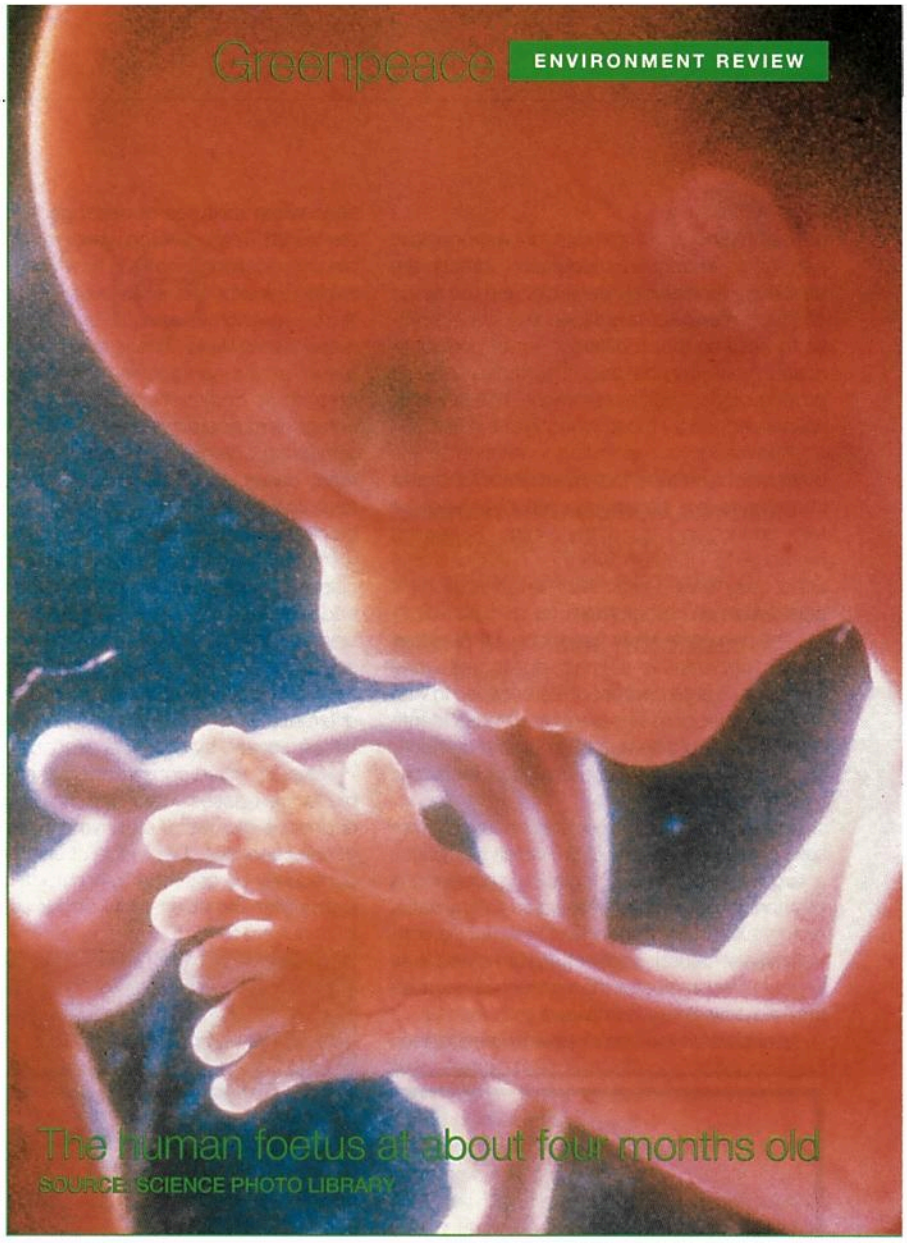
The chemical industry has accused Greenpeace of twisting the endocrine disruption issue to suit its campaigns against PVC and the chlorine industry. Here, scientists at the Greenpeace research laboratory at the University of Exeter in the UK have their say. By Ruth Stringer and Paul Johnston.



The human foetus at about four months old
SOURCE: SCIENCE PHOTO LIBRARY

Time to take fresh stock of the risks

Rarely has a topic of environmental toxicology developed as rapidly or had greater ramifications for the regulation of chemical pollutants as that of endocrine disruption. The publication in 1992 of the results of the Wingspread Session, a workshop drawing together research on the causes and effects of hormone disruption in humans and wildlife, provided the first assembly of data from diverse areas. This stimulated interest among environmental scientists, many of whom realised their data was consistent with the theories being proposed.

Also in 1992, a Danish group published a crucial paper analysing medical data from the previous 53 years. This suggested a significant and widespread decline in sperm density and semen volume and received a great deal of public attention. Subsequently, numerous articles, popular and scientific, have been published and many seminars held to report and discuss the ever-increasing data set. Interest in the subject continues to increase and all signs indicate that this is a major breakthrough in our understanding of the environmental effects of anthropogenic chemicals.

Endocrine disruption has profound implications for toxicology and the way chemicals are regulated. Toxicology has progressed from evaluation of the most simple end-point, death, to embrace sublethal effects such as reproductive toxicity and long-term effects such as cancer. Opinion has remained divided as to the importance of biochemical responses; alterations, for example, in enzyme activity are often regarded as an adaptive response useful as a biomarker, but not necessarily indicative of harmful changes. The realisation of the profound nature of potential effects at the individual and species level, due to slight alteration in endocrine function, demands this attitude be reconsidered. Risk assessment, which has become the foundation of the regulation of many chemicals, is also seriously undermined.

Firstly, recognition of effects of hormone disruptors at concentrations which are orders of magnitude lower than previously observed no-observed effect levels exemplifies the inadequacy of the testing regimes upon which previous risk assessments have been based.

Furthermore, endocrine disruption endpoints will not realistically be suitable for incorporation into future risk assessment protocols. Risk assessment depends upon blunt, easily measurable end-points such as lethality or

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cancer. Although in vitro tests for oestrogenicity and other endocrine modulation effects are becoming more widely available, and the range of effects measurable is expanding, it is simplistic to assume that a different set of hormone-related tests can be added to those used to provide data for risk assessment. This is widely acknowledged by those working in the field.

Knowledge is expanding in relation to the other sex hormones, but other areas of similar importance (eg: growth regulation) will not be fully understood for many years. Screening methods to establish whether chemicals can affect less well researched endocrinological parameters do not yet exist.

The degree of effect cannot be extrapolated from in vitro tests to animals, nor to real-world situations. Large discrepancies between in vitro and in vivo responses have already been identified. These could be due to a number of mechanisms including bioaccumulation or metabolic activation.

Interaction of anthropogenic chemicals with sex hormone binding globulin, which inactivates a large proportion of circulating endogenous hormones has not been assessed to any satisfactory extent. Xenoestrogens may not be controllable by natural feedback systems and their impact may be greater than expected because they are only slowly inactivated.

In addition, synergistic responses have been seen when mixtures of oestrogenic chemicals are tested. Testing of the whole range of possible chemical combinations to which humans or wildlife are exposed is obviously impossible, but in the meantime, serious underestimation of responses is likely. This is also true where mixtures exhibit antagonism since differential breakdown or excretion rates may prevent this antagonism operating in vivo. Measurement of circulating chemicals is not only impractical in many cases (eg: in utero) but presents serious analytical problems. Importantly, agents which block hormone receptors may have effects without altering the actual concentrations of circulating biochemicals. Natural variations of endogenous hormones can be measured in animals and have profound effects upon the subsequent behaviour and social interaction of the individuals. It would be extremely hard to differentiate these from potentially harmful effects caused by chemical exposure.

Overall, these constraints make it impossible for risk assessment realistically to include endocrine disruption as anything other than a general concept. The range of effects that can confidently be ascribed to hormone disruptors exemplifies the insensitivity of risk assessment in its current form.

The research required to elucidate the effects of endocrine disruptors will take many years. Even then, risk assessment will still not be able to embrace the complexities necessary to predict quantitatively the extent of the damage that could be caused.

Nevertheless, both the extent of the potential problem and the way towards the solution are clear. The UK National Rivers Authority (now part of the Environment Agency) has persuaded the wool-scouring industry to phase out use of APE detergents whose oestrogenic breakdown products were affecting a number of rivers. Sweden seems set to phase out soft PVC because of concerns over the toxicity of the phthalates (added as softeners), some of which are oestrogenic. Unplasticised PVC containing harmful additives will be included in these plans.

Since risk assessment cannot tell us the extent of the risk posed by the endocrine disruptors nor the benefit from any specific course of action, it fails its most fundamental purpose. Given the potential repercussions of the sorts of reproductive and other effects attributed to endocrine disruptors, a more robust approach must be taken. A precautionary approach implemented via the immediate phasing out of the most problematic chemicals will be seen by many as the only practical way to minimise future environmental and human exposure to endocrine disruptors. Further, in order to achieve comprehensive protection against such environmental effects it will be necessary to screen new chemicals for the potential to disrupt hormone systems before they are allowed to enter the marketplace. ■