Genet. Res., Camb. (1986), **48**, *pp.* 133–135 Printed in Great Britain

BOOK REVIEWS

Risk Quantitation and Regulatory Policy, Banbury Report, no. 19. Edited by DAVID G. HOEL *et al.* Cold Spring Harbor Laboratory. 1986. 368 pages. $67. ISBN 0 87969 219 7.

The Banbury Reports have established themselves as presenting authoritative discussions on scientific aspects of environmental and medical problems, mainly in the fields of mutagenic and carcinogenic toxicology. The concept of a small group of recognized experts in their fields discussing in depth a limited and well-studied sector of a problem of great societal impact carries with it prospects of careful analysis leading to well-founded consensus, but also the threat of conventional, mutually self-supporting preservations of the prevalent in-trend. Obviously, the selection of the participants of the group will be crucial for the outcome of the exercise. Einstein has said something about the underlying theory determining the outcome of experiments, and something of the same may be true of meetings of this type.

The present report is the nineteenth in the series, and is concerned with Risk Quantitation and Regulatory Policy, obviously in relation to the American scene, and mainly focusing on environmental chemical carcinogens. Scientific, technical and legal features are discussed, partly in general terms, but mainly with reference to specific cases and procedures. Twenty-five papers are presented by the twenty-seven participants. All taken together, there emerges a broad and detailed picture of the confrontation between the ideas of modern society of not accepting any avoidable risk (see, for example, the Delaney clause) and the real world of activities leading to emissions, pollutions and contaminations with a wide spectrum of potentially harmful substances.

The scientific contribution to the basis for regulation is discussed in epidemiological and experimental terms, in reference to qualitative and quantitative test analyses, on the basis of dose–effect relationship models and theories of carcinogenesis, and so on. An excellent overview touching on a large fraction of the growing points of the field of environmental toxicology is the result. Much has been gained, but there remain the central problems of inter-species correlations, of the relationship between somatic (and *in vitro*) DNA damage to carcinogenic damage, and the clinical importance of the 'new' genetic end-points (*de novo* protein polymorphisms, and restriction fragment length polymorphism). These bottlenecks constitute of course the crucial transfer points between hazard identification and risk quantification.

So, one may ask, what is the significant gain in insight or information from this meeting. The answer is possibly the classical one: still confused, but on a higher level. The most precise statement on the gap between the scientific knowledge and the regulators' needs comes in the verbatim transcription of the discussions (these are, by the way, unusually informative and pertinent) following the presentation of EPA's Revised Interim Guidelines for the Health Assessment of Suspect carcinogens. The comment is : 'EPA's policy judgement...is not to take the best guess about what the truth is, but to take a conservative approach. I think this is sound public health policy, but don't mistake it for a scientific decision.'

If this conclusion is to be accepted it begs the question of where the public or political expertise is in this discussion. Agter Seveso, Bhopal, Three Mile Island and now Chernobyl it seems unavoidably imperative that public understanding and acceptance of risk situations must constitute an important element in every policy formulation. In Scandinavia we are now on the way to terminate by obligatory slaughter a major fraction of the reindeer and sheep on the basis of very refined but also quite tenuous estimates of radiation damage from the Chernobyl caesium release. In the same stroke we eliminate the basis for making a living for a section of the Lapp and high-ground farming community. The economics can be handled with relative ease by support from other sectors of society, but the pattern of life and cultural identity of the focal groups will probably be in danger. Those of us who sometimes worry about endangered species should perhaps also give some thought to the dangers of monoculture and loss of variability to our own extended phenotype. And above all, should these decisions be

taken by experts over the heads of those directly concerned? The problem has the distasteful aroma of the 'job or health' threat, but must be solved.

But this discussion would demand a different Banbury group of experts and laymen. No doubt, the series will continue.

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Genetics in Clinical Oncology. Edited by R. S. K. CHAGANTI and J. L. GERMAN. Oxford University Press. 1985 280 pages £35.00. ISBN 0 19 503609 3

The preface tells us that this book is aimed at the clinicians who take care of cancer patients. The chapters are contributed by the participating teachers of courses given in New York to help physicians appreciate the genetic aspects of cancer and so enable them to provide affected patients and their families with a better quality of medicine. In fact, the book works very well the other way round as well. As a geneticist working on one type of childhood tumour, I found much food for thought and useful, surprisingly up-to-date, references in several chapters. Obviously, fast-moving fields such as oncogenes are impossible to cover in multi-author books, which always have a long gestation period. Despite this, the chapter on 'viral and cellular oncogenes in cancer etiology' gives a solid introduction from which the reader can launch into the sea of recent research papers. Alas, clinical relevance has not yet been pinpointed for the observations that in some leukaemias and lymphomas activation of dominant oncogenes can be demonstrated and even followed by karyotypic analysis. This point is clearly made in the later chapters. The clinical value of the cytogenetic observations has to be confined to prognosis assessment for which much statistical evidence has been collected.

The multi-stage development of malignancy is discussed in different contexts throughout the book and the reader will eventually emerge with a fair overview. However, the discussion in the first chapter of the various models for genetic susceptibility to cancer could be better structured. It would be improved by distinguishing more clearly the variety of postulated mechanisms:

(1) Increased susceptibility to mutagenic agents due to (*a*) DNA repair problems, (*b*) increased likelihood of encountering mutagens because of allelic differences in enzymic detoxification or potentiation systems.

(2) Dominant predisposition to specific malignancies where a pre-existing heritable mutation in one gene increases the likelihood of overt cancer dramatically. (*a*) by mutation of the second allele at the same locus, (*b*) by further genetic change at a different locus.

The detailed genetics of the various types of cancer predisposition are confusing. It may take the reader some time to understand that retinoblastoma and Wilms' tumour can be found in both the dominant and the recessive categories. The information is, however, there. On careful reading of several chapters it becomes clear that there is a dominant predisposition to these embryonal tumours. Emergence of the tumour is associated with homozygous loss of function mutations which lead to uncontrolled proliferation. The kinetics of presentation of these childhood malignancies are consistent with a two-hit hypothesis for tumour evolution.

Throughout the text suitable warnings are sounded about some possible pitfalls, such as likely genetic heterogeneity in apparently similar cancers segregating in different families. Another worthwhile point made to research workers is that many of the cancer predispositions, such as the chromosome breakage syndromes or xeroderma pigmentosum, are numerically very rare but may help elucidate important steps in tumorigenesis.

The biochemical basis of even the strongest predispositions (e.g. retinoblastoma, Wilms' tumour) still remains to be identified. The prospects for defining the less-clearcut genetic variability which must exist in the family cancer syndromes (breast and colon cancers) must be correspondingly more distant. The chapters which deal with the clinical management of families with genetical predispositions to cancer are very well written and offer useful advice at practical and ethical levels, not forgetting even the emotional problems which the disclosure of cancer-proneness can bring. One author boldly states that surveillance in such families is of no proven value, and if it is to be undertaken this should be done in a coordinated manner so that its effectiveness can eventually be assessed. One comment, dear to the heart of a non-clinical scientist, is that physicians should arrange links between families being counselled and scientists with an academic interest in the disease. I hope all the clinicians from whom I want to receive clinical materials and information on patients read this book.

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Advances in Gene Technology: Molecular Biology of the Endocrine System. Edited by D. PUETT, F. AHMAD, S. BLACK, D. M. LOPEZ, M. H. MELNER, W. A. SCOTT AND W. J. WHELAN. Cambridge University Press. 1986. £27.5. ISBN 0 521 32685 3.

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