Parallel Symposium No. 8

Cancer Risk Assessment

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PS 8.1

Role of epidemiological studies in cancer risk assessment
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Cancer risk assessment can be defined as the estimation of the probability of developing cancer, given a defined situation of exposure. This approach is based both on experimental and epidemiological data. Its main limitation is the necessity of extrapolating cancer risk data estimated in experimental condition that are characterized by high levels of exposure to human populations. Epidemiological studies must be designed carefully to provide valid data for risk assessment: the exact quantification of human exposure is crucial. The use of biological markers of exposure (internal dose and target dose) must be encouraged. These markers (e.g. DNA adducts) can be measured both in animals and in human to improve the extrapolation of animal data to man and from high to low levels of exposure.

PS 8.2

ROLE OF LONG AND MEDIUM-TERM CARCINOGENICITY BIOASSAYS IN RISK ASSESSMENT. J.R.P. CABRAL, International Agency for Research on Cancer, Lyon, France, and Pathology Dept., NCU Medical School, Nagoya, Japan.

Risk assessment generally comprises factors such as hazard identification, dose response assessment, exposure assessment and risk characterization. Animal bioassays are important in providing information relevant to the two first factors. The first bioassays were largely devoted to model studies designed to find which animal systems should be used, what protocols were feasible, and the spontaneous tumour incidence in available strains of rodents. The protocols presently adopted in long-term studies have been thoroughly discussed by the IARC (1986). The IARC, in collaboration with IPCS of WHO, coordinates a small network of laboratories involved in the long-term testing of chemicals for carcinogenicity in rodents. Because the number of new compounds being introduced annually has over-burdened the world laboratory capacity, comprehensive long-term studies cannot be undertaken for each new compound. Over the past several years, some medium-term bioassays have been developed as a further tool in identifying carcinogenic risks (Ito et al., 1988). One of these, the liver bioassay system, in which it is easy to detect preneoplastic foci, has proved a very useful model for detecting risk of agrochemicals (Cabral et al., 1991). Some examples will be discussed.

PS 8.3

"Role of Pharmacodynamic Studies in Cancer Risk Assessment." (Curtis C. Travis, Ph.D., Health and Safety Research Division, Oak Ridge National Laboratory*, Oak Ridge, Tennessee 37831-6109.) While there is universal acknowledgement that quantitative risk assessment is far from precise, incorporation of mechanistic models of carcinogenesis has the potential to vastly improve the process. The author will review the recent use of pharmacodynamic models in risk assessment and discuss their potential to reduce uncertainty. Topics discussed will be the role of cellular proliferation in carcinogenesis, the nature of progression and transformation, the existence of thresholds, partial lifetime exposures, and interspecies extrapolation. (*Managed by Martin Marietta Energy Systems, Inc., under contract no. DE-AC05-84O21400 for the U.S. Department of Energy.)

PS 8.4

GENOTOXIC AND NON-GENOTOXIC FACTORS IN HAZARD EVALUATION. S. Parodi, D. Malacarne and M. Taningher. Istituto Nazionale per la Ricerca sul Cancro-Genova, Istituto di Oncologia Clinica e Sperimentale dell'Università di Genova, CIRC-Genova-Italy.

At the level of experimental oncology it was well known for many years that both genotoxic and non-genotoxic events concur in the carcinogenetic process. More recent studies in the applied field of hazard evaluation have confirmed the knowledge that had been obtained at the level of basic research. If we examine the Data Base of L. Gold and collaborators for carcinogenic potencies (about 1050 chemicals, about 50% positive for carcinogenicity), we can try to subdivide the positive carcinogens in genotoxic and non-genotoxic compounds. For the analysis of genotoxicity we have used the Data Base of F.E. Würgler and collaborators. For the majority of chemical carcinogens (= 70%) genotoxicity or lack of it cannot be established clearly (conflicting or insufficient results). Of the remaining 30%, = 60% can be defined as genotoxic and = 40% as non-genotoxic carcinogens. This explains in part why the capability of short-term genotoxicity tests of predicting overall carcinogenicity is moderate at best. The possibility of establishing tests for non-genotoxic activities is discussed.