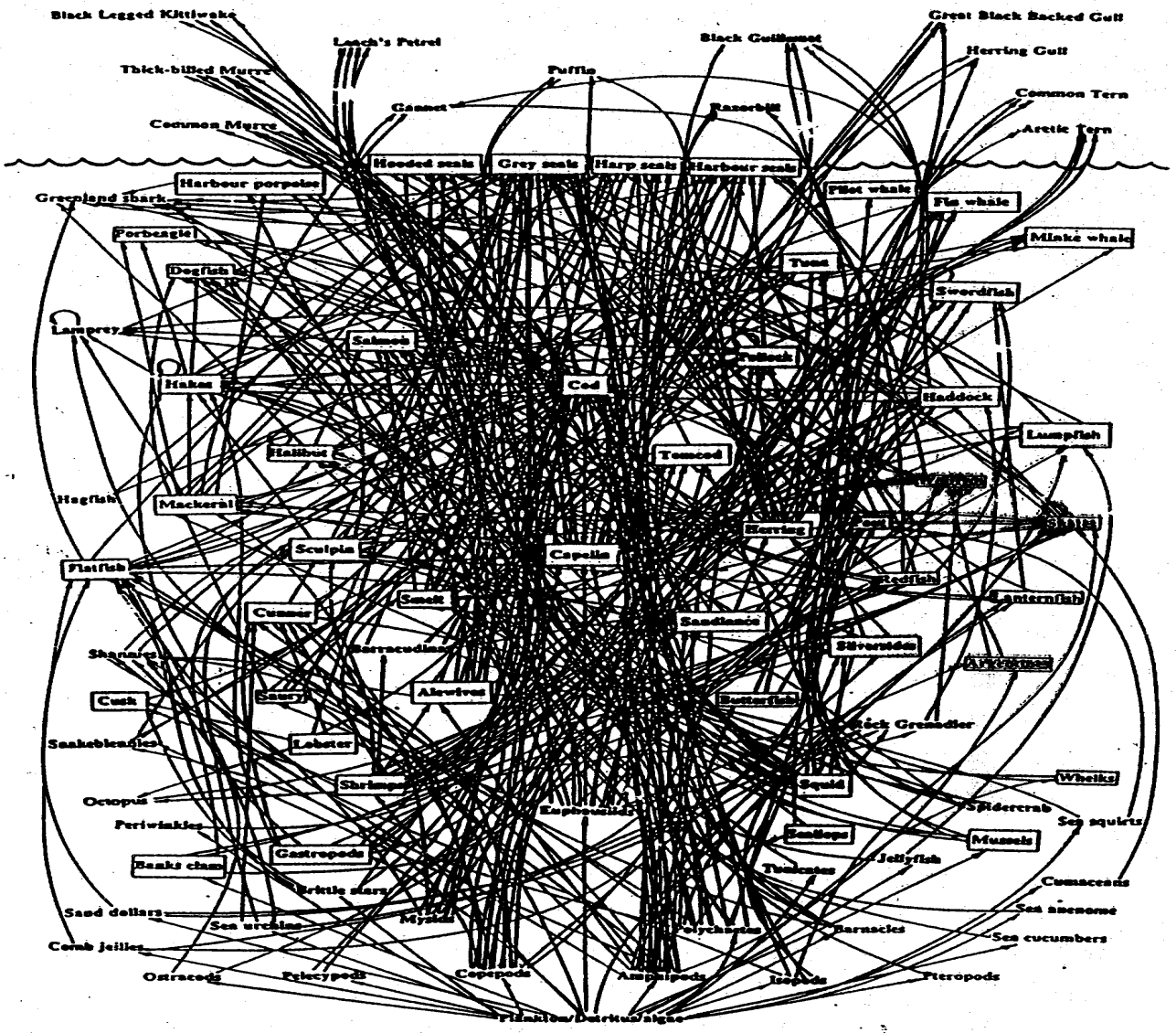


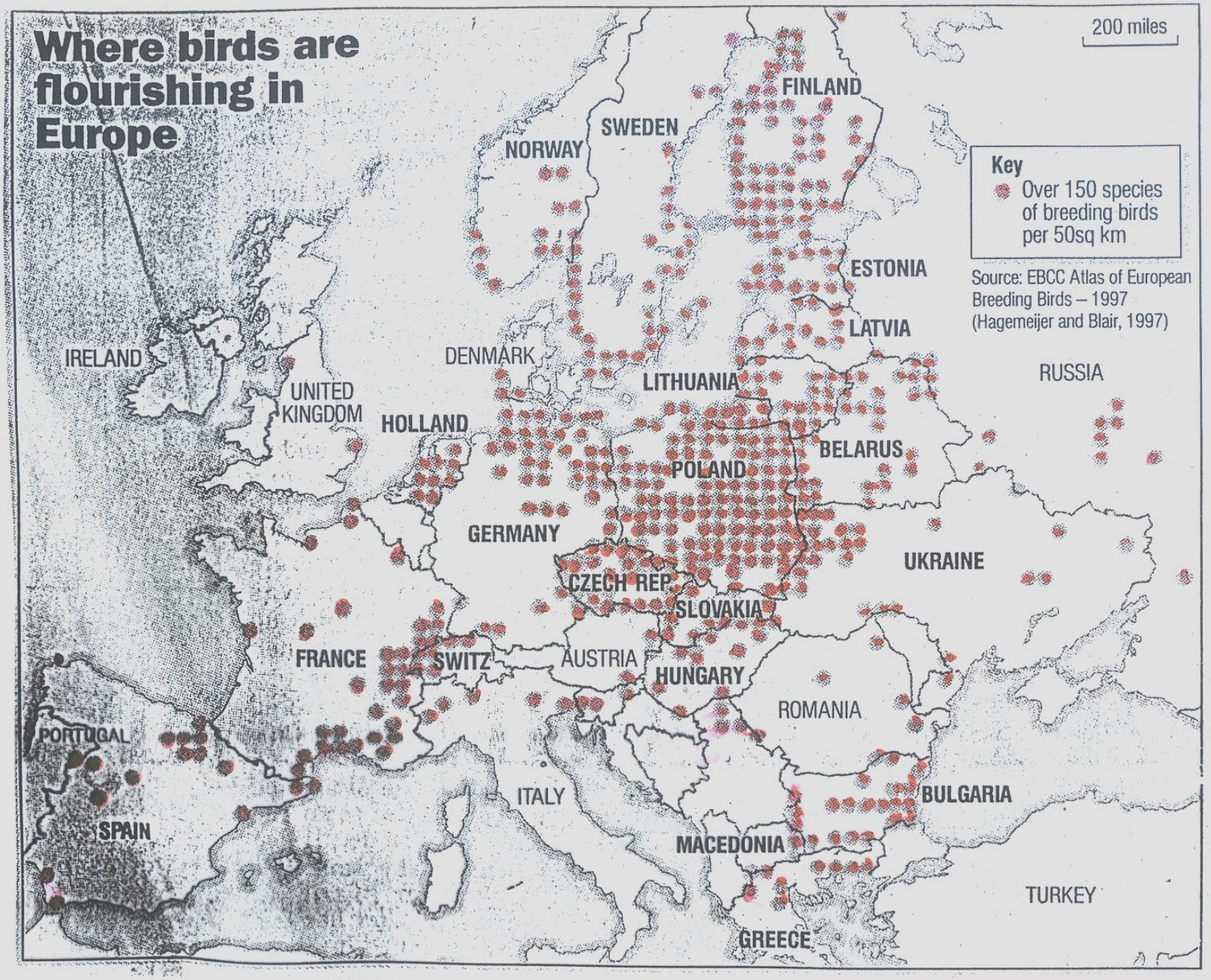
Figure 3.5: The Scotian Shelf food web. This is a well known system with a huge amount of links among species. It is quite obvious that in this ecosystem lacks any hierarchical principle and that a change in a single link may affect some species in an unexpected fashion.

There can be no room for doubt when commerce is at stake

- How well would GM food sell if it was admitted that:
  - we didn't fully understand the technology, the toxicology, the ecological consequences
  - That it wasn't 100% safe (Prof V. Moses)
  - That many of the predicted hazards had already happened (gene stacking, horizontal gene flow, unpredicted toxicity etc)

Formal Risk Assessment is a recent development

- Regulators have belatedly 'reacted' to disasters in the past, rather than anticipating harm.
- The 'Green Revolution' in agriculture is a case in point –introduced because "we are all going to starve", massive use of pesticides has led to:
  - Loss of biodiversity
  - Soil degradation
  - Pollution of biota


Where birds are flourishing in Europe
200 miles
Key
Over 150 species of breeding birds per 50sq km
Source: EBCC Atlas of European Breeding Birds – 1997 (Hagemeijer and Blair, 1997)
FINLAND
SWEDEN
NORWAY
ESTONIA
LATVIA
IRELAND
DENMARK
LITHUANIA
RUSSIA
UNITED KINGDOM
HOLLAND
BELARUS
POLAND
GERMANY
UKRAINE
CZECH REP.
SLOVAKIA
FRANCE
SWITZ
AUSTRIA
HUNGARY
ROMANIA
PORTUGAL
ITALY
BULGARIA
SPAIN
MACEDONIA
TURKEY
GREECE

It is clear that a mode shift was required

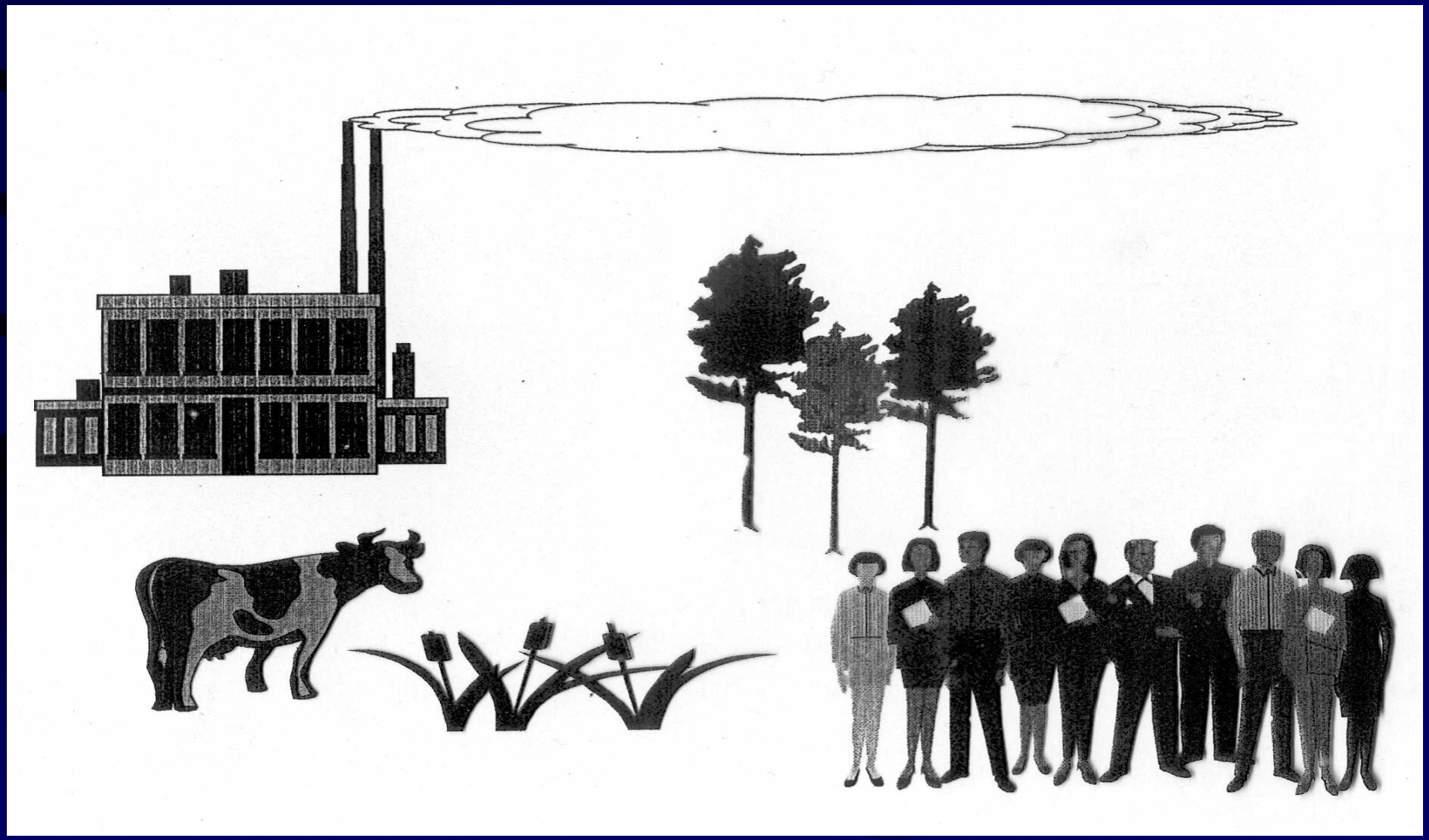
- Simply reacting to disasters was seen to be an inadequate approach
- Man was clearly capable of causing changes to the environment and health on a global scale
- There was a desire to adopt an anticipatory mode to try to avoid failures by using past experience to predict likely areas of hazard
- The options available are:
  - Hazard assessment
  - Risk assessment
  - Precaution

Of Risk Assessment..

- A former director of the US EPA said:

- *"We should remember that risk assessment can be likened to the captured spy: if you torture it long enough, it will tell you anything you want to know"*

If you ask the wrong question – you get the wrong answer



An example of a fact-free model in environmental chemistry

- '… summary data is presented of the estimates in the Environmental Statement for the worst case situation for the rate of deposition of various chemicals from the refuse to energy plant on local crops assuming continuous exposure. The human risk from consuming these is assessed for a hypothetical *maximally exposed individual.* This individual is presumed to consume largely (60% of total intake) vegetables grown in the area (eg: from allotments) of the maximum impact of the stack plume (i.e. having maximum long term GLC values). As discussed above, continual emission is presumed. These are worst case assumptions. (Professor J. W. Bridges)

A failure of hazard recognition

- There is an important un-stated "***fact-free assumption***" in this approach. It was assumed that all members of the population had no appreciable prior exposure to dioxin and that therefore it was quite safe for them to receive a further pollution burden.

A failure of hazard characterisation

- Not a single physical measurement of any kind is presented in the exposure assessment. Everything was modelled in computers. It would have been easy enough to measure the average body burden of the local population living at the modelled site of maximal ground level concentration.

GMO Areas of potential hazard

- Genetic instability – transgenes are inherently unstable
- Horizontal gene transfer (eg antibiotic resistance)
- Pleiotropic effects: allergy, toxicity

Substantial Equivalence

- A chemical test of composition
- Not predictive of biological effects
- What is needed is knowledge of:
  - Allergenicity
  - Unpredicted toxicological effects

‘Risk Assessment’ from Ag-Bio manufacturers

ii. Potential for gene transfer

Brief Description of Hazard	Potential Harmful Effects	Probability of Realisation	Risk of damage
Transfer by Pollen to Plants	Low	Negligible	Effectively zero
Transfer by Vector to Plants	Low	Negligible	Effectively Zero

Pollen production will be prevented by the removal of whole "bolter" (flowering) plants before flower formation. The trials will be checked periodically for the presence of bolters.

There are no precedents to support the hypothesis that genetic material may be transferred by a virus/aphid vector interaction.

iii. Phenotypic and genetic stability

Brief Description of Hazard	Potential Harmful Effects	Probability of Realisation	Risk of Damage
Phenotypic Modifications	Negligible	Low	Effectively Zero

Previous experiments with these transformed lines of cultivated beet have shown the phenotypic stability of this material over several generations. Any phenotypic modifications in subsequent generations would not be expected to enhance the ecological success of the modified plants and would not be expected, therefore, to adversely affect the environment. In any event, bolter removal will ensure no propagation of unexpected modifications.

Monsanto risk assessment for GM sugar beet in Eire

D. EVALUATION OF OVERALL RISK

i. Risk of individual hazards causing damage

Description of Hazard	Risk of Damage
Theft of plant material from trial site	Low
Grazing of plant material by wildlife	Low
Movement of plant material on field machinery	Low
Loss of plant material during transit incident	Effectively Zero
Loss of viable plant material during sampling/processing	Effectively zero
Vegetative regeneration	Effectively Zero
Gene transfer by pollen to other relative plants	Low
Gene transfer by virus/aphid vectors to other plants	Effectively Zero
Phenotypic modification caused by gene insertion/tissue culture	Effectively Zero
Transfer of harmful characteristics from donor organisms	Effectively Zero
Use of *Agrobacterium tumefaciens* vector	Effectively Zero
Ingestion of glyphosate tolerance proteins	Effectively Zero
Ingestion of beta glucuronidase protein	Effectively Zero
Selective advantage of modified beet	Low

ii. **Summary assessment of all risks**

The overall risk of damage is assessed as <u>low to effectively zero</u>.

Chardon LL – T25 fodder maize

- Purified PAT protein taken from another plant species – Canola
- Fed to a non-relevant species – rat
- Irrelevant anti-nutrient, phytate, assessed
- Non-substantial equivalence ignored (changes in fatty acid expression)
- No whole food feeding trial to cattle

How much hazard assessment is being performed on GM crops?

- Dr Arpad Pusztai won a grant of £1.6 million from the Scottish Office to *develop* hazard assessment methods
- He has published his results in *Lancet*
- Industry did not like his results
- This type of work appears to have stopped

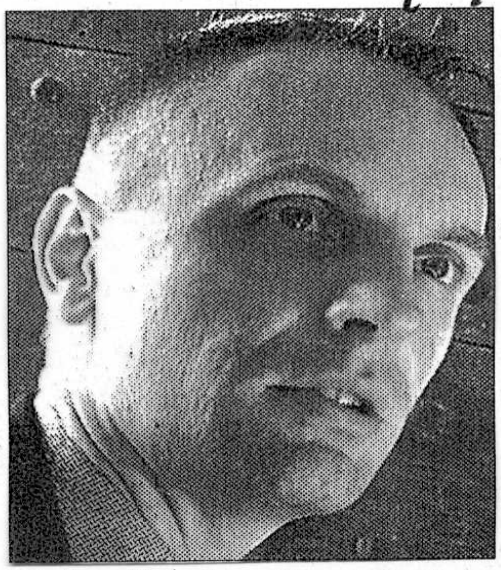
Peer pressure???

Top pro-GM food scientist threatened me, says editor

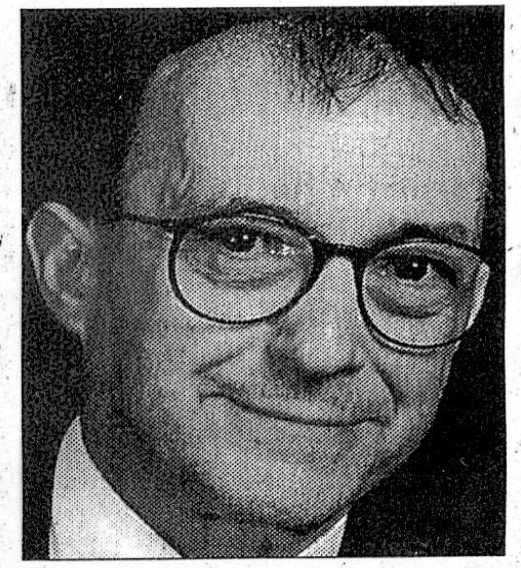
Guardian 1/11/99

◂ **Page 1** publishing both papers. He said there was intense pressure on the Lancet from all quarters, including the Royal Society, to suppress publication. The campaign, he said, was "worthy of Peter Mandelson".

The Guardian has learned that these interventions are taking place in an unusual context. According to a source the Royal Society science policy division is being run as what appears to be a rebuttal unit. The senior manager of the division is Rebecca Bowden, who coordinated the highly critical peer review of Dr Pusztai's work. She joined



Richard Horton: Royal Society behaving 'like a star chamber'



Peter Lachmann: admits call to editor but denies th[illegible]ats

Coin-operated consultants?

- "All policy makers must be vigilant to the possibility of research data being manipulated by corporate bodies and of scientific colleagues being seduced by the material charms of industry. Trust is no defence against an aggressively deceptive corporate sector."
- - THE LANCET, April 2000

Standard format for risk assessments?

- Pro-forma listings of:
  - All hazards identified
  - Those hazards identified but not assessed
  - Those hazards not assessed but modelled
  - Areas of uncertainty identified
  - Levels of confidence in the results
  - Time scale over which the risk assessment can be considered to be valid

Pervasive Technologies

- Society should consider whether certain activities should be reclassified:
  - Strict liability
  - Temporary licensing
  - Full transparency of hazard assessments

No risk is acceptable if it is avoidable

- Biotech industry spokesmen tell us that "nothing is 100% safe"
- Traditional foods have been tested for thousands of years, GM foods for 6 years
- We are being asked to risk eating GM food (not 100% safe) for no immediate benefit except to the manufacturers
- The rationale is that "we are all going to starve"

Precaution – the best option

- Decision on the balance of probabilities
- Reverse onus
- Strict liability for “Pervasive Technologies”
- Prior debate on a societal level before the development of new pervasive technologies
- The use of risk assessment only in situations where it is appropriate