The position and problems of toxicology

Like a living system, this and other scientific journals have a dynamic that reflects the developing professional interests, capabilities and needs of readers and editors. They will respond to changes in scientific capabilities and understanding, to the requirements of industry, to new demands placed upon Toxicology by governments advancing or reacting to new scientific, political and economic ideas and to fluctuating public concerns about ‘Toxicity’ as one among the many risks to life. It would be encouraging to be able to write that advances in scientific knowledge were paralleled by equal improvements in understanding by professionals and users of their findings about toxicity; but it would be more honest to admit that one-sided arguments, misdirected or unbalanced investigations and biased campaigns affect our science at least as much as any that lie at interfaces between the public, industry and governments. Aristotle wrote ‘The fruits of education are bitter but necessary’! It is painful to see how often that has been a repetitive process in toxicology and a continuing source of professional and even personal difficulties for toxicologists.

It is now 35 years since Paul Turner and his colleagues started this journal as Human Toxicology, and it became Human and Experimental Toxicology (HET) in 1987 in cooperation with the British Society of Toxicology. The initial aim was to publish clinical accounts of ‘poisoning’ in humans and experimental investigations into its causes, mechanisms and treatment, but it soon extended to include other species, the environment and basic experimental investigations into its causes, mechanisms and treatment, but it soon extended to include other species, the environment and basic experimental investigations, both in vitro and in vivo, as the importance and power of mechanistic studies increased. A key point is that it has always attempted to reflect the ways in which toxicity has been understood and used at different times. Looking back at the material published in the past 35 years shows something of the growth of science of toxicology, its practices and many successes but also its many failures over critical issues.

The problem areas have often come from a narrow focus on a mechanism or an effect in isolation without giving equal weight to the biology of the system or species and the exposure involved. There has sometimes been a lack of caution in extrapolating toxicity to other species and circumstances. How often do we have to relearn even Paracelsus’ fundamental point about the primacy of the dose in causing toxicity? New science and novel causes and consequences may be exciting, but past experience is only overlooked at the risk of unnecessary anxieties aggravated by the common tendency to be swayed more by emotional appeals to ‘(pseudo)science’ than by accurate but dispassionate analyses. The result has been an excuse for campaigns floated on excessive suspicion more than fact. Remember the scares about artificial sweeteners, pesticide residues in foods, genetically modified organisms, fluoride in toothpaste and drinking water, plasticizers, and baseless fears about the toxicity of mixtures? HET has presented material on many of these themes and may continue to do so as long as authors present manuscripts of a sufficiently high standard.

What might be regarded as the most important developments in toxicology over the past 35 years as represented in HET and other journals as I see them? Note, I have not written most valuable or interesting or fundamental advances or even changes in that period because that would depend on too individual a judgement. Toxicology can be seen as a strictly academic discipline in which harmful toxic actions or their absence are investigated as a way to explore basic biological processes across the complete spectrum from reactive molecules and subcellular components to organized populations of humans and other species in the environment. However, it is probably more commonly experienced as Applied Toxicology directed to detecting types of harm in laboratory experiments, predicting the risk that they will occur in practice and defining circumstances to avoid, limit or treat them. It draws upon more basic sciences, such as chemistry, biochemistry, immunology, pharmacology, physiology and pathology, human and veterinary medicine and the broader biology of the environment with epidemiology interposed among the other disciplines. The principles and ideas of toxicology are
widely deployed in society as a whole because public and political beliefs about *toxicity* and its avoidance have extended into basic economic and legal areas affecting where and how we live, permissible industries and the utility of their products and into concerns about the environment at large.

The concepts of *hazard* and *risk* are invaluable principles defining the strategies and often the tactics of investigating and predicting the effects of possible exposure to chemical and physical factors on every living and environmental system. That has long been associated with standardized investigations done to ensure consistent prediction of hazards and risks before actual exposure has occurred and to permit benefit–risk and *cost* assessment of the consequences of exposure. Achievements and difficulties in these areas have been presented in *HET*, still with some concentration on the humans in its original title, but looking more widely as scientific interests and capabilities have evolved.

There is much still to be learnt even by balanced and critical investigators and a great deal still to be understood about how to explain in a neutral way what a *risk* and its *cost* really are, how to convey the difference from a *hazard* and how to estimate *benefit* in ways that can be balanced against *cost* expressed in the same understandable units. Without a clear explanation and understanding, there can only be confusion and the dangers of bias and anxiety leading to irrational and potentially costly mistakes. In the case of medicines, balancing risks against the benefits of potential exposure to a therapy might seem relatively straightforward although the experience of National Institute of Health Care and Excellence in Britain demonstrates the contrary, but it has proved far more difficult in broader areas such as foods and pesticides, industrial practices, cosmetics and atmospheric and environmental pollution from sources that are wanted but may also be harmful under certain circumstances, such as air pollution from motor vehicles and trace residues of pesticides in food and water.

What then might be possible or likely areas of development in *toxicology* in the future on which authors might submit papers and readers of *HET* might wish or expect to read about?

Every editor and reader will have his/her own list but my tentative suggestions (not ranked in feasibility) are listed below. They are directed towards *Applied Toxicology* and not to the related basic sciences because I cannot make a useful forecast of major advances in fundamental biology and how they will affect our discipline.

- Increased understanding of how genomic and epigenetic factors can explain individual differences in susceptibility to toxicity.
- Related to that will be how to modify standardized test procedures to explore individual characteristics and their consequences after a given exposure. Growing interest in *systems toxicology* akin to systems biology, in which the harmful effect comes from incoordination or disruption of complex interacting processes at the levels of the subcellular, intercellular, organ and complete individual organism or even within entire populations.
- Increasing emphasis on functional as much as conventional biochemical, immunological, pharmacological and pathological responses. This should include exploiting some of the more refined techniques now common in the neurosciences to explore possible effects on higher level brain functions. Greater consideration of the toxicological implications of increasingly aged populations.
- How to find and predict very late effects of an exposure, such as the concern now raised about the increased incidence of heart attacks in people treated with certain statins.
- Better understanding of what the ‘public’ really perceives as *hazard* and *risk* and the *cost* evaluated in cost–benefit/risk assessments and on what bases and how do people make conscious and the default unconscious decisions about the acceptability of risks and costs.
- How might the professional education of toxicologists change to reflect these wider applications and what corresponding changes might there be in the training of the specialized economists, regulators and lawyers who rely on our findings?
- The best ways to provide open and unbiased facts and evaluations to the public and media in ways that all can understand?

Most of these issues involve other technical areas of applied sciences, too, but *toxicology* has long had a key position in battles over the limits of acceptability of technical possibilities in our industrialized societies, ranging from the universal exposures associated with power generation, waste disposal and the use of
genetically manipulated organisms to the more individual risks from eating manufactured foods, using domestic products, new medical therapies, and the many other ways in which the circumstances of modern living may be influenced for better or for worse by advances in technology.

Toxicologists should be active in the decision-making processes about our world within the broad ambit of what is being formalized into the new area of Science Policy - recognition of the need for scientific understanding of general issues, including recognition of the need for investigation of potential or even existing problems and for the resources required for investigations in a timely fashion, as well as translation of scientific findings into terms that are suitable for making a decision that something will entail that a cost is acceptably less than or unacceptably more than the likely benefit. There is much depth here involving political philosophy, government and economics, but toxicologists could and should contribute from their experience of these problems.

Applied Toxicology is not a pure science and it may lack the dramatic appeal of new fundamental discoveries that attract attention and general support. But its results, their critical evaluation and the subsequent decisions or failures to decide have direct and long-lasting consequences for us and our world. More appreciation of its roles and value should be encouraged.

The authors in this special anniversary issue of HET have generously given their time and shared their knowledge and skills in many of the important and active areas of Toxicology by revealing their expert understanding and their critical concerns about the detection, investigation and understanding of toxic hazards and risks.

The Editors and I are very grateful to them for allowing us to peer over their shoulders as they discuss many of the more important forms of toxicity, how to relate them to and to predict risks under many diverse circumstances and how to communicate their deep understanding of this complex of science and practice. It is to our benefit that they have not concealed weaknesses in understanding as well as showing scientific strengths.

There is an old saying ‘There is nothing so difficult to predict as the future’, but there can be no doubt that HET and the profession can only gain from continuing thoughtful involvement in progress in the understanding and practice of Toxicology.

AD Dayan
Guest Editor