Indicators of Genotoxic Exposure, Banbury Report 13. Edited by BRYN A. BRIDGES, BYRON E. BUTTERWORTH and I. BERNARD WEINSTEIN. Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, NY 11724. (December 1982). 580 pages, $62.50 ($75.00 outside U.S.). ISBN: 0 87969 212 X.

This volume contains papers presented at a Banbury Conference in April 1982 on the topic 'Indicators of Genotoxic Exposure'. In the preface this title is interpreted to include the effects of genotoxic exposure and our capacity to monitor them in man; however, there must be some initial uncertainty in the reader's mind as to whether the emphasis is on measuring exposures and monitoring them or on the genetic effects of exposure. In practice the book deals with both matters without always distinguishing between them.

Mutagenesis is a multi-step process which starts when the mutagen enters or is formed in the cell and interacts with the DNA. It ends with the production of a mutant individual. In between, a variety of cellular processes participate which include repair, DNA replication, RNA and protein synthesis. Monitoring can accordingly be performed at a variety of points which inevitably become less and less accurate as indicators of exposure as more of the components of cellular response to exposure are built into the endpoint measured. At the same time it has to be admitted that even the most accurate methods for measuring exposure alone do not always provide an indication of what the genetic or carcinogenic consequences will be. Our measurements provide information only on what we measure; the predictions we make from them will only be more certain when the details of mutagenic and carcinogenic processes in the cell are better understood. These problems are recognized in the first contribution of the meeting but thereafter largely ignored.

The meeting, and therefore the book, was organized into seven sections which roughly reflect the increasing complexity of monitoring techniques and the difficulty of interpreting their results. Session 2 deals with the monitoring of mutagens in body fluids, and the papers in this section describe the application of standard bioassay procedures to the detection of mutagens in urine, faeces and breast fluids in populations exposed to cigarette smoke or living in other elevated cancer risk situations. Techniques for analysing the stable components of complex mixtures can be applied in these studies, but the sensitivity of the method is limited by the genetic indicator organism as it is in other screening tests. In most cases the Ames Salmonella assay is used but it is very difficult to establish causal connections between identified Salmonella mutagens in the body fluids and human carcinogenesis.

Sessions 3 and 4 deal with two other methods of monitoring exposure, the measurement of repair activity evoked by damage to DNA from carcinogens and mutagens and the direct measurement of exposure in terms of DNA-adduct formation. The former approach relies on the assumption that biologically important DNA damage is likely to be repaired, and the techniques described were designed to measure the extent of the repair activity (unscheduled DNA synthesis) in a range of tissues; hepatocytes of rat and humans, spermatocytes of rats (Butterworth *et al.*), rat lymphocytes (Skinner *et al.*) the pyloric mucosa of the rat stomach (Furihata & Matsushima). DNA damage can, of course, also be directly assayed in a variety of ways, and several of these are presented in this section. Parodi *et al.* describe attempts to test the predictive value for carcinogenicity of the alkaline elution method of measuring single-strand breakage, and conclude that it shows a predictivity which overall is similar to other short-term tests. Other techniques described include the coupling of HPLC and sensitive fluorometric techniques for methylated purines in the DNA (unfortunately this interesting paper by Swinburg *et al.* suffers from a confusing legend reversal), the use of monoclonal antibodies against specific adducts, and possibly the most sophisticated of the molecular developments described,

that by Low *et al.* These workers used a small reiterated sequence in human DNA and applied methods of DNA sequencing adapted to allow the sites of the DNA lesions to be pinpointed and their amounts to be estimated. The method could be used to compare the same DNA treated in a purified form as well as in the intact cell. Coupled with the post-labelling technique developed by Haseltine and independently by Randerath these techniques must constitute some of the most significant developments described in the book.

In Section 3 also, three papers are presented which describe the use of haemoglobin binding methods to estimate exposure *in vivo*. The stability of haemoglobin and its freedom from the repair effects which can affect the number of lesions remaining in DNA at the time of the assay makes this a useful cumulative measure of exposure in spite of the effect of background levels of alkylated aminoacids in lowering sensitivity.

Session 5 deals with cytogenetics and sister chromatid exchange in a variety of systems and from several points of view. The usefulness of rodent lymphocytes for studying cytogenetic damage and the possible role of metabolic differences in determining species, tissue and strain response specificities to mutagens and carcinogens are dealt with by Kligerman *et al.* and Allen *et al.* respectively. The use of sister chromatid exchange and other cytogenetic endpoints in human lymphocytes derived from populations exposed to a number of agents (cigarette smoke, ozone, ionizing radiation, cytostatic drugs) is dealt with in papers by Carrano, Evans, Sorsa and others, and they demonstrate how much is still being learnt about the behaviour of the lymphocyte system and the influence of this behaviour on the yield of SCEs, to say nothing of the effects of treatment.

The two final sessions deal with recent developments in mutagenicity tests in lymphocytes and questions of risk evaluation in man. There were few new developments of note here. However, one important report was that a major artifact in the detection of thioguanine-resistant mutants, the expression of TG^R phenotype by cycling sensitive cells, can be avoided if the cells are frozen (Albertini).

The last section reviews techniques for studying germ-cells of mammals. Methods for the measurement of repair activity in mouse spermatocytes and the study of chromosome aberrations in de-condensed sperm DNA are presented and are important parts of attempts to achieve a clearer estimation of risks to man. Lastly, the sperm morphology test is described and used in a specific monitoring context. Although the results of the latter were suggestive, additional data are required. Evans also correctly points out the possible involvement of several other non-mutagenic factors in producing sperm morphology changes.

All in all the volume is a useful summary of the general position in the field of ascertaining the consequences of exposure to mutagenic agents.

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Drug Resistance in Bacteria: Genetics, Biochemistry and Molecular Biology, Third Tokyo Symposium. Edited by SUSUMU MITSUHASHI. Japan Scientific Societies Press, 6-2-10 Hongo, Bunkyo-ken, Tokyo 113, Japan; Thieme-Stratton Inc. – 381 Park Avenue South, New York, NY 10016, U.S.A. (1982). 429 pages, DM 148.00. ISBN 0 86577 085 9.

This book contains the 57 papers given at the Third Tokyo Symposium, and has a slightly misleading title since it by no means presents a balanced picture of recent developments in this field. Rather, it gives a sample of the work of those able to attend the symposium, including that of a few major Western research teams and of probably